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Fire toxicity

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Dedication

To the millions of people who have lost their lives through fire in recent decades – the majority of whom died from inhalation of toxic fire effluents. It is our sincere belief that better understanding of this tragic problem will contribute to a reduction in the number of such deaths in the future.

Preface

The origins of this work can be traced back to three factors: the tragic human consequences of inhaling toxic fire effluents; the realisations that this high toxicity was a relatively recent phenomenon; and, similar to the pronouncements from the tobacco industry in the 1970s, that there will always be some 'experts' who, for whatever reason, refuse to acknowledge the severity of the problem. Thankfully, in the last decade, progress has been made and deaths from the inhalation of toxic gases are now in decline. This must in part be due to improvements in understanding the problem. It is our sincere hope and belief that this book will hasten this process.

Fire science is multidisciplinary, spanning chemistry, physics, engineering and computer modelling through to human behaviour. In fire toxicity, the range of subject matter is broader still, and the problems more challenging. The conditions in real fires are difficult to recreate on a laboratory scale; fire effluents are difficult to analyse; quantifying the impact on human subjects can only be obtained through surrogates, originally live animals, but now predominantly through biological models or chemical analysis; and fire effluents are dynamic, changing composition as they travel, requiring sophisticated computational models to predict their concentrations. To describe all these phenomena in a single volume is a tall order! We are indebted to our world-leading contributors, each with unique expertise in their specific area of fire toxicity. Working with such expertise has been a humbling but enjoyable experience. It will become clear to the reader that there are still areas of uncertainty within fire toxicity, and we have encouraged our contributors to follow their own beliefs, and not be constrained by a drive towards uniformity.

The book opens with an introductory chapter providing an overview of the field of fire toxicity. It is recommended that readers new to the subject start here, and then select the sections most relevant to their needs. The second chapter describes how different fire conditions influence the nature and yields of toxic products. Chapters 3 to 5 describe the effects of different toxicants on the human physiology. The range of biological assessments, from animal exposure to *in vitro* methods such as cell culture and whole lung exposure are covered in

Chapters 6 to 10. Physical methods for fire effluent generation and chemical methods of analysis, from bench to large scale, are dealt with in Chapters 11 to 13, while typical yields and their predicted toxicity from a range of common materials are covered in Chapters 14 and 15. The current international regulatory framework and the more elaborate suite of ISO standards being developed for toxicity assessments for performance-based design for fire safety engineering are described in Chapters 16 and 17. The volume concludes with three chapters (18 to 20) covering one of the least well-developed areas, that of modelling fire toxicity.

Anna Stec
Richard Hull

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We owe our gratitude to our families, for their tolerance and understanding during the preparation of the book, particularly to Artur and Helen.

Abbreviations

AAIB	Air Accident Investigation Branch (UK Department of Transport)
AAS	atomic adsorption spectroscopy
ABS	acrylonitrile butadiene styrene copolymer
ADP	adenosine diphosphate
AEGL	Acute Exposure Guideline Levels of Hazardous Substances
AMP	adenosine monophosphate
ANSI	American National Standards Institute
APCI	atmospheric pressure chemical ionisation
APP	ammonium polyphosphate
APS	aerodynamic particle sizer
ASET	available safe escape time
AT	apnoea time
ATH	hydrated aluminium oxide or aluminium hydroxide, $Al(OH)_3$
ATP	adenosine triphosphate
ATPS	ambient temperature and pressure, saturated
BAL	bronchoalveolar lavage
BSI	British Standards Institution
BSL	Building Standards Law (Japan)
CAAT	Center for Alternatives to Animal Testing (Johns Hopkins University)
CAIPE	chloroformic acid isopropylester
C_6F-ketone	dodecafluoro-2-methylpentane-3-one
CEN	European Committee for Standardization
CENELEC	European Electrotechnical Committee for Standardization
CFAST	The Consolidated Model of Fire and Smoke Transport (a multi-zone model produced by NIST)
CFD	computational fluid dynamics
CFK	Coburn Forster Kane equation
CO	carbon monoxide

CO_2	carbon dioxide
$COCl_2$	phosgene
COF_2	carbonyl fluoride
COHb	carboxyhaemoglobin
CPU	central processing unit
CS	*ortho*-chlorobenzylidene malonitrile
CSF	cerebrospinal fluid
DBA	di-*n*-butylamine
DIN	Deutsches Institut für Normung
DL_{CO}	limiting value for uptake of carbon monoxide
DLPI	Dekati low pressure impactor
DMSO	dimethyl sulphoxide
DNPH	2,4-dinitrophenyl hydrazine
DNS	direct numerical solution/simulation
DTGS	deuterated triglycine sulphate (FTIR detector)
EC	electron capture
ECG	electrocardiogram
EDIT	Evaluation-guided Development and new *In vitro* Tests
EELs	emergency exposure limits
EEPS	engine exhaust particle sizer
ELPI	electrical low pressure impactor
EPA	Environmental Protection Agency (US)
EPFM	Eulerian particle flamelet model
ER	endoplasmic reticulum
ERPG	Emergency Response Planning Guidelines
ESTIV	European Society of Toxicology *In Vivo*
ET	expiratory time
ETFE	ethylene tetrafluoroethylene copolymer
EVA	ethylene vinyl acetate copolymer
EVCAM	European Centre for the Validation of Alternative Methods
ϕ	(phi) equivalence ratio
FAA	Federal Aviation Administration (US)
FAI	Fatal Accident Inquiry
FAR	Federal Aviation Regulations (US global)
FDF	filtered density function
FDM	finite differences method
FDS	Fire Dynamics Simulator
FEC	fractional effective concentration
FEC_{smoke}	fractional effective concentration of smoke
FED	fractional effective dose
FEM	finite element method
FIC	fractional irritant concentration
FID	flame ionisation detector

FLD	fractional lethal dose
FPD	flame photometric detector
FPV	flamelet/progress variable
FR	fire retardant (sometimes flame retardant)
FRAME	Fund for Replacement of Animals in Medical Experiments
FTIR	Fourier transform infrared spectroscopy
FTP Code	Fire Test Procedures Code (IMO)
FVM	finite volume method
GC	gas chromatography
GC-MS	gas chromatography combined with mass spectrometry
GER	global equivalence ratio (ϕ_g)
GFRP	glass fibre reinforced polyester composite
GRP	glass reinforced polyester
GSH	glutathione
H_2O_2	hydrogen peroxide
H_3PO_4	phosphoric acid
Halon 1301	bromotrifluoromethane
HBr	hydrogen bromide
HCl	hydrogen chloride
HCN	hydrogen cyanide
HF	hydrogen fluoride
HFC 125	pentafluoroethane
HFC 227ea	heptafluoropropane
HGV	heavy goods vehicle
HNCO	isocyanic acid
HPC	high performance computing
HPIC	high performance ion chromatography
HPLC	high performance liquid chromatography
HRR	heat release rate
IC_{50}	irritant (or inhibitory) concentration affecting 50% of the population
ICCVAM	Interagency Coordinating Committee on the Validation of Alternative Methods
IDLH	immediately dangerous to life or health
IEC	International Electrotechnical Commission
IL-8	interleukin 8
IMO	International Maritime Organisation
IPL	isolated perfused lung
ISE	ion-specific electrodes
ISO	International Organization for Standarization
IT	inspiratory time
IVTS	*In Vitro* Toxicology Society
KB	kenacid blue

KCN	potassium cyanide
LC	liquid chromatography
LC_{50}	lethal concentration affecting 50% of the population (often referring to the concentration causing death of 50% of the test population during or after a 30 min exposure)
LCt_{50}	median lethal concentration per minute which is the product of the concentration of a toxic component and the exposure time causing lethality in 50% of test animals
LDH	lactate dehydrogenase
LDPE	low density polyethylene
LEM	linear eddy modelling
LER	local equivalence ratio
LES	large eddy simulation
LFM	Lagrangian flamelet model
LoD	limits of detection
LoQ	limits of quantification
MCT	mercury–cadmium–telluride (FTIR detector)
MDF	medium density fibreboard
MDI	methylene diphenyl diisocyanate
MEIC	Multicenter Evaluation of *In vitro* Cytotoxicity
MetHb	methaemoglobin
MgB	magnesium borate ($Mg_3B_2O_6$)
MH	magnesium hydroxide $Mg(OH)_2$
MIC	methyl isocyanate
MLIT	Ministry of Land, Infrastructure, Transport and Tourism (Japan)
MMAD	mass median aerodynamic diameter
MS	mass spectrometry
MTS	3-(4,5-dimethylthiazol-2-yl)-5-(3-carboxymethoxyphenyl)-2-(4-sulphophenyl)-2H-tetrazolium (assay)
MTT	3-4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide
NaF	sodium fluoride
NaOH	sodium hydroxide
NBS	National Bureau of Standards (US) (now NIST)
NC	nanoclay
NDIR	non-dispersive infrared spectroscopy
nf ox	non-flaming oxidative thermal decomposition
NH_3	ammonia
NIOSH	National Institute of Occupational Safety and Health
NIST	National Institute of Standards and Technology (US)
N_2O_4	nitrogen tetroxide
NO	nitric oxide
NO_2	nitrogen dioxide
NOAEC	no observed adverse effect concentration

NO_x	nitrogen oxides (NO and NO_2 treated collectively)
NP	nasopharyngeal
NRU	Neutral Red uptake (assay)
O_2	oxygen
O_2Hb	oxyhaemoglobin
OD	(smoke) optical density
ODT	one-dimensional turbulence
OEL	occupational exposure limit
P	pulmonary
PA-6	polyamide-6
PA-6.6	polyamide-6.6
PAH	polycyclic aromatic hydrocarbons
PAN	polyacrylonitrile
PBDDs/ PBDFs	polybrominated dibenzodioxins and dibenzofurans
PBS	phosphate buffer system
PBT	polybutylene terephthalate
PCBs	perchlorinated biphenyls
PCDDs/ PCDFs	polychlorinated dibenzodioxins/dibenzofurans
PDF	probability density function
PE	polyethylene
PES	phenazine ethanosulphate
PET	polyethylene terephthalate
PFIB	perfluoroisobutylene (gas)
PFOS	perfluorooctanesulphonates
PMMA	polymethylmethacrylate
PMS	phenazine methosulphate
POPs	persistent organic pollutants
PP	polypropylene
ppm	parts per million
PPgMA	polypropylene-graft maleic anhydride
PS	polystyrene
PSA	pressure swing adsorption
PTFE	polytetrafluoroethylene
PUR	polyurethane
PVC	polyvinyl chloride
RADS	reactive airways dysfunction syndrome
RANS	Reynolds-averaged Navier–Stokes
RD	Respiratory rate depression
RD_{50}	the concentration causing a 50% decrease in respiration rate
RMV	the respiratory volume per minute
RSET	required safe escape time

SBI	single burning item (test)
SC	subcommittee
SGS	subgrid scale
SIVB	Society of *In Vitro* Biology
SLFM	steady laminar flamelet model
SMLD	statistically most likely distribution
SMPS	scanning mobility particle sizer
SO_2	sulphur dioxide
SPR	smoke production rate
SSCT	Scandinavian Society for Cell Toxicology
STELs	short-term exposure limits
STP	standard temperature (0 °C) and pressure (760 mmHg)
STPD	standard temperature (0 °C) and pressure (760 mmHg) dry
TB	tracheobronchial compartment
TC	thermal conductivity; technical committee
TDI	toluene di-isocyanate (monomer)
TEOM	tapered element oscillatory microbalance
THC	the total (amount of unburned) hydrocarbons
TLC	total lethal concentration
TMPP	trimethylol propane phosphate
TSA	thermal swing adsorption
TSP	total smoke production
TV	tidal volume
UHTP	unusually high toxic potency
UV-VIS	ultraviolet – visible (spectrophotometry)
V_A	the alveolar ventilation
V_D	lung dead space
V_E	respiratory minute volume, the minute volume of air inhaled
VOC	volatile organic compounds
WG	working group
ZB	zinc borate ($2ZnO3B_2O_3{\cdot}3.5H_2O$)
ZS	zinc hydroxystannate ($ZnSn(OH)_6$)

Standards

ASTM E 662 Test for specific optical density of smoke generated by solid materials

ASTM E1678 Standard method for measuring smoke toxicity for use in fire hazard analysis

ASTM E 2058 – 02a Standard test methods for measurement of synthetic polymer material flammability using a fire propagation apparatus (FPA), 2002

ASTM E662-06e1 Standard test method for specific optical density of smoke generated by solid materials

BS 476-13:1987 Fire tests on building materials and structures. Method of measuring the ignitability of products subjected to thermal irradiance

BS 476:Part 7:1971 Fire tests on building materials and structures. Surface spread of flame tests for materials

BS 476-13:1987 Fire tests on building materials and structures. Method of measuring the ignitability of products subjected to thermal irradiance

BS 6853 Code of practice for fire precautions in the design and construction of passenger carrying trains

BS 6853:1999-01 Code of practice for fire precautions in the design and construction of railway

BS 7990:2003 Tube furnace method for the determination of toxic products yields in for effluents

BS 476 Part 7 Fire tests on building materials and structures Part 7: Method of test to determine the classification of the surface spread of flame of products

BS 7899-2:1999 Code of practice for assessment of hazard to life and health from fire. Guidance on methods for the quantification of hazards to life and health and estimation of time to incapacitation and death in fires

DEF-STAN 02 – 713 (NES 713) Determination of the toxicity index of the products of combustion from small pieces of material

DIN 53436 Producing thermal decomposition products from materials in an air stream and their toxicological testing – Part 1: Decomposition apparatus and determination of test-temperature, 1981-04; Part 2: Thermal decomposition method, 1986-08; Part 3: Method for testing the inhalation toxicity, 1989-11; Part 4: Thermal decomposition method for liquids, 2003-07; Part 5: Method to calculate the toxicity, 2003-07

DIN 5510-2:2007-10 Preventive fire protection in railway vehicles – Part 2: Fire behaviour and fire side effects of materials and parts – Classification, requirements and test methods

EN 13501-1:2007 Fire classification of construction products and building elements – Part 1: Classification using data from reaction to fire tests

EN 13823:2002 Reaction to fire tests for building products - Building products excluding floorings exposed to the thermal attack by a single burning item

EN 50266-1 Common test methods for cables under fire conditions – Test for vertical flame spread of vertically-mounted bunched wires or cables, Part 1: Apparatus

EN ISO 5659-2 Plastics – Smoke generation – Part 2: Determination of optical density by a single-chamber test, 2006

EN TS 45545-2:2006 Railway applications – Fire protection on railway vehicles. Part 2: Requirements for fire behaviour of materials and components

GA 132-1996 Smoke and toxicity of fire effluents

GOST 12.1.044-89 Part 4.20 Method for the experimental definition of a toxicity index for combustion gases from polymeric materials (1989)

GOST 12.1012 UDSSR Imo Standard Fb/353, Toxic potency of effluents (1984)

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IEC 60695 Fire hazard testing – Part 7-50 Toxicity of fire effluents – Estimation of toxic potency. Apparatus and test method

IEC 60695 Fire hazard testing – Part 7-51 Toxicity of fire effluent – Estimation of toxic potency. Calculation and interpretation of test results

IEC TS 60695-7-50 Fire hazard testing Part 7-50: Toxicity of fire effluent Estimation of toxic potency Apparatus and test method

ISO 9705:1993 Fire tests – Full-scale room tests for surface products

ISO 13344:2004 Estimation of lethal toxic potency of fire effluents

ISO 13571:2007 Life-threatening components of fire – Guidelines for the estimation of time available for escape using fire data

ISO 16312-1:2006 Guidance for assessing the validity of physical fire models for obtaining fire effluent toxicity data for fire hazard and risk assessment – Part 1: Criteria

ISO 19700:2007 Controlled equivalence ratio method for the determination of hazardous components of fire effluents – Currently at the technical specification (TS) stage (Oct 09)

ISO 19701:2005 Methods for sampling and analysis of fire effluents

ISO 19702:2006 Toxicity testing of fire effluents – Guidance for analysis of gases and vapours in fire effluents using FTIR gas analysis

ISO 19703:2005 Generation and analysis of toxic gases in fire – Calculation of species yields, equivalence ratios and combustion efficiency in experimental fires

ISO 19706:2007 Guidelines for assessing the fire threat to people

ISO 24473:2008 Fire tests – Open calorimetry – Measurement of the rate of production of heat and combustion products for fires of up to 40 MW

ISO 27368 Analysis of blood for asphyxiant toxicants — Carbon monoxide and hydrogen cyanide

ISO 5657:1997 Reaction to fire tests-Ignitability of building products using a radiant heat source

EN ISO 5659-2 Plastics – Smoke generation – Part 2: Determination of optical density by a single-chamber test, 2006

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ISO 5660-1:1993 Fire tests – Reaction to fire – Part 1: Rate of heat release from building products (cone calorimeter method)

ISO 5660-2: 2002 Reaction-to-fire tests – Heat release, smoke production and mass loss rate – Part 2: Smoke production rate (dynamic measurement)

ISO TR16312-2 Guidance for assessing the validity of physical fire models for

obtaining fire effluent toxicity data for fire hazard and risk assessment – Part 2: Evaluation of individual physical fire models

ISO/TR 9122-1:1989 Toxicity testing of fire effluents – Part 1: General

ISO/TS 19700:2007 Controlled equivalence ratio method for the determination of hazardous components of fire effluents

LSZH Low Smoke Zero Halogen

NF C32-070:1979-06-01 Tests for the classification of wires and cables according to their reaction to fire

NF P92-507:2004-02-01 Fire safety – Building – Interior fitting materials – Classification according to their reaction to fire

NF X10-702-1:1995-11-01 Determination of the opacity of the fumes in an atmosphere without air renewal. Part 1: description of the testing device and method for control and adjustment of the testing device

NFX 70-100 Analysis of pyrolysis and combustion gases. Tube furnace method. Part 1: Methods of analysis of gas generated by thermal degradation. Part 2: Method of thermal degradation using tube furnace

PD IEC 60695-7-3:1998, Part 7-3 Toxicity of fire effluent, use and interpretation of test results

PN-88/B-02855 Fire protection of buildings. Method for testing emission of toxic products of decomposition and combustion of materials

prEN 2824 (Aerospace Series) Burning behaviour, determination of smoke density and gas components in the smoke of materials under the influence of radiating heat and flames – Test equipment apparatus and media, prEN2825 – Determination of smoke density, prEN 2826 – Determination of gas concentrations in the smoke

prEN 50399:2007 Common test methods for cables under fire conditions – Heat release and smoke production measurement on cables during flame spread test

1

Introduction to fire toxicity

T. R. HULL and A. A. STEC, University of Central Lancashire, UK

Abstract: Fire toxicity is the largest cause of death and injury in fires. These toxic gases contain asphyxiants, carbon monoxide (CO), and hydrogen cyanide, and irritants, such as hydrogen chloride (HCl), hydrogen bromide (HBr), a wide range of organo irritants, including acrolein and formaldehyde, oxides of nitrogen (NO_x), and sulphur (SO_x). Fire effluents also contain particulate matter (soot particles) which can penetrate deep into the lung. Both asphyxiants and irritants cause death in fire, as any incapacitation is likely to impede escape, and increase the chance of becoming trapped.

Key words: fire, fire toxicity, fire effluent, smoke, carbon monoxide, fire statistics.

1.1 Fire toxicity

Fire continues to pose a threat to life and property. The widespread use of synthetic polymers has increased this threat. Although the majority of fire deaths and injuries are attributed to inhalation of fire effluents, most of the recent research in development of fire safe materials is focused on preventing ignition and fire growth. From the 1970s until the early 1990s, fire toxicity was recognised as a serious problem, and some high quality research was undertaken. However, it became apparent that much higher levels of toxicity were found in real fires than in small-scale laboratory tests, but the difficulties of replicating real fires on a bench scale appear to have discouraged further studies in fire toxicity.

The extensive adoption of the cone calorimeter as the tool for development and assessment of fire safe materials coincided with a diminution of research into fire toxicity, shifting the focus of the fire safety towards reducing peak heat release rates. Although overall numbers of fire deaths fell in the UK from 1990 to 2006, the numbers of deaths from fire toxicity have remained static while the numbers of injuries have steadily increased. Recently there has been a clear resurgence of interest in fire toxicity. This has been driven by three factors:

- The progressive replacement of prescriptive codes by performance-based design approaches to ensuring fire safety.
- The development of tools to make meaningful assessments of fire toxicity.

- The gradual recognition that the problem of fire toxicity had not been addressed by the emphasis on heat release in fire safety engineering.

Fire toxicity has also played an important role in forensic investigations, where blood samples are routinely analysed for carbon monoxide, to ensure the victim was breathing after the fire started, or to explain deaths remote from the fire. However, this has led to the simplistic assumption that because elevated carbon monoxide levels were easily quantified in the blood, this must be the only important toxicant.

Studies of fire effluent toxicity create a fascinating multidisciplinary area where both the fuel chemistry, and the conditions of the complex process of fire have significant influences. Its importance is underlined by its serious, life-threatening impact. It requires understanding of the stages of fire growth, from ignition to ventilation controlled burning; the behaviour of fire on different scales; the product formation from flaming polymer pyrolysates; the behaviour of the aerosol particulates; the response of living organisms to the components present; the chemical quantification of those fire effluents and their relationship to the toxicity; and the application of this knowledge to fire safety.

The growing need to address the flammability of all materials, particularly synthetic polymeric materials, has led to a substantial increase in the use of fire and flame retardant (FR) systems in recent years. In some cases the FR systems themselves have the potential to increase the range and yield of toxic and irritant species released during a fire. However, this must be balanced against the benefits of FR systems in reducing the incidence and severity of fire, and thus reducing the risks of injury and death.[1]

In addition to the potential for causing incapacitation, injury and death, fires and fire effluents may also cause harm to the environment. Several well-documented large fires in recent years have highlighted the often severe, widespread and prolonged contamination of the atmosphere, soil and water courses with the resulting ecological damage.

Although all fires may be regarded as unique, burning behaviour and toxic product yield depend most strongly on a few factors. Material composition, temperature and oxygen concentration are normally the most important. The generalised development of a fire has been recognised, and used to classify fire growth into a number of stages, from smouldering combustion and early well-ventilated flaming, through to fully developed under-ventilated flaming.[2] The development of these stages is discussed in Chapter 2. Although on some occasions smouldering (oxidative pyrolysis) can generate toxicologically significant quantities of effluent (for example smouldering cotton, or polyurethane foam), the rate of reaction, and hence the amount of toxic species generated, will be small, so unlikely to affect anyone outside the immediate vicinity. Similarly, well-ventilated fires are generally small, and the fire effluent moves across the ceiling above head height, so extinguishment and escape are both feasible. As

fires grow, they become ventilation controlled, and in enclosures such as buildings rapidly change from well ventilated to under-ventilated (or vitiated). These fires are much larger, and therefore consume more oxygen and produce greater volumes of effluent, affecting occupants over a much wider part of any building. While well-ventilated fire scenarios are routinely used for assessment of flammability, because the object is to stop the fire growing to the out of control stage, where fire toxicity is concerned, the important fire stages are under-ventilated. There are two reasons for this:

- The volume of effluent is much greater.
- The yields of the major toxic products (carbon monoxide and hydrogen cyanide) will be much greater.

In tests performed in our laboratory, the NBS Smoke Chamber (ISO 5659) was not capable of replicating under-ventilated burning, because the flame simply went out, although inexplicably it is currently being proposed as a standard method for fire toxicity (ISO DIS 21489).

Almost all unwanted fires are diffusion flames, with inefficient mixing of fuel and oxygen. In contrast, combustion for energy release normally premixes the fuel and oxidant, for example by allowing air access to the base of the flame, giving a much cleaner burn and higher combustion efficiency. The interior of large flames are always under-ventilated, because oxygen cannot penetrate the flame. At a certain flame height (known as the smoke point height), there is an opening at the tip of the flame and smoke starts to appear, which is dependent on the nature of the fuel.[3] Thus, for large fire there will always be a significant yield of carbon monoxide (CO), hydrocarbons and smoke.

Data from large-scale fires[4,5] in enclosures, such as a room, show much higher levels of two of the major toxicants, carbon monoxide and hydrogen cyanide (HCN) under conditions of developed flaming. It is therefore essential to the assessment of toxic hazard from fire that each fire stage can be adequately replicated, and preferably the individual fire stages treated separately. The drive for internationally harmonised methods for assessment of combustion toxicity, through adoption of international standards, such as those of the International Organization for Standardization (ISO) (see Chapter 17), provides the framework for meaningful and appropriate use of toxic potency data in the assessment of fire hazard.

Fire toxicity is most important in areas where escape is restricted. Thus, most mass transport applications, such as airlines, railways and passenger ships, include requirements to quantify the fire toxicity of internal components. In buildings, regulations vary from country to country, several imposing restrictions on the use of materials with high fire toxicity. In many other countries, there are no restrictions on the fire toxicity of building components, and none exists for goods carried in road tunnels. Regulatory requirements for fire toxicity are discussed in more detail in Chapter 16.

As structures and means of transportation become larger and more complex, there is movement away from the more traditional methods of ensuring fire safety by prescriptive codes, towards fire risk assessments and engineering solutions. Reliable rate of heat release, fire effluent toxicity and smoke generation data are all essential elements of such an assessment. This is described in Chapters 18 and 19.

Although most fire deaths are attributed to inhalation of smoke and toxic gases, it has been argued correctly that preventing such fires would save these lives. Unfortunately this view has been distorted by those industries that fear restriction in the application of their products if fire toxicity were to be more widely regulated. This has led to contradictory claims, in the scientific literature and elsewhere, removing clarity from the urgently needed debate on fire effect toxicity. From the statistics presented later in this chapter, it is clear that despite the widespread use of fire retardants, fire toxicity deaths and injuries continue at an unacceptably high level.

1.2 Hazards to life from fire

1.2.1 Fire hazard assessment

The replacement of prescriptive standards by performance-based fire codes requires a fire hazard assessment, which includes prediction of the toxic product distribution within the building from a fire.[6] Analysis of fire hazard requires data describing the rate of burning of the material, and data describing the toxic product yield of the material. These are not material properties, but are scenario dependent. The rate of burning will depend on the ignitability, heat release and rheological properties of the material, and on the material orientation (horizontal, vertical, etc.) proximity to a heat sink, thickness, fire conditions and so forth. While some materials clearly burn less easily than others, there is no consensus on how materials may be ordered in terms of increasing flammability, because of the parameters outlined above. Fire toxicity is also scenario dependent, but clear relationships have been demonstrated between the yield of toxic products (for example in grams of toxicant per gram of polymer) and the fire condition, as a function of material. Analysis of fire statistics shows that most fire deaths are caused by inhalation of toxic gases.[7] Prediction of toxic fire hazard is increasingly being recognised as an important factor in the assessment of fire hazard. This depends on two parameters:

- Time–concentration profiles for major products. These depend on the fire growth curve and the yields of toxic products.
- Toxic potency of the products, based on estimates of doses likely to impair escape efficiency, or cause incapacitation or death.

Toxic product yields depend on the material composition,[8] and the fire conditions. The most significant differences arise between flaming and non-

flaming combustion. For flaming combustion the most significant factor is the fuel:air ratio, although the oxygen concentration and the compartment temperature can also affect the yields. As an enclosure fire develops, the temperature increases and the oxygen concentration decreases. This has been set out as series of characteristic fire types,[9] from smouldering to post-flashover. Carbon monoxide is generally considered to cause the greatest number of fire deaths, and the evolution of carbon monoxide is highly dependent on conditions, the most significant of which are difficult to create on a small scale.

1.2.2 Heat, smoke, asphyxiants and irritants

The toxic hazards associated with fire and the inability of victims to escape from fire atmospheres may be considered in terms of major hazard factors: heat, smoke and toxic combustion products.[10] Each of these factors, and their effect on escape behaviour, are considered briefly below. The time available for escape is the interval between the time of ignition and the time after which conditions become untenable, such that occupants can no longer take effective action to accomplish their own escape. This can result from exposure to radiant and convected heat; visual obscuration due to smoke; inhalation of asphyxiant gases; and exposure to sensory/upper-respiratory irritants. Fire gases contain a mixture of fully oxidised products, such as carbon dioxide (CO_2), partially oxidised products, such as carbon monoxide and aldehydes, fuel and fuel degradation products, such as aliphatic or aromatic hydrocarbons, and other stable gas molecules, such as hydrogen halides (HCl, HBr) and hydrogen cyanide.[11] Heat, smoke and irritant gases may impair escape, and frequently lung damage causes death in those exposed victims who manage to escape.

Heat

There are three ways in which exposure to heat can lead to life threat: hyperthermia; body surface burns; and respiratory tract burns. When the sum of fractional doses of heat and radiant energy exceeds the safety threshold, this defines the time available for escape. To predict life threat due to heat exposure in fires, only the threshold of second degree burning of the skin, and exposure where hyperthermia is sufficient to cause mental deterioration and therefore threaten survival, need to be considered. Burns to the respiratory tract from inhalation of dry air (<10% water vapour) do not occur in the absence of burns to the skin or the face; thus, tenability limits with regard to skin burns are normally lower than for burns to the respiratory tract. However, burns to the respiratory tract can occur on inhalation of air above 60 ºC when saturated with water vapour. The tenability limit for exposure of skin to radiant heat is approximately 2.5 kW m^{-2}. Below this, exposure can be tolerated for 30 min or longer without significantly affecting the time available for escape. As with

toxic gases, an exposed occupant may be considered to accumulate a dose of radiant heat over a period of time. Similar predictions of the time to incapacitation for exposure to convective heat from dry air can be made. Thermal tolerance data for unprotected skin of humans suggest a limit of about 120 ºC for convected heat. Above this there is considerable pain, which results in burns within minutes. Convective heat below this temperature can also cause hyperthermia.

Smoke obscuration

As smoke accumulates in an enclosure, it becomes increasingly difficult for occupants to find their way. This increases the time required for escape. Moreover, at some degree of smoke intensity, occupants can no longer discern boundaries, and become unaware of their location relative to doors, walls, and windows, even if they are familiar with the building. When this occurs, they can become so disoriented that they are unable to effect their own escape. The time at which this occurs represents the upper limit for the time available for escape due to smoke obscuration. It has been estimated that when confronted with a fuel mass loss concentration of $20\,g\,m^{-3}$ for well-ventilated fires, or $10\,g\,m^{-3}$ for under-ventilated fires, occupants literally cannot see their hands in front of their faces and thus become disoriented. The effects of smoke on escape are discussed in more detail in Chapter 3.

Asphyxiant and irritant gases

The main toxic combustion products are divided into two classes: asphyxiant gases, which prevent oxygen uptake by cells, with loss of consciousness and ultimately death; and irritant gases which cause immediate incapacitation, mainly by effects on the eyes and upper respiratory tract, and longer-term damage deeper in the lung. The effect of asphyxiants and deep lung irritants depend on the accumulated doses, the sum of each of the concentrations multiplied by the exposure time, for each product; upper respiratory tract irritants are believed to depend on the concentration alone.[12] The most common toxic components of fire effluent are presented in Table 1.1. The specification of gases to be determined in particular standard tests is somewhat arbitrary, and may not adequately define the effluent toxicity.[6] There is also the potential for species to be present in the fire gas which have not been well characterised in terms of chemical structure or toxicity. It would be difficult to identify or to assess their toxic hazards, although the existence of important acute toxicants which have yet to be characterised is less likely than for toxicants with longer-term or delayed effects.

Table 1.1 List of main asphyxiant and irritant gases[6]

Asphyxiant gases	Irritant gases	Other components which should be monitored
Carbon monoxide (CO) Hydrogen cyanide (HCN)	Hydrogen fluoride (HF) Hydrogen chloride (HCl) Hydrogen bromide (HBr) Nitrogen dioxide (NO_2) Sulphur dioxide (SO_2) Organo irritants	Oxygen (O_2) Carbon dioxide (CO_2)

1.3 Important toxicants

In order to introduce the main toxicants present in fire effluents, a brief outline of their occurrence and effects is given here alongside reference to the chapter where they are discussed in detail.

1.3.1 Asphyxiant gases

Asphyxiant or narcotic gases cause a decrease in oxygen supplied to body tissue, resulting in central nervous system depression, with loss of consciousness and ultimately death. The severity of the effects increases with dose.[10] The main asphyxiants, carbon monoxide and hydrogen cyanide have been widely studied and are the best understood.[6] In addition, asphyxiation can also occur as a result of lowered oxygen concentration, and affected by the carbon dioxide concentration. The effects of asphyxiant gases are discussed in more detail in Chapter 4.

Oxygen depletion, also a feature of fire gases, which can be lethal once the oxygen concentration has fallen below tenable levels (~6%). However, from a fire toxicity perspective it is generally assumed that heat and other gases will have already prevented survival, while other toxicants, such as carbon monoxide or hydrogen cyanide, will be present in lethal quantities further from the fire where the oxygen depletion would not be considered harmful.

The carbon dioxide content in fresh air varies 300 ppm to 600 ppm, depending on location, and is almost always present at higher levels in fire gases. Inhalation of carbon dioxide stimulates respiration, increasing both rate and tidal volume, and causes acidosis (an increase in the acidity of the blood). The result is an increase in inhalation of oxygen and toxic gases produced by the fire. It also has moderate toxicity in its own right: exposure to a 50 000 ppm (5%) concentration for 30 minutes produces signs of intoxication; above 70 000 ppm unconsciousness results in a few minutes.

Carbon monoxide

The toxic effect of carbon monoxide is characterised by a lowered oxygen delivery capacity of the blood, even when a partial pressure of oxygen and the rate of blood flow rate are normal. Carbon monoxide binds to the haemoglobin in red blood cells resulting in the formation of carboxyhaemoglobin (COHb), with stability 200 times greater than that of oxyhaemoglobin, impeding the transport of oxygen from the lungs to the cells in the body. This causes deterioration in mental and muscular performance. Carbon monoxide also combines with myoglobin in the muscle cells, impairing diffusion of oxygen to cardiac and skeletal muscles.[13] Carbon monoxide has a cumulative effect, from which the body takes time to recover. About 50% of blood carbon monoxide is eliminated in the first hour, while complete elimination takes from several hours to a few days. When inhaled, carbon monoxide impairs an individual's ability to escape, causing different effects at different concentrations of carbon monoxide. At exposure to carbon monoxide levels of 10 ppm for short periods, impairment of judgement and visual perception occur; exposure to 100 ppm causes dizziness, headache and weariness; loss of consciousness occurs at 250 ppm; and inhalation of 1000 ppm results in rapid death. Chronic long-term exposures to low levels of carbon monoxide are suspected of causing disorders of the respiratory system and the heart.[14]

Hydrogen cyanide

Hydrogen cyanide is approximately 25 times more toxic than carbon monoxide through the formation of the cyanide ion formed by hydrolysis in the blood.[10] Unlike carbon monoxide which remains primarily in the blood (as COHb), the cyanide ion is distributed throughout the extracellular fluid of tissues and organs.[6] Two mechanisms have been identified for the toxic effects of cyanide. The first is by combination with the ferric ion in mitochondrial cytochrome oxidase, preventing electron transport in the cytochrome system and inhibiting the use of oxygen by the cells. The second results in a brief stimulation, followed by severe depression, of respiratory frequency, also starving the body of oxygen, and causing convulsions, respiratory arrest and death.[15] Whether one or other of these mechanisms predominates, or their interrelationship, remains unclear. Hydrogen cyanide also causes rapid incapacitation, preventing escape, and then, with carbon monoxide, contributes to death from asphyxiation. One analysis of fire victim's blood showed a trend of declining carboxyhaemoglobin and a rise in cyanide concentrations,[16] probably because of increased use of nitrogen-containing synthetic polymers. The uptake, distribution, metabolism and excretion of cyanide is much more complex than for carbon monoxide, and quantifying CN^- in fire victims is more expensive and not routinely undertaken. Therefore the contribution of hydrogen cyanide to fire deaths is difficult to

assess, and analysis for CN^- is limited to cases where lethal concentrations of carbon monoxide are absent.

1.3.2 Irritant gases

In contrast to the well-defined effects of asphyxiants, the effects of exposure to irritants are more complex. Incapacitating irritants and smoke can prevent escape from fire, although the victim is likely to have an elevated blood carboxyhaemoglobin, which will be reported as the cause of death. Most irritant fire effluents produce signs and symptoms of both sensory and upper respiratory tract irritation, and of pulmonary irritation. However, in post-mortem analysis these are similar to the effects of heat exposure (see Chapter 5). Sensory and upper respiratory tract irritation stimulates the trigeminal and vagus nerve receptors in the eyes, nose, throat and upper respiratory tract, causing discomfort, then severe pain. The central nervous system's response to acidic and organic irritant gases in mice is to inhibit breathing, causing the respiration rate to fall to 10% of its normal value, while in primates and humans the same stimulus results in hyperventilation, increasing the uptake of other toxicants. The effects of irritants range from tears and reflex blinking of the eyes, pain in the nose, throat and chest, breath-holding, coughing, excessive secretion of mucus, to bronchoconstriction and laryngeal spasms.[13] At sufficiently high concentrations, or when attached to submicron particles, such as soot, most irritants can penetrate deeper into the lungs, causing pulmonary irritation, which may cause post-exposure respiratory distress and death, generally occurring from a few hours to several days after exposure, due to pulmonary oedema (flooding of the lungs).[6] The effects of irritant gases are discussed further in Chapter 3.

Hydrogen halides

Hydrogen chloride (HCl) and hydrogen bromide (HBr) are strong acids which dissociate entirely in water. Both may be present in fire gas, for example from poly(vinyl chloride) (PVC) or brominated flame retardants, and since the damage caused by the acidity (the H^+ ion) is independent of the anion (Cl^- or Br^-), the discussion on hydrogen chloride is also applicable to HBr.

Hydrogen fluoride (HF) is a highly irritating, corrosive gas. Reaction with water is rapid, producing heat and hydrofluoric acid. However, hydrofluoric acid is a weak acid, whose toxicity does not derive from its acidity. Hydrogen fluoride is a severe irritant to the eyes, skin and nasal passages; high concentrations may penetrate to the lungs, resulting in oedema and haemorrhage. The ISO indicates a threshold for incapacitation of 500 ppm, while the United States Environmental Protection Agency (EPA) give 10 and 30 minute AEGL-3 concentrations are 170 ppm and 62 ppm respectively, based data on irritant

effects in humans and lethal and sublethal effects in six species of mammal to develop acute exposure guideline levels (AEGLs).[17] (AEGL-3 is 'the airborne concentration of a substance above which it is predicted that the general population, including susceptible individuals, could experience life-threatening adverse health effects or death').

Hydrogen chloride is an acidic gas which results in severe irritant effects at low concentrations (around 100 ppm) but only causes death at very high concentrations (in mice 2600 ppm, and in rats 4700 ppm for 30 minute exposures[18]). The difficulty in quantifying a threshold level for incapacitation, and the high levels of hydrogen chloride evolved during decomposition of certain materials has led to a long-running controversy over the maximum atmospheric concentrations of hydrogen chloride in fire gas from which escape is still possible.

There is only one report of human exposure to hydrogen chloride gas at concentrations relevant to fires,[19] which found that humans could tolerate exposure to 10 ppm hydrogen chloride, while at 70 and 100 ppm humans had to leave the room because of intense irritation, coughing and chest pains, indicating that 100 ppm is intolerably irritating to humans. The data have led to guidelines[20] that the maximum concentration tolerable for 1 hour is between 50 and 100 ppm, and that 1000 to 2000 ppm is dangerous for even short exposures. These guidelines were corroborated using an animal model that correctly predicted intolerable irritation levels for humans for other inorganic gases such as sulphur dioxide, ammonia, chlorine and a wide variety of organic chemicals, including formaldehyde and acrolein,[21,22] indicating that 300 ppm would be intolerable to humans.[23] However, other authorities and regulatory agencies have proposed much higher limits on 'acceptable' hydrogen chloride concentrations.

Nitrogen oxides

Nitric oxide (NO) and nitrogen dioxide (NO_2) are non-flammable gases present in fire effluents. At high concentrations nitric oxide is rapidly oxidised in air to form nitrogen dioxide; however, at the concentrations found in fire gases, most of the nitric oxide remains unchanged. Nitrogen dioxide dissolves rapidly in water to form nitric and nitrous acids. At high concentrations these acids can cause pulmonary oedema and death.[24,25] Conversely, nitric oxide gas at low concentrations has been used to aid breathing in the treatment of respiratory disorders.[26] However, in the blood it combines with oxyhaemaglobin to form methaemoglobin, between 5 and 20 times faster than oxygen and the resulting compound breaks down slowly,[24] giving effects similar to hypoxia; it forms nitrates; and if the blood oxygen concentration is low it can combine with haemoglobin to form nitrosohaemoglobin. Excessive levels of nitric oxide in blood have been shown to cause low blood pressure. However, it has been

reported that tobacco smoke can contain up to 1000 ppm of nitric oxide but this does not cause death.[24,27]

Organo irritants

Large numbers of known irritant chemicals have been found to occur in fire atmospheres.[28,29] The irritant chemicals released in fires are formed during the pyrolysis and partial oxidation of materials, and the combinations of products from different materials are often remarkably similar.[29] However, for many organic materials and particularly for simple hydrocarbon polymers such as polypropylene or polyethylene, the main pyrolysis products, which consist of various hydrocarbon fragments, are innocuous.[13] Thus when polypropylene is pyrolysed in nitrogen the products such as ethylene, ethane, propene, cyclopropane, formaldehyde, butane, acetaldehyde, toluene, styrene are produced,[13] and such an atmosphere was found to have no effect upon primates.[28,30] However, when these products are oxidised during non-flaming decomposition in air, some are converted to highly irritant products, and such atmospheres were indeed found to be highly irritant to both mice and primates. In reports of mouse exposure experiments, some fire retardant materials, which could be induced to flame only intermittently, with considerable smoke production, were found to produce atmospheres up to 300 times more irritant than the same polymer in its non-fire retardant state, which burned cleanly.[31] Table 1.2 shows some of more toxic, commonly encountered organic species in fire gas, with the concentration considered by the National Institute of Occupational Safety and Health (NIOSH) as immediately dangerous to health or life (IDLH).[32]

The difficulty in quantifying each organic component present in a fire effluent has led to an approximation by Purser[13] that an organics concentration of 10 mg/litre is sufficient to cause incapacitation. For comparison, the 500 ppm IDLH value for benzene corresponds to 1.6 mg/litre.

Table 1.2 Common organo irritants found in fire gas with IDLH values[32]

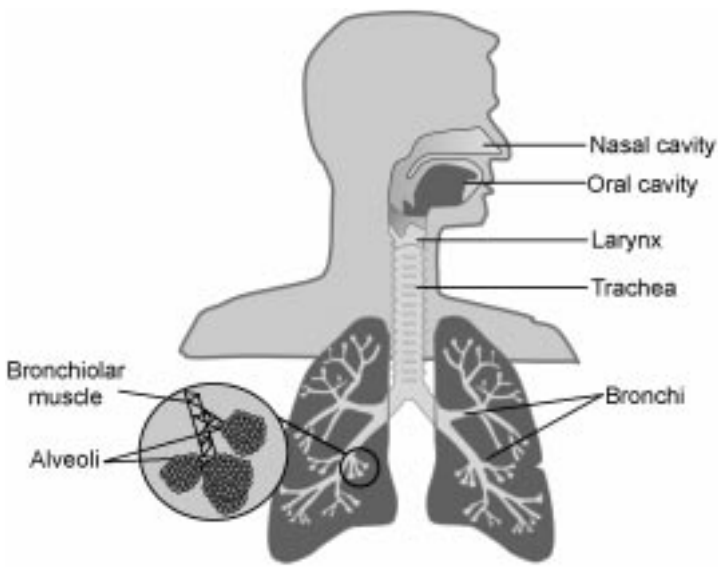
Substance	IDLH value (ppm)
Acetaldehyde	2000
Acrolein	2
Benzene	500
Crotonaldehyde	50
Formaldehyde	20
Phenol	250
Toluene	500

1.3.3 Particulates

Death in fire may be caused either by gases which are directly toxic or which cause such irritation that they impair vision and breathing, preventing escape, or by smoke which not only impairs escape ability by visual obscuration, but also contains particulate matter which is sufficiently small to pose a respiratory hazard. Despite the large amounts of particulates which are generated in a fire, relatively few investigations have been made on the particles (size, distribution and composition) from such fires.[33] Live animal exposure experiments, discussed in Chapter 6, show that the toxicity of fire effluents cannot be ascribed to the simple asphyxiants and irritants alone, and uncharacterised species, such as particulates, play a key role.

The particle size distribution is dependent on the material, temperature and fire conditions. Typical particle sizes of the spherical droplets from smouldering combustion are generally of the order of 1 μm, while those of the irregular soot particulates from flaming combustion are often larger, but much harder to determine and dependent on measuring technique and sampling position. The deposition areas for humans as a function of particle size are presented in Fig. 1.1.

The general effect of particulates is to cause fluid release and inflammation, preventing gas exchange in the alveolae. Inflammation of the terminal bronchioles can result in complete blockage. Passage of oxygen through the blood–gas barrier can only occur in the absence of excess fluid in the lungs.[34] Oedema fluid disrupts the dispersion of the lung surfactant, causing collapse of



1.1 Particle deposition in respiratory system.

the alveolae from higher surface tension of the fluid. The smallest particles (<0.5 μm) penetrate into the lung interstitium (between the alvelolar surface and the blood capillaries), where they have been shown to be particularly dangerous, causing interstitial and luminal oedema. They can also transcend the blood–gas barrier and enter the bloodstream, triggering dangerous immune responses from the white blood cells, including polymer fume fever, and increased platelet stickiness leading to heart attacks. Particulates and other irritants can change lung efficiency by increasing the stiffness of the lung tissue and through airways becoming blocked or flooded. In addition the particulates can act as vehicles for transport of noxious molecules deep into the lungs.

1.3.4 Firefighting agents

Although outside the scope of this book, reference should be made in passing to the toxicity of the breakdown products of fire fighting agents. The thermal decomposition products of four fire extinguishing agents, bromotrifluoromethane (Halon 1301), pentafluoroethane (HFC 125), heptafluoropropane (HFC 227ea) and dodecafluoro-2-methylpentane-3-one (C_6F-ketone) have been reported.[35] The concentrations required for extinction were determined using a cup burner in an 8 litre volume, and the thermal breakdown was studied by introducing the agent into a propane flame in a tubular burner. It was found that both hydrogen fluoride and carbonyl fluoride (COF_2), both of which are very toxic, were produced from each of the four firefighting agents.

1.4 Quantification of toxic hazards from fire

The replacement of prescriptive standards by performance-based fire codes requires a fire hazard assessment, which includes prediction of the toxic product distribution within the building from a fire.[6] The goal of any toxicity assessment is to generate reliable bench-scale toxicity data. Within the European Union, and other jurisdictions where routine animal testing is unacceptable,[36] this effectively means reliable quantification of yields of toxic products.

1.4.1 Estimation of fire effluent toxicity from chemical composition data

Exposure to toxic fire effluents can lead to a combination of physiological and behavioural effects of which physical incapacitation, loss of motor coordination and disorientation are only a few. Furthermore, survivors of a fire may experience post-exposure effects, complications and burn injuries, leading to death or long-term impairment. A significant number of studies aimed at relating the toxicity of fire effluents to the concentration of each component using animals as indicators of the toxicity[11,25,37] have been reported. Mice, rodents or

primates were exposed to pure gas mixtures or fire gases to determine incapacitation or lethality. The major effects, such as incapacitation or death, may be predicted by quantifying the fire effluents in different fire conditions in small-scale tests, using only chemical analysis, without animal exposure.

The estimation of fire effluent toxicity is a recurrent theme throughout the book, and the different established approaches are considered here. Methods for estimation of incapacitation and lethality are discussed in Chapter 8. The general approach in generating toxic potency data from chemical analysis is to assume additive behaviour of individual toxicants, and to express the concentration of each as its fraction of the lethal concentration for 50% of the population for a 30 minute exposure (LC_{50}). Summing these contributions generates a fractional effective dose (FED). An FED equal to 1 indicates that the sum of concentrations of individual species will be lethal to 50% of the population over a 30 minute exposure. These types of approaches have used existing rat lethality data, as described in ISO 13344[38] or more recently, based on the best available estimates of human incapacitation thresholds as described in ISO 13571.[6] Two equations have been developed for the estimation of the FED for lethality from the chemical composition of the environment in the physical fire model, based on the same set of lethality data. Each begins with the precept that the fractional lethal doses of most gases are additive, as developed by Tsuchiya and Sumi.[39]

Both equations have been taken from ISO 13344[38] and use LC_{50} values for lethality to provide reference data for the individual gases to calculate toxic potency, based on rats exposed for 30 minutes. The N-gas model, in Equation 1.1, assumes that only the effect of the main toxicant carbon monoxide is enhanced by the increase in respiration rate caused by high carbon dioxide concentrations (expressed as a step function with one value of m and b for carbon dioxide concentrations below and another for those above 5%):

$$\text{FED} = \frac{m[\text{CO}]}{[\text{CO}_2] - b} + \frac{21 - [\text{O}_2]}{21 - \text{LC}_{50,\text{O}_2}} + \frac{[\text{HCN}]}{\text{LC}_{50,\text{HCN}}} + \frac{[\text{HCl}]}{\text{LC}_{50,\text{HCl}}} + \frac{[\text{HBr}]}{\text{LC}_{50,\text{HBr}}} + \ldots \quad 1.1$$

The Purser model, presented in Equation 1.2, uses V_{CO_2} a multiplication factor for carbon dioxide driven by hyperventilation, therefore increasing the FED contribution from all the toxic species, and incorporates an acidosis factor A to account for toxicity of carbon dioxide in its own right.[38] An updated version of this equation is presented in Chapter 8, but this is the version published in reference 36:

$$\text{FED} = \left\{ \frac{[\text{CO}]}{\text{LC}_{50,\text{CO}}} + \frac{[\text{HCN}]}{\text{LC}_{50,\text{HCN}}} + \frac{[\text{AGI}]}{\text{LC}_{50,\text{AGI}}} + \frac{[\text{OI}]}{\text{LC}_{50,\text{OI}}} \ldots \right\} \times V_{\text{CO}_2} + A + \frac{21 - [\text{O}_2]}{21 - 5.4} \quad 1.2$$

$$V_{\text{CO}_2} = 1 + \frac{\exp(0.14[\text{CO}_2]) - 1}{2}$$

where [AGI] is the concentration of acid gas irritants, [OI] is the concentration of organic irritants and A is an acidosis factor equal to $[CO_2] \times 0.05$.

Both of these equations relate only to lethality, or *cause of death*. However, many people fail to escape from fires because of the incapacitating effect of smoke (obscuring visibility) and its irritant components which cause pain, inhibiting breathing resulting in incapacitation the *reason for death*. As described earlier ISO 13571[6] considers the four major hazards from fire which may prevent escape (toxic gases, irritant gases, heat and smoke obscuration). It includes a calculation for prediction of incapacitation of humans exposed to fire effluents, indicating, in a non-normative appendix, that the effects of heat, smoke and toxicants may be estimated independently. Equations 1.3 and 1.4 have been taken from ISO 13571. They calculate the FED of asphyxiants, carbon monoxide and hydrogen cyanide, but without taking oxygen depletion or carbon dioxide driven hyperventilation into account, and the fractional effective concentration (FEC) of sensory irritants in the fire effluent which limit escape:

$$\mathrm{FED} = \sum_{t_1}^{t_2} \frac{[\mathrm{CO}]}{35\,000}\,\Delta t + \sum_{t_1}^{t_2} \frac{\exp([\mathrm{HCN}]/43)}{220}\,\Delta t \qquad 1.3$$

$$\mathrm{FEC} = \frac{[\mathrm{HCl}]}{\mathrm{IC}_{50,\mathrm{HCl}}} + \frac{[\mathrm{HBr}]}{\mathrm{IC}_{50,\mathrm{HBr}}} + \frac{[\mathrm{HF}]}{\mathrm{IC}_{50,\mathrm{HF}}} + \frac{[\mathrm{SO_2}]}{\mathrm{IC}_{50,\mathrm{SO_2}}} + \frac{[\mathrm{NO_2}]}{\mathrm{IC}_{50,\mathrm{NO_2}}} + \frac{[\mathrm{acrolein}]}{\mathrm{IC}_{50,\mathrm{acrolein}}} + \frac{[\mathrm{formaldehyde}]}{\mathrm{IC}_{50,\mathrm{formaldehyde}}} + \sum \frac{[\mathrm{irritant}]}{\mathrm{IC}_{50,\mathrm{irritant}}} \qquad 1.4$$

Equation 1.2 describes the generally accepted case that there are only two significant asphyxiant fire gases, carbon monoxide and hydrogen cyanide. The FED value is calculated using the exposed dose relationship (concentration–time product, Ct) for carbon monoxide. The lethal Ct product corresponds to the incapacitating dose (Ct) for carbon monoxide of $35\,000\,\mu l\,l^{-1}$ min (approximately equal to ppm min), equal to around 1170 ppm for 30 min exposure and an exponential relationship for hydrogen cyanide (because asphyxiation by hydrogen cyanide exposure does not fit a linear relationship). Equation 1.4 uses a similar principle to Equation 1.1 to estimate the combined effect of all irritant gases.

The additive model is almost certainly an over-simplification, because the effects occur in different organs (lungs, muscles, brain, etc.), although it is as likely to be an overestimate as an underestimate. There are several gases where the additive methodology is known to be wrong. For example, at carbon dioxide concentrations of 5% (common in diluted fire effluents) the respiratory volume per minute (RMV) increases by a factor of 3, increasing the dose of fire gas inhaled. Purser's model addresses this by applying a correction factor (itself a function of carbon dioxide concentration) to all the individual toxicant ratios,

Table 1.3 Toxic gas concentrations leading to death (ISO 13344) and incapacitation impairing escape (ISO 13571) for a fixed concentration for a 30 minute exposure

	Concentration leading to death giving FED = 1 using ISO 13344 (ppm)	Concentration leading to incapacitation giving FEC/FED = 1 using ISO 13571 (ppm)
CO	5700	1170
HCN	165	100
HCl	3800	1000
NO_2	170	250

not just carbon monoxide.[38] However, ~50 ppm nitric oxide (usually present in fire gas) opens up the airways, allows improved respiration, but also greater exposure to other toxicants. Hydrogen cyanide initially increases the respiration rate, and then severely suppresses it; irritant gases such as hydrogen chloride suppress it by a factor of around 10 in stationary rats and mice.[40] There is also growing evidence that other chemical species present in fire gas (such as particulates and isocyanates), which are not normally included in these predictions of fire gas toxicity, can be some of, or even the most toxicologically significant species.

More controversy surrounds the toxic potency values used in these models (Table 1.3). These range from direct application of rat lethality data for single gas exposures to humans, to estimates made by committees of experts.[6] Data exist to show that both simplifications are unjustified.[41,42]

In order to relate the fire effluent toxicity to a maximum permissible material loading for example in a room or railway carriage, the FED can be related to the mass of material in a unit volume which would cause 50% lethality for a given fire condition. Thus the fire toxicity of a material can be expressed as an LC_{50}, which in this case is the specimen mass M of a burning polymeric material which would yield an FED equal to one within a volume of 1 m^3. The relation to the FED from the N-gas model is given in Equation 1.5:

$$LC_{50} = \frac{M}{\text{FED} \times V} \qquad 1.5$$

where V is the total volume of diluted fire effluent in m^3 at standard temperature and pressure (STP). The accuracy of LC_{50} values determined in this manner is quoted as $\pm 30\%$ if the concentrations of all the contributing toxicants are measured and included.[9,43] Comparing the toxic potencies of different materials, the lower the LC_{50} (the smaller the amount of materials necessary to reach the toxic potency) the more toxic the material is. LC_{50} values should be referenced to the fire condition under which they were measured.

1.4.2 Effect of toxicants on different species

The difficulties in making reliable estimates of the effects of fire effluents on humans are outlined here, and discussed in more detail in Chapters 3, 4, 7 and 8. The effect of fire effluents on human life cannot be measured directly for legal and ethical reasons. It may be estimated from the effect on animals either directly, using animal exposure, or indirectly from tables of concentrations leading to a particular effect (such as the limit below that causing irreparable damage, death or incapacitation of 50% of the population, etc.). Simple application of the data relies on the untested assumption that effects on animal subjects (usually rats) may be simply extrapolated to humans. However, there is no direct relationship between these data and the limits for humans. Some data indicate that the mechanism of toxicity of some gases is the same in rodents and humans. For other gases the response is known to be different.[13] Other reports suggest that the use of mice may not be reliable because of their very fast respiration rate and narrow airways. Differences between species such as respiratory rate and volume, may produce different relative results in toxicity tests. It has been reported[25] that rat data cannot be extrapolated to baboon data when irritant gases are the principal toxicants. A paper by Hartzell *et al.*[37] suggests that when considering acute lethal effects, primates may resist about 1.3 times greater concentrations of hydrogen chloride and hydrogen cyanide than rats and about 1.6 times greater concentrations of carbon monoxide than rats. Nitric oxide also has different effects on different species. Exposure of rats to 1500 ppm for 15 min and to 1000 ppm for 30 min, and of lambs to 80 ppm for 60 to 180 min does not cause adverse effects, but the exposure of rabbits to 5 ppm for 14 days causes interstitial oedema. It is necessary to understand the accuracy and uncertainties of animal testing methods for fire hazard assessment.

Table 1.4 presents and compares lethal toxic potencies of the most common fire effluents for different animal species,[38] showing considerable variation between species.

Table 1.4 Comparison of LC_{50} (30 minute exposure) for different animals[38,44]

Chemical agent	Mice	Rats	Primates
CO (ppm)	3500	5300–6600	2500–4000
HCN (ppm)	165	110–200	170–230
HCl (ppm)	2600	3800	5000
Low O_2 (%)	6.7	7.5	6–7

1.5 Bench-scale generation of fire effluents

Controlled laboratory methods for generation of fire effluents are discussed in detail in Chapter 12. Since real fires do not occur under controlled conditions bench-scale methods are the principal methods for generating toxic fire effluents under controlled conditions. Guidance on assessment of physical fire models has been published in ISO 16312-1,[45] and reviewed elsewhere.[46]

In all fire smoke toxicity tests, specimens are decomposed by exposure to heat, resulting in 'forced combustion' driven by an applied heat flux from a flame, radiant panel, etc. Some tests use a pilot flame or spark igniter to facilitate ignition, while others rely on self-ignition of the sample. When flaming combustion occurs, this will increase the radiant heat flux back to the sample, typically between 2 and 10 times. This will have two significant effects on the fire effluent. First, the existence of flames will help to drive the combustion process to completion, by increasing the temperature and hence the reaction rates, which will tend to reduce the toxicity of the fire effluent (favouring carbon dioxide over carbon monoxiode and organic molecules). Secondly, the higher heat flux will pyrolyse more material at a greater rate, increasing the amount of volatiles in the vapour phase, and reducing the concentration of oxygen, both of which will increase the toxicity of the fire effluent.

Unfortunately, these effects are so large that, rather than cancelling each other out, they can result in very large differences in the toxic product yield between different fire toxicity tests. Clearly, the presence or absence of flaming combustion is critical to the interpretation of the results from combustion toxicity assessments. In some conditions, specimens will either pyrolyse or self-ignite, but the scatter of results will be very large if flaming combustion is inconsistent. Once flaming is established, combustion will drive itself to completion (and hence the toxicity will be reduced), provided there is sufficient oxygen, and the flame is not quenched. If the flame is cooled rapidly, e.g. by excessive ventilation or a cool surface, the yield of toxic products will increase. Ultimately the value of the bench-scale toxicity assessment is dependent on its ability to predict large-scale burning behaviour, and therefore validation must involve comparison with large-scale test data.

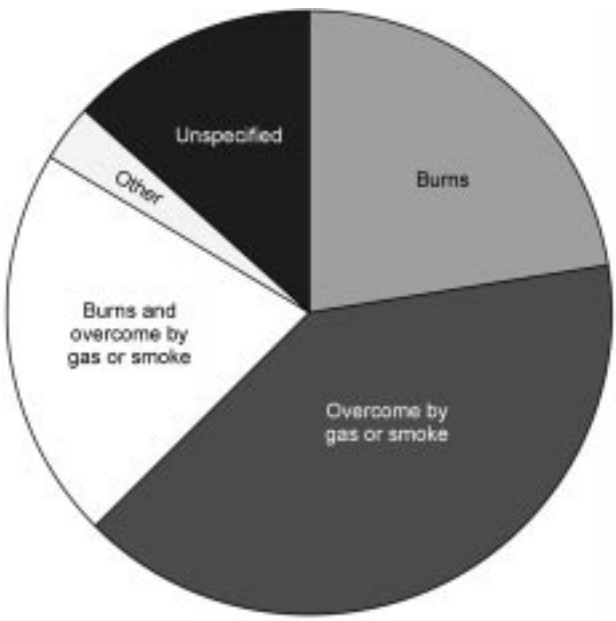
Unfortunately most large-scale test data have been obtained under well-ventilated conditions, and when data from under-ventilated fire scenarios, such as the ISO 9705 room test,[47] are made available the change of sample mass and the air flow to the fire during the test is not generally known. Of the standard methods used for toxicity assessment, there are three general types: well-ventilated or open methods, closed box tests and tube furnaces. Of these, the steady-state tube furnace ISO 19700 has shown the greatest potential to adequately replicate each fire stage individually. It achieves this by driving a linear sample into a long furnace under a controlled flow of air, such that the heat flux applied to the sample increases until ignition occurs. Flaming then

stabilises and the rate of burning equals the sample feed rate. This has proved to be the most reliable method for replicating the highly toxic condition of under-ventilated burning.

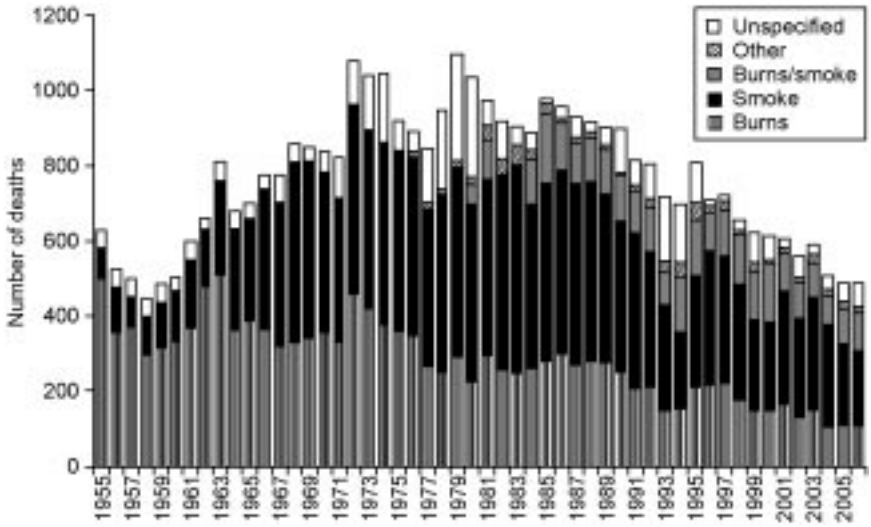
1.6 Fire death and injury statistics

In the UK fire statistics are collected nationally, using a standardised form filled in by lead firefighters after each call-out. Supplementary information on fire victims is added as it becomes available. The statistics can probably be assumed to be representative of most northern European countries. The assignation of cause of death is made by the pathologist (see Chapter 5). Figure 1.2 shows the causes of fire deaths in the UK.[48] In many cases it has not been possible to unambiguously identify the cause of death, since the victim may be severely burnt, but also have a high level of carboxyhaemoglobin in their blood. Given that some of the unspecified deaths may also have been overcome by toxic gas and smoke it is reasonable to assume that fire toxicity is responsible for over 50% of fire deaths in the UK.

Figure 1.3 shows the trend in causes of fire deaths[48,49] from 1955 to 2006. This shows a significant increase from the 1950s to the 1980s, generally ascribed to the replacement of natural materials (e.g. wood, cotton, wool and leather) with synthetic polymers, for example as fabrics and foams in soft furnishing. In 1988 in the UK, the Furniture and Furnishings (Fire) (Safety) Regulations were

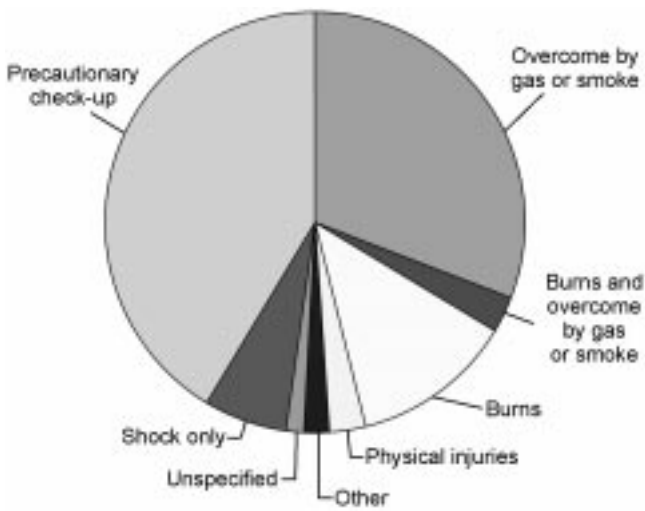


1.2 Cause of UK fire deaths 2006.

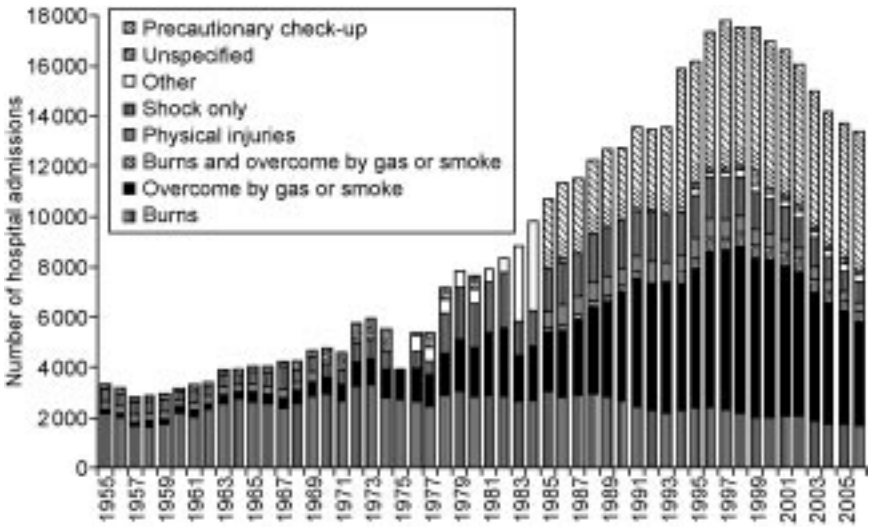


1.3 Causes of UK fire deaths 1955–2006.

introduced, which not only banned the sale (new or second-hand) of non-fire retarded furniture, but also made it illegal to rent furnished property containing such furniture. However, it was also around this time that low-cost smoke alarms became available. The noticeable drop in fire deaths from 1988 to 1994 can almost certainly be attributed to one or other of these changes. In 1981, a new category, 'burns and smoke', was introduced to identify where the cause of death was ambiguous. It is apparent that while all fire deaths have fallen, the



1.4 UK non-fatal injuries requiring hospital treatment.



1.5 UK non-fatal fire injuries requiring hospital treatment, 1955–2006, excluding precautionary check-up.

reduction in deaths from burns has been more dramatic than those from toxic gas inhalation.

Figure 1.4 shows the non-fatal injuries requiring hospital treatment.[48] Disregarding the large proportion requiring only a precautionary check-up, this also shows a much higher proportion suffering from toxic gas inhalation than burns. The figures do not report longer-term injuries resulting from fire.

Figure 1.5 shows the longer-term trend in non-fatal fire injuries requiring hospital treatment, excluding the increasing proportion attending hospital only for a precautionary check-up.[48,49] In contrast to the fire deaths, this shows a very large rise in the fire toxicity injuries, with a later peak, around 1998, which is only now falling to 1988 levels. If the figures for those overcome by gas or smoke are considered, these have failed to decrease significantly and are currently still at the high levels seen around 1990. This demonstrates that the problems associated with fire effluent toxicity have not gone away, and are becoming more important as the overall numbers of fire and fire deaths decrease.

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2

Fire scenarios and combustion conditions

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Abstract: Fire effluent toxicity and toxic hazard in fires are highly dependent on the fire conditions. This chapter describes the stages of fire growth, the different types of fires in terms of fire scenario, combustion conditions, and the typical toxic products from each stage. The main fire types described are non-flaming, smouldering, well-ventilated flaming, under-ventilated pre-flashover and post-flashover fires. Under ventilated fires produce the high yields of toxic products that are considered responsible for most fire injuries and deaths.

Key words: under-ventilated, pyrolysis, equivalence ratio, vitiated, flashover, compartment fires, toxic hazard.

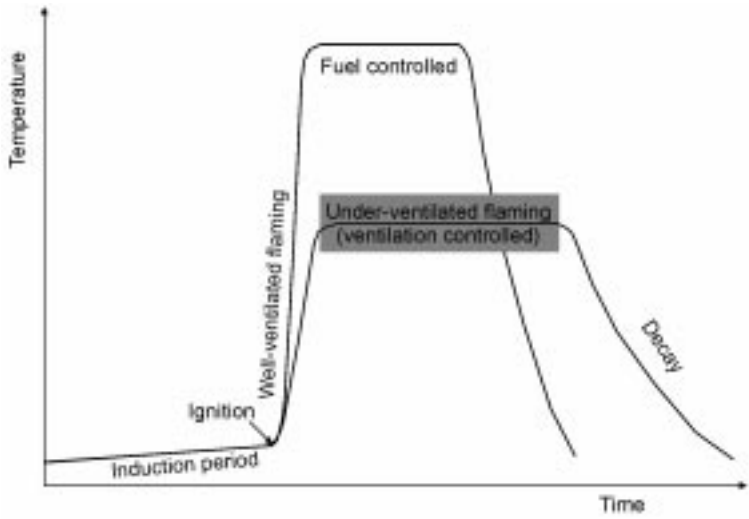
2.1 Introduction

Fire effluent toxicity is highly dependent on the fire conditions. This chapter describes the stages of fire growth, the different types of fire in terms of fire scenario and combustion conditions, and the typical toxic products from each stage.

Fire gases contain a mixture of fully oxidised products, such as carbon dioxide (CO_2); partially oxidised products, such as carbon monoxide (CO), hydrogen cyanide (HCN) and aldehydes; fuel or fuel degradation products, such as aliphatic or aromatic hydrocarbons, carbonaceous particulates and other stable gas molecules, such as nitrogen and hydrogen halides. A large number of other toxic and irritant gas species also contribute to the hazard from fire gases to a lesser extent. The yields of most of these species will depend on both the material properties (especially the elemental composition) and the fire conditions.

2.2 Idealised fire growth and typical toxic products

A simplified growth curve for a fire in an enclosure is shown in Fig. 2.1. In terms of the overall fire scenario and the combustion conditions, fires can be characterised by stages or types. The graph shows an example of a fire passing though all the main stages. Fires often begin by a non-flaming induction period, which may involve smouldering. After an indefinite period ignition may occur

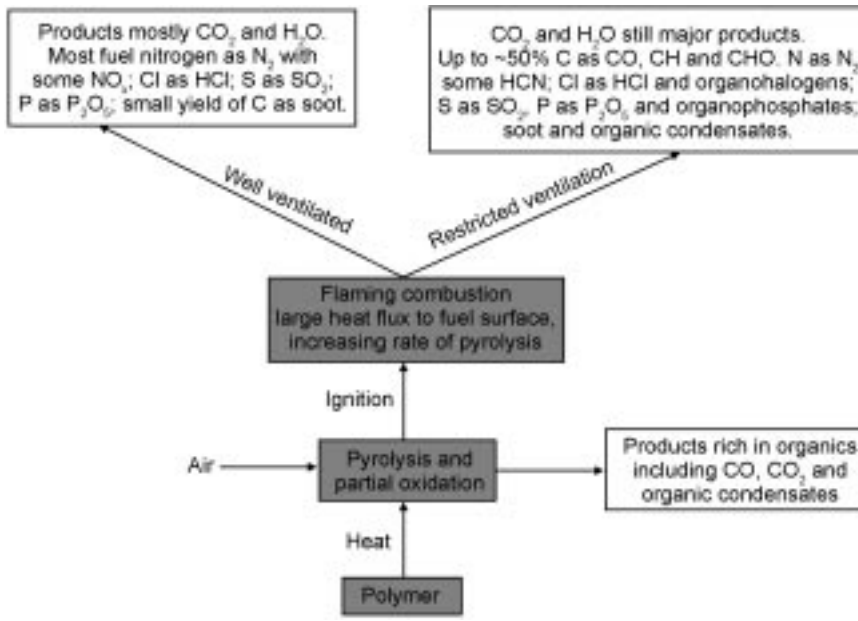


2.1 Idealised fire growth curve and typical temperatures.

with transformation to flaming combustion. During the early stages of flaming fires, when the fire is small compared with the enclosure size, it is usually well ventilated, with an ample air supply to support combustion. This often leads to a period of rapid fire growth until the size of the fire becomes limited, either by the rate of fuel supply (a fuel-controlled fire) or by the rate of air supply (ventilation-controlled fire). The fire then reaches a quasi-steady state, continuing in either form until the fuel or air supply is used up, whereupon the fire decays and eventually self-extinguishes. Depending upon the conditions, any particular fire may remain at one of these stages throughout most of its life, so that it may be referred to as a particular type of fire: non-flaming, smouldering, small/early well ventilated, developed fuel controlled or developed ventilation controlled.

Full-scale compartment fires (such as most flaming fires inside buildings) usually become ventilation controlled, and under these under-ventilated (oxygen-depleted or 'vitiated') combustion conditions, the yields of toxic products are usually much greater than those produced under well-ventilated (fuel-controlled) combustion conditions.[1] For most materials the yields of toxic species have been shown to depend critically on the fire conditions.[1] Figure 2.2 illustrates the generalised change in toxic product yields during the growth of a fire from non-flaming through well-ventilated flaming to restricted ventilation. Although the toxic product yields are often highest for non-flaming combustion, the rates of burning and the rate of fire growth are much slower, so under-ventilated flaming is generally considered the fire stage presenting the greatest toxic hazards.

The main products of importance with respect to survival and injury in fires are as follows:



2.2 Effects of fire stages on toxic gas production.

- *Asphyxiant gases*: carbon monoxide, carbon dioxide, hydrogen cyanide and oxygen depletion (with a small contribution from oxides of nitrogen).
- *Irritants*: inorganic acid gases (hydrogen halides, sulphur oxides, nitrogen oxides, phosphoric acid), organic irritants and smoke particulates.

The dangerous concentrations of some important toxic fire gases are shown in Table 2.1 alongside the influence of ventilation condition on their yields. Painful irritant effects of acid gases (HF, HBr, HCl, SO_2) and organic irritants (acrolein, formaldehyde and other irritant oganics) occur immediately, depending upon the exposure concentration. Incapacitating asphyxiant effects of carbon monoxide and hydrogen cyanide, and lethal lung injuries from irritants, occur after exposure to significant concentrations over a period of time (dose-related effects – see Chapters 3 and 4). Consensus estimates of the concentrations are presented for immediate incapacitation (IC_{50}) of humans by irritant gases;[2] for asphyxiant incapacitation of humans following a 30 min exposure and for estimated lethality for all gases in humans following a 30 min exposure. Estimates of lethal exposures are based on rat exposure data[3] (measurements of 30 min LC_{50} concentrations – which represents death of 50% of the population during or after a 30 min exposure).

The yields of acid gases and nitrogen-containing products depend upon the proportion of the appropriate elements in the materials burned and the efficiency of conversion. In general conversion efficiencies are high for halogen acid gases.

Table 2.1 The main irritant and asphyxiant components in fire gases and their toxic potencies in terms of incapacitating and lethal concentrations for a 30 minute exposure period (as specified in ISO 13571 and ISO 13344)

Yield largely independent of fire condition	Yield decreases as ventilation decreases	Yield increases as ventilation decreases
HF (500; 2900 ppm)	CO_2 (~7%, ~10%) also replaces O_2 and increases respiration rate	CO (1170; 5700 ppm)
HCl (1000; 3800 ppm)	NO_2 (170; 250 ppm)	HCN (82; 165 ppm)
HBr (1000; 3800 ppm)	SO_2 (150; 1400 ppm)	Acrolein (30; 150 ppm) Formaldehyde (250; 750 ppm) Aromatics, aldehydes, ketones, etc.

Note: incapacitating effects immediate for all except CO and HCN.

Most fuel nitrogen is released as N_2, but under well-ventilated combustion conditions a proportion is released as oxides of nitrogen (mainly NO) and under vitiated combustion conditions a proportion is released as HCN.[4] Carbon monoxide yields are generally very low under well-ventilated conditions (in the absence of halogens) but increase considerably under vitiated combustion conditions. Acrolein and formaldehyde are formed especially from cellulosic materials under non-flaming decomposition conditions, but products of vitiated combustion contain other organic irritants.

2.3 Studies on methane flames

2.3.1 Carbon monoxide production

The combustion chemistry of methane is often studied as the simplest organic fuel, although it is unusual in having four hydrogen atoms to one carbon atom, while most organic fuels have two or fewer hydrogen atoms per carbon atom. The influence on fire conditions on the toxic product yield can be illustrated by consideration of the formation of carbon monoxide and higher hydrocarbons in methane flames.[5] The free radical processes typical of flaming combustion lead to very rapid reactions, once a critical free radical concentration has been reached. These gas phase processes occur at temperatures above 500 °C and are normally associated with flaming combustion. Since the number of radicals is much smaller than the number of molecules, any reduction in the radical concentration is likely to lead to incomplete combustion. For ignition and fire growth to occur, there must be an increase in the number of free radicals, involving chain branching steps. Oxidative thermal decomposition will generate the species responsible for the initial attack on methane.

$$H\cdot + O_2 \rightarrow OH\cdot + \cdot O\cdot$$

$$\cdot O\cdot + H_2 \rightarrow OH\cdot + H\cdot$$

$$H_2O + \cdot O\cdot \rightarrow OH\cdot + OH\cdot$$

Most of the hydroxyl (OH·) radicals are produced by the reaction:

$$H\cdot + H_2O \rightarrow H_2 + OH\cdot$$

The methyl radical ($CH_3\cdot$) is formed by attack of one of these radicals on methane (CH_4):

$$CH_4 + OH\cdot \rightarrow CH_3\cdot + H_2O$$

$$CH_4 + H\cdot \rightarrow CH_3\cdot + H_2$$

$$CH_4 + \cdot O\cdot \rightarrow CH_3\cdot + OH\cdot$$

The methyl radical $CH_3\cdot$ can then react with oxygen to form methanal (HCHO) (formaldehyde):

$$CH_3\cdot + O_2 \rightarrow HCHO + OH\cdot$$

Since very little methanal is observed in methane flames this must be followed by a rapid removal step such as:

$$HCHO + OH\cdot \rightarrow HCO\cdot + H_2O$$

and then

$$HCO\cdot + OH\cdot \rightarrow CO + H_2O$$

If sufficient oxygen is present, carbon monoxide is consumed by reaction with a further OH· radical:

$$CO + OH\cdot \rightarrow CO_2 + H\cdot$$

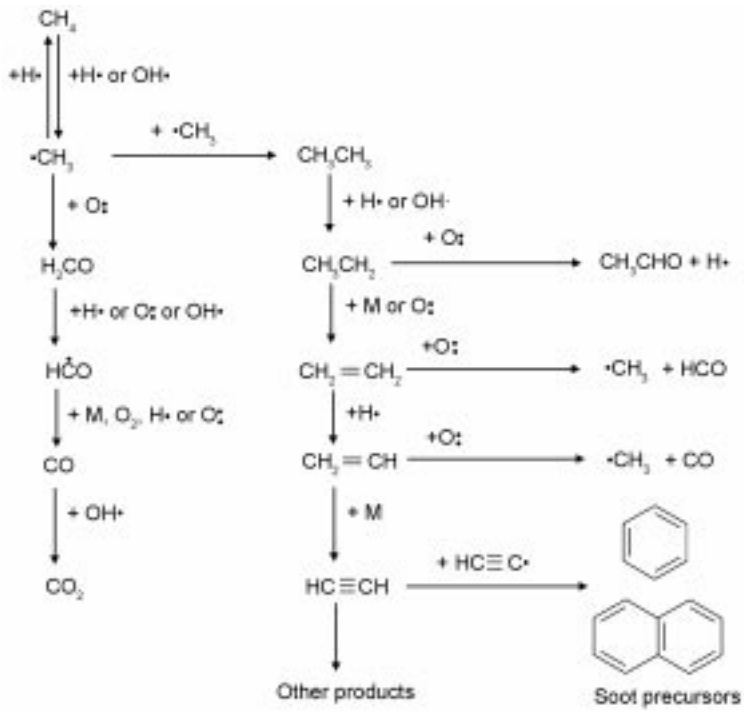
This is the only gas phase process by which carbon dioxide is formed from carbon monoxide, and any reduction in the availability of hydroxyl radicals (OH·) can dramatically increase the carbon monoxide yield. It is also one of the main energy releasing steps in fire reactions. Since OH· radicals are relatively scarce, this prevents oxidation of carbon monoxide until higher in the flame. Crucially, if the H· radicals cannot diffuse back to the lower part of the flame, they will not be able to generate enough OH· radicals to convert carbon monoxide to carbon dioxide. Thus although carbon monoxide always results from incomplete combustion, this can arise from:

- insufficient heat (e.g. during smouldering, which is dominated by reactions at the fuel surface, rather than gas phase free radical processes);
- quenching of the radical flame reactions (e.g. when halogens are present in the flame, forming free radicals which are stable enough to leave the flame zone without further reaction, or excessive ventilation cools the flame);

- the presence of stable molecules which do not succumb to attack by free radicals, such as aromatics which survive longer in the flame zone, giving high carbon monoxide yields in well-ventilated conditions, but lower than expected yields in under-ventilated conditions;[6]
- insufficient oxygen reducing the availability of OH· radicals for the carbon monoxide oxidation stage (e.g. in under-ventilated fires, large radiant heat fluxes pyrolyse the fuel even though there is not enough oxygen to complete the reaction).

2.3.2 Higher hydrocarbon and soot production

In reduced oxygen environments two methyl radicals can combine, forming ethane (CH_3CH_3), which may then be oxidised to acetaldehyde (CH_3CHO) or dehydrogenated to ethene ($CH_2{=}CH_2$), then ethyne ($CH{\equiv}CH$), which can combine to form benzene (C_6H_6), higher aromatics and ultimately a carbonaceous soot particle. Figure 2.3 summarises this process. At high temperatures H· atom abstraction reactions with the major radical species, H·, OH·, and ·O· occur rapidly and the hydrogen atoms of the fuel are stripped off one by one, leaving



2.3 Flow diagram for methane combustion in a stoichiometric methane–air flame at atmospheric pressure.

carbon monoxide. The final step in the oxidation reaction is the reaction of CO with OH· to generate CO_2.

Depending on the fuel : air ratio and conditions, hydrocarbon radical recombination may compete with abstraction and subsequent degradation, leading to the formation of higher hydrocarbon species. Under conditions of incomplete oxidation, compounds such as ethyne (acetylene) and the ethynyl radical ($\cdot C_2H$) can react to give the basic building constituents for soot formation. In polymers and other condensed phase materials, both carbon monoxide and carbon dioxide can also be formed by oxidative degradation on the surface at lower temperatures (below 500 ºC) which often produces high yields of carbon monoxide.

2.4 The equivalence ratio ϕ

The high yields of carbon monoxide from under-ventilated fires are held responsible for most deaths through inhalation of smoke and toxic gases, but this under-ventilated burning is the most difficult to create on a bench scale. Research predicting the carbon monoxide evolution from flames of simple hydrocarbons, reviewed by Pitts,[7] has shown the importance of the equivalence ratio ϕ, and introduced the concept of a global equivalence ratio ϕ_g.

$$\phi = \frac{\text{actual fuel to air ratio}}{\text{stoichiometric fuel to air ratio}}$$

		Typical CO yield (g/g)
$\phi < 1$	fuel lean flames	0.01
$\phi = 1$	stoichiometric flames	0.05
$\phi > 1$	fuel-rich flames	0.2

In recognition of the fact that the reaction can occur in the fire plume, or above it in the hot upper layer, and additional air may be added to this upper layer, sometimes the equivalence ratio needs to be more precisely defined. The overall, or global equivalence ratio ϕ_g can be used, to distinguish it from the plume equivalence ratio ϕ_p. In one set of experiments, the fire plume was contained in a hood, and the products were allowed to escape from the bottom of the hood, then upwards, to form an upper layer, where further reactions could take place, and additional oxygen could be added. The work has shown that in some circumstances only ϕ_g is needed to predict the concentration of carbon monoxide in the products, while in others, the hot or upper layer temperature must also be taken into consideration. In both cases for simple hydrocarbons, including polyethylene, there is only a marginal dependence on the fuel. In fuel-rich conditions, the carbon monoxide yield was found to be more or less constant at 0.2 g per g of fuel, for fuels containing only carbon and hydrogen (such as propane, hexane or polyethylene), and about 0.25 g per g of fuel for fuels containing oxygen (such as methanol and propanone). A surprisingly low result for toluene (0.11 g carbon monoxide per g) was ascribed

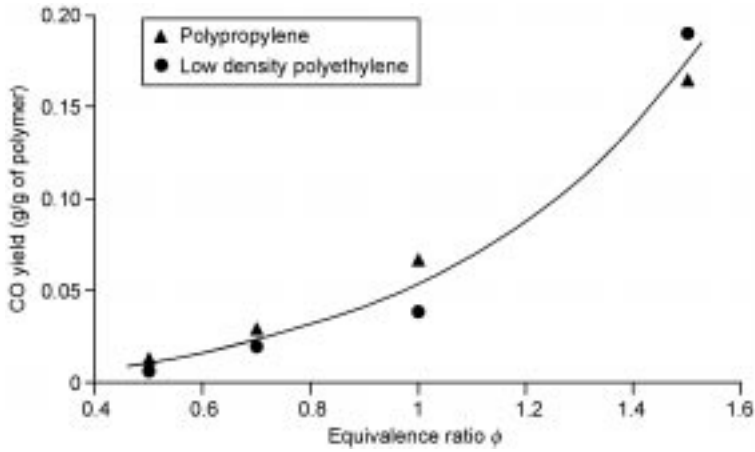
to its thermal stability leaving more OH· available to oxidise the carbon monoxide to carbon dioxide.

Since this review, the relationship between equivalence ratio and yields of carbon monoxide and other products has been studied in detail for a wide range of materials using two small-scale apparatus designed specifically for this purpose – the ASTM E2058 fire propagation apparatus[8] and the ISO 19700 tube furnace apparatus,[9] in conjunction with a series of large-scale experiments used for validation.[4,10,11] The findings from these studies have corroborated and extended those of the Pitts review, demonstrating that yields of different toxic products are highly dependent on equivalence ratio (and either positively or negatively correlated), but also to a lesser extent, on other parameters such as temperature, oxygen concentration, elemental and molecular composition of the material. These aspects are reviewed in Chapter 14.

The applicability of the global equivalence ratio concept according to Pitts is summarised in Table 2.2. Thus in studies above 625 ºC, where there is no direct entry of air to the reactive upper layer, it should be possible to relate the carbon monoxide yield to the equivalence ratio. In general air entrainment into horizontally flowing plumes is relatively low, while entrainment into plumes

Table 2.2 Applicability of global equivalence ratio concept[7]

Upper layer temperature (ºC)	Upper layer composition	Comments
< 425	Exclusively from plume	Upper layer non-reactive. Relative production rates of combustion products very similar for full range of ϕ_g.
> 625	Fuel lean	Similar to fully ventilated fires. CO levels low unless soot present to catalyse $CO_2 \rightarrow CO + \cdot O \cdot$.
> 625	Exclusively from plume	Prediction of combustion products possible over the full range of ϕ_g. When $\phi_g > 1.5$, CO yields are relatively constant.
425–625	Exclusively from plume	Relative generation rates for combustion products dependent on upper layer temperature and upper layer residence time. Global equivalence ratio concept needs to be modified to correct for temperature dependence.
> 625	Direct entry of air to upper layer	This situation is commonly reported in some real enclosure fires. The remaining fuel is oxidised to CO in preference to CO_2 in the upper layer. CO likely to be greater than predictions based on ϕ_g. Any air introduced via this route needs to be taken into account when determining equivalence ratio.



2.4 Small-scale data from the steady-state tube furnace showing the relationship between equivalence ratio and CO yield.[6]

turning vertically can be large. This can occur for example when doorway plumes rise into calorimeter hoods in room calorimeter fire experiments, or when a doorway plume from a burning shop turns vertical as it flows up into shopping centre atrium. When such secondary air entrainment occurs it is necessary to take it into consideration with respect to equivalence ratio estimations. Similarly if additional fuel is introduced into a hot upper layer (for example in the case of a ceiling lined with wood panels) then this may also affect overall fuel–air ratios and hence equivalence ratios in the fire scenario.

In a fully developed fire, with low ventilation, ϕ can be as large as 5, although flames are often extinguished at lower values. For many hydrocarbon polymers, carbon monoxide yield increases rapidly with increase in ϕ, somewhat independent of polymer, as shown in Fig. 2.4. In addition, a close correlation between carbon monoxide formation and hydrogen cyanide formation has been established in full-scale fire studies,[12] as the formation of both species appear to be favourable under the same poorly ventilated fire conditions.

2.5 Types of fire and stages of growth

Both in terms of the fire chemistry and the development of fire conditions and toxic hazards it is possible to classify full-scale fires into a small set for which the decompositions conditions can be replicated in small or large-scale tests in order to measure toxic product yields. Fires often grow quickly from well-ventilated flames and relatively clean products to dense sooty flaming with high concentrations of toxic products. Figure 2.5 shows a sequence of fire development from an experiment involving a full-scale room burn.

2.5 Images of each stage of fire development Stages 2, 3a and 3b (Table 2.3): (a) early flaming, smoke already forming upper layer, (b) well-ventilated flaming, (c) well-ventilated flaming showing smoke layer, (d) pre-flashover under ventilated (dark smoke layer), (e) post-flashover (luminous, reactive smoke layer), (f) post-flashover, vented flaming.

2.5.1 ISO classification of fire stages

The stages of a fire, from non-flaming, to well-ventilated flaming, and finally to under-ventilated flaming, have been classified by the ISO (Table 2.3) in terms of heat flux, temperature, oxygen concentration (to the fire, and in the fire effluent), and $CO_2 : CO$ ratio, equivalence ratio ϕ (the actual fuel-to-air ratio divided by the stoichiometric fuel-to-air ratio) and combustion efficiency (the % conversion of fuel to fully oxygenated products, such as carbon dioxide and water). While some real life fires may be represented by a single fire stage, other fires may pass through several different stages.[13] It should be noted that the current ISO 19706 standard incorrectly assigns a value of the equivalence ratio (normally only applied to a flaming environment) for non-flaming combustion, which is not consistent with established practice in fire science; these values have not been shown here.

The use of $CO : CO_2$ ratios can only be used to characterise fire stages for materials which do not contain chlorine or bromine since these elements significantly increase the carbon monoxide yield in well-ventilated fires. Additional information about the fire stage may be apparent from the yields of combustion products, and the ratios of 'telltale' second-order products of incomplete combustion, such as an aldehyde : CO_2 ratio.

2.6 Combustion conditions in full-scale compartment fires

The stages of fire growth and fire types, and their contribution to the toxic hazard[12] are discussed in more detail in the following sections because of their important influence on the toxic product yield.

2.6.1 Non-flaming and smouldering fires

Although non-flaming and smouldering decomposition has been studied in large-scale compartment fire experiments, such fires generally show relatively minor interactions between the decomposing material and the fire compartment, since compartment temperatures usually remain near ambient and compartment oxygen concentrations are not lowered. In general the decomposition conditions relate to the local heat and air exposure of the material, so that bench-scale and intermediate scale experiments can be used to study decomposition processes.

The first set of fire types in Table 2.3 are non-flaming and smouldering fires. Non-flaming thermal decomposition occurs when the temperature is high enough to produce thermal breakdown of the polymer structure. The simplest pyrolysis (Stage 1c in Table 2.3) occurs in inert atmospheres, and under these conditions most polymeric materials decompose into a limited range of organic compounds, some of which often resemble the parent polymer or its monomers.

Table 2.3 ISO classification of fire stages, based on ISO 19706[13]

Fire stage	Heat ($kW\,m^{-2}$)	Max temp (°C)		Oxygen (%)		Equivalence ratio ϕ	V_{CO}/V_{CO_2}	Combustion efficiency (%)
		Fuel	Smoke	In	Out			
Non-flaming								
1a. Self-sustained smouldering	n.a.	450–800	25–85	20	0–20	–	0.1–1	50–90
1b. Oxidative, external radiation	–	300–600		20	20	–		
1c. Anaerobic external radiation	–	100–500		0	0	–		
Well-ventilated flaming								
2. Well-ventilated flaming	0 to 60	350–650	50–500	~20	0–20	<1	<0.05	>95
Under-ventilated flaming								
3a. Low vent. room fire	0 to 30	300–600	50-500	15–20	5–10	>1	0.2–0.4	70–80
3b. Post-flashover	50 to 150	350–650	>600	<15	<5	>1	0.1–0.4	70–90

Although simple pyrolysis occurs to some extent under non-flaming conditions, the most common form of thermal decomposition occurring in fires is oxidative thermal decomposition characterised in Stage 1b.

In the presence of air, reaction with oxygen will occur on the surface of the material, and also possibly in the gas phase. In the absence of large ignition sources, oxidative pyrolysis (Stage 1b in Table 2.3) is often the precursor to flaming combustion. Initial application of heat results in a mainly endothermic pyrolysis and exothermic oxidative thermal decomposition. Oxidative thermal decomposition occurs in most materials at temperatures exceeding approximately 300 ºC.

For non-char-forming materials oxidative thermal decomposition can continue until the entire organic specimen mass has been decomposed, leaving either no residue or a residue of inorganic components or fillers if present, so that final yields are partly a function of decomposition temperature and heating time.

For char-forming materials, decomposition is a two-stage process. Initial application of heat results in a mainly endothermic pyrolysis and oxidative thermal decomposition, leaving a carbon-rich residue. For these materials stable side groups leave the main chain of the polymer, so that an open porous carbon-rich residue may be formed. This may then continue to be decomposed by exothermic oxidation in the solid phase. If the air supply is sufficient, a glowing char may be formed. This constitutes smouldering decomposition, whereby the residual carbon is oxidised mainly to carbon monoxide and carbon dioxide.

In self-sustained smouldering, which can only occur to porous materials, such as foams or other cellular structures or residues, such as the char from burning wood (Stage 1a in Table 2.3), exothermic oxidation of the porous material drives the endothermic thermal decomposition of adjacent undecomposed material, so that the overall product yields depend on the combined effects of the two processes. Another variable affecting species yields and rates of decomposition is the air supply, so that yields increase at a given temperature under well-ventilated conditions. For char formers, increased ventilation can considerably increase the specimen temperature and rate of decomposition, ultimately leading to flaming combustion.

The primary thermal decomposition products of different materials range from species related to the structure of the original material, often spanning a wide range of molecular weights, through rearrangements bearing little resemblance to the original structure, to partially and fully oxygenated products. For aliphatic materials such as polyethylene (PE) or polypropylene (PP), consisting only of carbon and hydrogen, pyrolysis in inert atmospheres produces a series of saturated and unsaturated aliphatic and aromatic hydrocarbons, which are generally non-irritant and not acutely toxic. For materials containing oxygen or other elements a wider range of products is formed, some of which may be irritant or otherwise toxicologically significant. In addition to aliphatic and

aromatic hydrocarbons, partially oxidised organic compounds are present such as carbonyl compounds, organic acids, and higher molecular weight polycyclic aromatic hydrocarbons (PAHs).

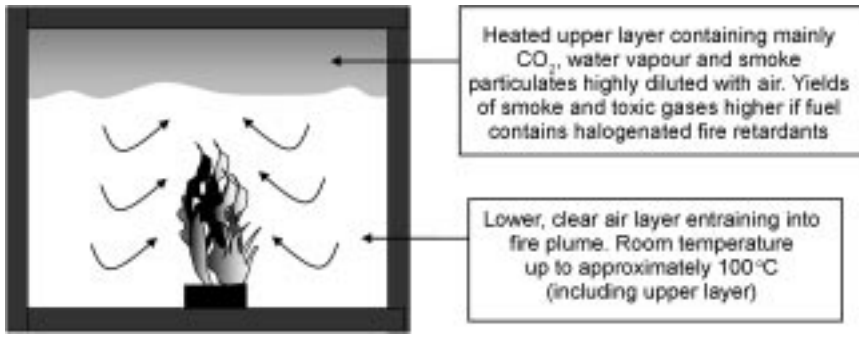
Non-flaming decomposition in air increases the yields of oxidised products. The products released with the higher yields are usually carbon monoxide and carbon dioxide, with $CO : CO_2$ mass yield ratios between approximately 1 : 1 and 1 : 3, plus a wide range of organic compounds depending partly on the material composition. These organic species are produced at relatively high yields, constituting a high proportion of the total mass loss and have been found to be highly irritant when animals are exposed to them.[14,15] They tend to be rich in partially oxidised organic species.[16] The rate of product formation and yields under non-flaming decomposition conditions generally increase with temperature and to some extent with ventilation over the fuel surface. Smouldering decomposition of char-forming materials further increases the yields of more completely oxidised species such as carbon monoxide and carbon dioxide. The decomposition chemistry of many major polymers is discussed in more detail in Chapter 14.

In general, low rates of endothermic decomposition under externally applied heating from non-flaming fires, although not rapidly hazardous, can lead to toxic concentrations of carbon monoxide and irritants developing over timescales of hours and transition to flaming may occur followed by rapid fire growth.

2.6.2 Well-ventilated (Stage 2) flaming fires

Almost all flaming fires are initially well ventilated (Stage 2 in Table 2.3), and remain so as long as the fire is small in comparison with the size and ventilation of the enclosure it is burning in. Most large-scale fire calorimeter tests, and hence most large-scale fire data, are obtained under these conditions. In early flaming fires the hot gases rising in the flame entrain air, which mixes with the fuel gases from the burning object (Fig. 2.6). The mixture of hot gases and air burn efficiently (at least in the absence of gas phase flame inhibitors), producing heat, carbon dioxide, water and small amounts of sooty smoke while yields of partially combusted fuel products such as carbon monoxide are very low. The yields for specific materials are discussed in more detail in Chapter 14. Part of the heat is fed back to decompose more fuel, so that the fire tends to grow and spreads at a rapidly increasing rate providing fuel and fresh air are freely available.

The fire effluent rises and forms a layer under the ceiling. The main hazards are from the heat radiated near the fire and from a dilute and relatively low toxicity smoke spreading to upper levels of the building. The rising plume of hot gases entrains a large mass of air into the hot flame zone which has an average temperature around 1000 ºC (but with flamelet regions at considerably higher and lower temperatures) and an equivalence ratio of less than 1 (typically



2.6 Early well-ventilated flaming fire in a small enclosed compartment ($\phi < 1$).

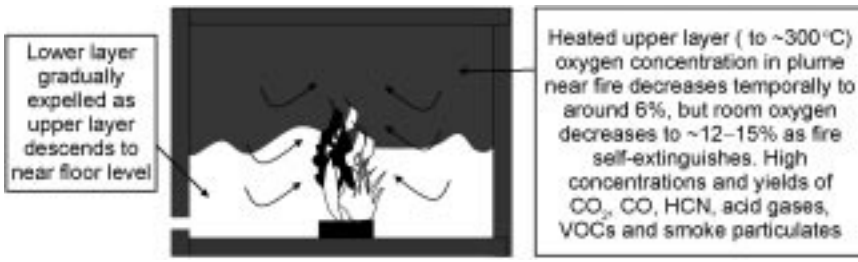
$\phi \sim 0.7$) so that combustion is very efficient. If the fire is very large, then more fuel-rich regions will exist in the heart of the plume, since oxygen cannot get to the middle of the flame, so that even fires burning in the open will involve regions of under-ventilated combustion if they are sufficiently large, with a proportion of the fuel being combusted at higher equivalence ratios. For enclosure fires, the heated products of well-ventilated combustion are diluted with plenty of air, and rise to the ceiling where they form an upper layer, which gradually fills the enclosure, from the top down. The transition from well-ventilated to under-ventilated flaming is driven by the mass of air entrained into the fire plume and the upper layer, and the rate of fuel pyrolysis. The mass of air entrained is proportional to the height to the upper layer above the base of the fire. The mass of fuel generated depends upon the volatility of the fuel, the back-radiation from the flames (or other radiation sources) and the fire area.

In large enclosures such as a warehouse, shopping centre atrium or theatre, the fire may continue to grow while remaining well ventilated for some time, especially if smoke extraction is operational. The main hazard is then from the heat of the spreading fire, and from smoke at the upper levels.

This is probably the least important stage in terms of fire toxicity. By their nature, fires at such an early stage are generally small, and will not generate sufficient quantities of effluent to cause harm, except in a very small enclosed space. During this stage both escape and extinguishment are often still possible. In addition, the smoke will rise to the ceiling away from head height. Although the yields for specific materials at this stage are discussed in more detail in Chapter 14, the toxic products from well-ventilated flaming of most non-halogenated fuels would not normally constitute a significant input into a fire hazard assessment.

2.6.3 Low ventilated (Stage 3a) fires

A characteristic of many spaces in buildings and transport vehicles is that they consist of essentially enclosed compartments with low ceilings, or a series of



2.7 Under-ventilated (vitiated) fire in enclosed compartment.

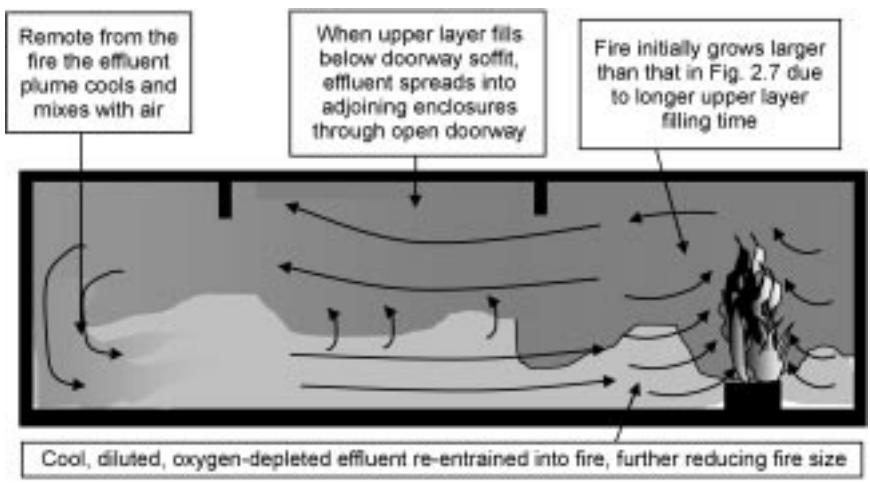
interconnected enclosures (such as an apartment with interior doors open). In such enclosures vitiated Stage 3a fires often dominate. As the fire grows the upper layer fills down until part of the flames penetrate into the upper layer as shown in Fig. 2.7. The filling time depends upon the rate of fire growth and the area (and hence the upper layer volume) of the enclosure, so that the most rapidly vitiating case is that of a small fire in a domestic-sized room. As the upper layer descends, an increasingly greater proportion of the flames is burning in the upper layer, which gradually becomes depleted in oxygen. Also, the mass of fresh air entrained into the now larger fire is reduced as the layer height decreases. The result is that the mass or air (and in particular the mass of oxygen) entrained per unit mass of fuel is decreased. The global equivalence ratio then exceeds unity and combustion becomes increasingly vitiated and inefficient. The yield of carbon dioxide (and oxides of nitrogen) decreases and the yields of other products (carbon monoxide, hydrogen cyanide, volatile organic compounds (VOCs, including oxidised organic irritants) and smoke particulates) increase. The heat of combustion of the fuel also decreases, as combustion becomes increasingly inefficient, and when the layer upper layer descends to the level of the base of the fire, the fire is extinguished. At this point the product mix in the compartment is dominated by the products of later, vitiated combustion, because the fire was larger during this stage and yields of toxic products were higher. However, especially in small enclosures, the fire may be extinguished with only moderately high concentrations of toxic gases. The oxygen concentration in the enclosure is typically between 12% and 15% at the time the fire is extinguished, depending upon the combustion properties of the burning fuels.[12]

Fires in small enclosed compartments

For fires in small enclosed compartments (as illustrated in Fig. 2.7) the filling time can be rapid, so that the fire may self-extinguish without spreading beyond the item first ignited. In such fires smoke and toxic gases usually become hazardous before heat exposure, although room temperatures can reach high levels before the fire extinguishes.

Fires in larger enclosed compartments

Figure 2.8 illustrates a typical fire in an apartment, in which the interior doors are open but exterior doors and windows closed. The fire begins well ventilated, continuing to grow as the upper layer descends below the doorway soffit, and spreads horizontally down the corridor and into associated rooms. As the upper layer fills the interior rooms beyond the fire enclosure, it continues to deepen throughout the apartment. The effluent plume cools gradually as it moves beyond the fire enclosure, partly by losing heat to the structure and partly as it mixes with cool air down to floor level, and is re-circulated into the fire enclosure. At this stage the fire becomes under-ventilated, with the global equivalence ratio exceeding one. The upper part of the flames burn in the oxygen-depleted upper layer, while the oxygen concentration of the air entering the fire in the lower layer decreases, owing to the presence of the re-circulated fire gases. In the absence of more oxygen, for example from a window breaking, the fire gradually subsides and becomes self-extinguishing as the oxygen concentrations in both the upper layer and the incoming air decrease. Although the fire may continue to burn with an oxygen concentration in the upper layer in the vicinity of the fire of 4–6%, it becomes extinguished when the oxygen concentration in the lower layer decreases to 12–15%. Fires of this type produce high yields of toxic gases, as in other fully enclosed fires. Fuels and fuel gases can be burnt at different equivalence ratios, different decomposition temperatures and different oxygen concentrations at different times and locations in the fire enclosure. In the room of origin the main hazards are from exposure to smoke and toxic gases followed closely by heat. In areas beyond the room of origin the temperatures are not usually hazardous, while the combination of smoke and toxic gases can be rapidly life-threatening.



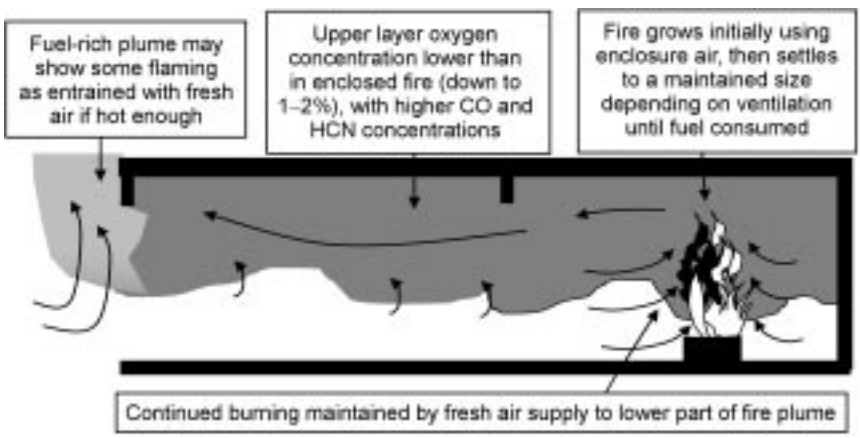
2.8 Vitiated fire in larger enclosed compartment (Type 3a).

Fire in vented compartments

Another common under-ventilated fire scenario occurs when fresh air is supplied to the lower layer, so that the fire continues to burn until the fuel is consumed. The rate of air supply to the fire, and hence the size of the fire, depends on the mass of fuel available and the size of the door or window openings. For a fire enclosure with a single open doorway, leading to a corridor with an open external door as depicted in Fig. 2.9, the fire size is limited by the size of the smallest opening (either the enclosure doorway or the external doorway). If either is small, the fire grows under well-ventilated conditions until the upper layer descends to below the level of the flames. Combustion then becomes vitiated and the layer continues to descend until equilibrium is established, from which point the fire burns at a relatively steady rate (though sometimes with dramatic oscillations) until the fuel is consumed. Under such conditions the upper layer becomes very vitiated, with very low oxygen concentrations (for example 1–2% O_2 and with CO concentrations of up to 6% and yields of 0.24 g/g from burning wood cribs).[12] Upper layer temperatures also depend upon the ventilation conditions in the range 400–700 ºC.

In under-ventilated (pre-flashover) fires there are three main regions where combustion reactions occur:

- at the interface between the fuel and the base of the flame, where fuel materials are decomposed and partially oxidised to form the gaseous fuel for the fire;
- in the lower part of the flame zone, where air and fuel gases combine to produce heat and primary products;
- in the under-ventilated hot layer in and above the upper part of the flame, where hot, partially combusted fuel gases continue to react with limited amounts of oxygen to produce high yields of toxic products.



2.9 Type 3a vitiated fire in vented apartment.

In upper layer regions more remote from the fire area, the gradual cooling and lack of oxygen result in the composition becoming more stable. With larger, hotter fires of this type more reactivity may occur at the boundary between the hot upper layer flowing out of the enclosure and fresh air entering in the lower layer. If the fire size and upper layer temperature become high enough then flashover may occur. Sudden oscillations in effluent flows or sudden changes in ventilation (for example due to failure of a window) may lead to backdraught events as rapid mixing of air and fuel-rich gases results in a sudden transient combustion of the upper layer.

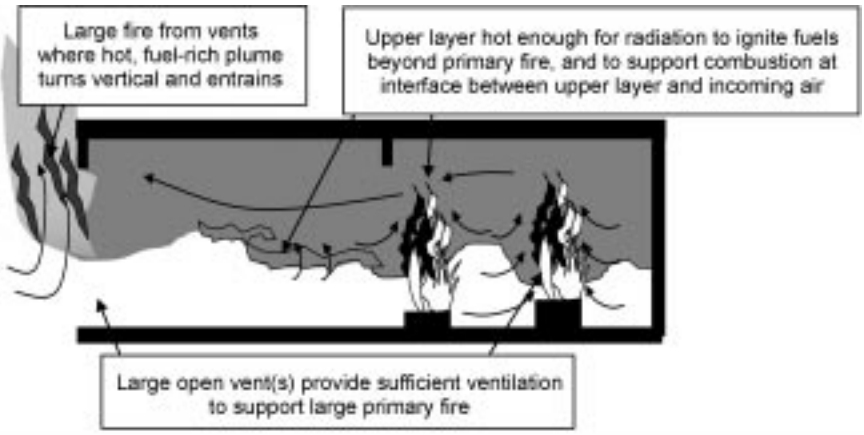
Hazards to occupants in under-ventilated fires

These fires are usually relatively small, often being limited to the item first ignited, or involving some decomposition of combustible materials at high levels in the room. Since the temperatures beyond the fire enclosure are not particularly high, the main hazard is from the inefficient combustion, which leads to high yields of asphyxiant gases (CO and HCN), and irritant smoke. Of critical importance to survivability and escape is the height of the upper layer during the period when occupant may be attempting to escape, the extent of mixing of smoke into the lower layer, and the availability of breathable air beneath it.

2.6.4 Post-flashover fires

If there is sufficient fuel available and the vents are large enough, the fire may reach flashover conditions (Stage 3b in Table 2.3), when the temperature of the hot layer is high enough to be fully reactive, and radiate heat downwards to ignite all combustible materials in the enclosure. This results in extremely rapid and widespread fire growth. The fire then becomes ventilation controlled and vitiated, producing very large amounts of hot, toxic fire effluent. Potential flashover conditions occur when the upper layer becomes sufficiently hot and reactive to support flaming combustion. This transition is characterised by flaming, red-orange streaks appearing in the hot layer. Firefighters refer to these as ‘angels’ fingers’, giving a stark reminder of the impending danger. At this point, downward radiation can ignite fuels at low level remote from the original fire. This condition is illustrated in Fig. 2.10.

The upper layer temperature required to induce flashover is approximately 500–600 ºC in the lower part of the upper layer, although considerably higher temperatures may exist in the upper layer closer to the ceiling and closer to the fire. For fully furnished rooms and similar compartments there is more fuel gas produced than air available for complete combustion, so the combustion conditions in flashed-over fires are under-ventilated. The main differences between pre-flashover and post-flashover are the size of the fire, the existence of higher



2.10 Under-ventilated post-flashover fire.

temperatures in some regions, and very low upper layer oxygen concentrations, around 1%. The combination of a very hot fuel-rich upper layer flowing away from the fire and fresh air flowing towards it in the lower layer can cause flaming at the interface between the two layers as some mixing occurs. In such circumstances, flame spread can be extremely rapid. As the effluent in the upper layer flows horizontally away from the fire, the plume gradually cools and combustion reactions cease. These conditions also favour the formation of very high yields of asphyxiant gases, particularly carbon monoxide and hydrogen cyanide, as well as irritant gases and smoke. Thus the flashed-over enclosure provides a massive amount of very hot, toxic smoke which pours out, filling building spaces with a lethal atmosphere.

Where the hot upper layer leaves the fire enclosure through windows or doorways it rises vertically and entrains air. If the plume temperature is high enough the mixed air and fuel-rich plume may form a secondary flame, remote from the original fire. Since this secondary fire is in a well-ventilated situation, the combustion tends to be efficient, so that more heat is released and the effluent is consumed to form high yields of carbon dioxide, with the yields of carbon monoxide and hydrogen cyanide decreasing as they are consumed in the secondary fire.

2.6.5 Fire stages associated with deaths in fires

A subject of some discussion is the extent to which building fire fatalities in different countries can be attributed to pre-flashover or post-flashover fires. This may depend partly upon how fire statistics are collected and interpreted, and partly upon building and living styles in different countries. As described in the previous sections, relatively small (pre-flashover) fires in enclosed buildings can

rapidly become under-ventilated and fill open areas with a lethal fire effluent. A proportion of building occupants (both in the room of origin and beyond) can be incapacitated and then die during this stage of a fire. However, particularly when a number of occupants are present in different locations, it is common for exterior doors and windows to be opened during an incident, either by occupants or rescuers from outside, resulting in rapid fire growth sometimes leading to flashover. Alternatively, depending upon the method of construction, fire may involve the fabric of a building, resulting in a large fire. An issue is then the extent to which the occupants in different locations are commonly overcome during the pre-flashover stage, or following the later transition to flashover.

In the UK, and probably across Europe, where rooms and buildings tend to be smaller with less open layouts, and masonry construction is used, most fire deaths result from relatively small fires confined to the room of fire origin, but with spread of toxic smoke to other areas. Thus for approximately 70% of fatal fires in dwellings in the UK, the fire has not spread beyond the room of fire origin.[17] Just over half of fire deaths (55% in 2002 in the UK) occur in the room of fire origin with the remainder in another room on the same floor or another floor. Conversely in the US only 21% of fire deaths occur in the room of origin of the fire, and 67% occur on another floor.[18] Thus in the UK flashover fires are not the major cause of fire fatalities, whereas in the US it is believed that 80% of fire deaths could be avoided if flashover could be prevented. In general the conditions to enable flashover rarely occur when exterior doors and windows are closed, even in large rooms or open plan areas, but are likely if either two reasonably large windows or one door are fully opened. In major fire disasters involving large numbers of building occupants in large buildings, flashover conditions have tended to occur in some areas before all occupants have evacuated, so that deaths have been attributed to the post-flashover stage.

In all cases the main cause of deaths beyond the room of fire origin is exposure to toxic smoke.

2.7 Conclusions

The classification of different fire stages show that fire hazards, and particularly the toxic hazards, depend upon the combustion conditions. In buildings, the majority of fires that are hazardous to life are likely to involve vitiated flaming combustion, either pre- or post-flashover. Since in the UK the majority of injuries and deaths from fire occur in domestic dwellings (77%), most deaths can be attributed to pre-flashover vitiated combustion. However the greatest numbers of deaths from large multi-fatality fires are usually attributable to post-flashover vitiated conditions. In both pre-flashover and post-flashover fires the yields of toxic products are high, and the main cause of incapacitation and death for most victims is exposure to toxic fire effluents.

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3

Hazards from smoke and irritants

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Abstract: This chapter reviews the available data on the effects of irritants. It also considers the similarities and differences between the effects of irritants on humans and different animal species together with their implications for the prediction of effects on human fire victims. Different calculation models are given for prediction of time to escape impairment and incapacitation, effects on movement speed and time to inhalation of potentially fatal exposure doses.

Key words: smoke, sensory irritants, lung oedema and inflammation, escape behaviour, walking speed, respiratory rate depression, hydrogen chloride, CS gas.

3.1 Introduction

Irritant smoke presents major hazards to fire victims during the early stages of fire incidents, and some hours after an incident for people surviving the immediate fire exposure. Although not directly life threatening during a fire, exposure results in behavioural and physiological effects impairing escape capability and causing incapacitation. This often delays or prevents escape until conditions become lethal, owing to the effects of asphyxiant gases or heat. Smoke impairs escape behaviours and capability because of direct effects on visibility and walking speeds while smoke irritants augment these effects by causing immediate pain to the eyes and respiratory tract, accompanied by reflex responses, including eye closure and breathing difficulties. During exposure, an increasing dose of irritants is inhaled, which can lead to the development of lung injury involving oedema and inflammation, usually several hours after exposure. The severity of lung injury and the probability of death increase with the exposure dose.

Fire hazard analysis involves calculation of available safe escape time (ASET) and required safe escape time (RSET). The time during a fire when irritant smoke impairs escape or causes incapacitation represents an ASET tenability end point. Irritant smoke also affects RSET calculations due to effects on escape behaviours and walking speeds.

This chapter reviews the available data on the effects of irritants, which have been obtained from human exposures in fire incidents, industrial accidents, and

experimental studies of humans, other primates and rodents. Consideration is then given to the application of these data to the development of calculation models for prediction of time to escape impairment and incapacitation, effects on movement speed and time to inhalation of potentially fatal exposure doses. The applicability of different types of calculation models is discussed, including models based simply on exposure concentration, models involving $C^n t$ exposure dose concepts, and models involving dynamic uptake–removal/detoxification mechanisms. Similarities and differences between the effects of irritants on humans and different animal species are also considered and their implications for the prediction of effects on human fire victims.

3.2 Hazard assessment issues in relation to smoke and irritants

A major design requirement for any occupied enclosure (such as a building or transport vehicle) is to ensure that occupants are able to escape safely in case of fire. The main cause of injury and death in fires is exposure to toxic fire effluent (smoke and gases), while the next most important cause is exposure to heat. It is therefore necessary to ensure that, in the event of a fire, the conditions are such that occupants are able to escape before they are overcome by toxic smoke or heat. This is a regulatory performance requirement in the UK Building Regulations.

Requirement B1 of Schedule 1 to the Building Regulations 2000[1] states that 'The building shall be designed and constructed so that there are appropriate provisions for the early warning of fire, and appropriate means of escape in case of fire from the building to a place of safety outside the building capable of being safely and effectively used at all material times'. Fire hazard and fire safety depend upon the outcome of two parallel timelines: ASET, which is the time from ignition of the fire to the development of incapacitating conditions, and RSET, which is the time required for occupants to reach a place of safety.[2–4]

In carrying out a fire hazard assessment, it is important to consider any effects of fire effluent that might impair escape capability of increase escape time (for example by slowing walking speed). It is also necessary to determine any effects of fire effluent that might prevent escape or cause incapacitation. As discussed in Chapters 8 and 14, the components of fire effluent affecting escape and tenability are optical obscuration by smoke particulates, irritants and asphyxiant gases. The effects of smoke and irritants are considered in this chapter, while those of asphyxiant gases are considered in Chapter 4.

3.3 Effects of smoke obscuration and irritancy on escape and tenability

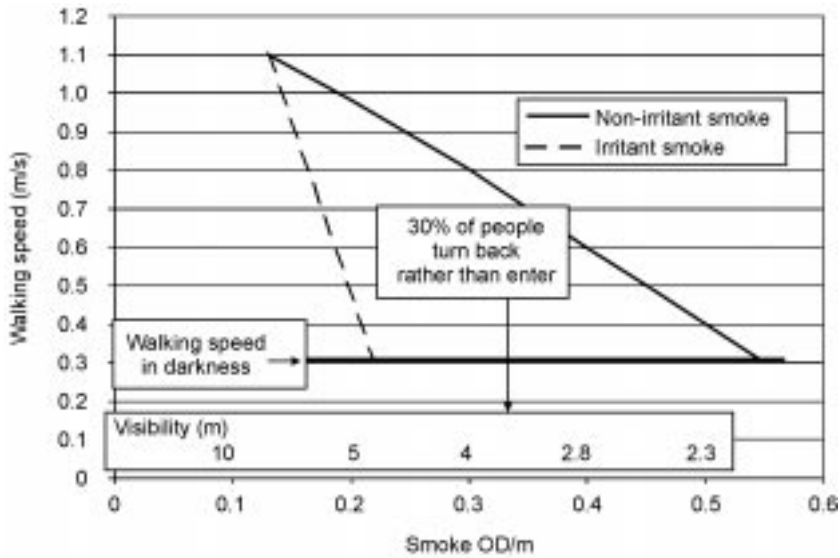
A primary concern with respect to smoke is the hazard presented by optical obscuration. All smoke is optically obscure to an extent depending mainly on the

concentration of smoke particles, but also on the particle size distribution and to some extent also the colour of the smoke. White smoke has a greater effect than black smoke, because in addition to the direct obscuration effects, light is scattered by white smoke particles. Some smokes have negligible toxicity, in which case the only hazards are from optical obscuration. This applies to some extent to the dry, carbonaceous soot particles evolved from some well-ventilated flaming fires, and to fogs of water vapour droplets. The hazards from such non-irritant smokes are predominantly behavioural and sensory.[5,6]

Purely behavioural effects occur when a building occupant sees smoke but is not immersed in it. For example a hotel room occupant might be in clear air in a room, but in response to a fire alarm finds the corridor smoke-logged. The occupant then has to decide whether to close the door and take refuge in the room, or to enter the smoke and attempt escape via the corridor. If the occupant decides to remain in the room they are effectively 'incapacitated', in that they do not escape. In some real-fire incidents room occupants have remained in safety until the fire was extinguished and were then able to escape, while in other cases they have died when the room later became filled with fire effluent.[7] In other incidents they have decided to enter the smoke, and have subsequently escaped or died from toxic smoke exposure while attempting to escape. If an enclosure or building has several exits or escape routes and one becomes smoke-logged, then occupants can be expected to use the unobstructed exits. In this context the smoke affects RSET, since the time required for occupants to escape depends upon the aggregate flow capacity of the available exits. For this reason it is normal practice to discount the largest exit (i.e. assume it will be unavailable) when calculating the design exit capacity for buildings.[1]

The decision on whether or not to attempt escape through smoke depends partly on the smoke density. People are more likely to attempt escape through thin smoke than dense smoke. From the studies of Wood in the UK[8] and Bryan in the US[9,10] around 30% of people were found to turn back rather than continue through smoke-logged areas, and the average smoke density at which people turned back was at a 'visibility' distance of 3 metres (0.33 optical density (OD)/m, extinction coefficient 0.76). The decision on whether to enter smoke also depends upon other aspects of the fire scenario. For example if a hotel occupant wakes in the night to find the room becoming smoke-logged, it is reasonable to assume that they are more likely to attempt escape. If a person hears an alarm and in addition, sees or smells a small amount of smoke contamination, they are more likely to attempt escape than if they hear an alarm alone.[11]

When occupants become immersed in smoke, behavioural, sensory and physiological effects occur. As with the previous situation, an occupant has to decide whether to continue to escape through the smoke, or to turn back and seek refuge in a less contaminated area. If they decide to continue, their ability to find their way to an exit depends upon the smoke density and irritancy, and



3.1 Relationships between smoke optical density, walking speed and behaviour for non-irritant and irritant smoke.[5,8,9,12,13]

other factors such as the size of the enclosure. In addition, their ability to move depends upon the visibility of their surroundings.

Since smoke is denser near ceilings, an early effect of fires is to reduce the overall illumination within a building. For subjects immersed in smoke, their ability to see nearby objects depends upon the smoke density and residual illumination. Experiments on people walking through non-irritant smoke have demonstrated a relationship between walking speed and smoke optical density as shown in Fig. 3.1.[12] This relationship can be used for RSET calculations of evacuation times for building occupants moving in smoke. As the figure shows, at an OD of around 0.55 (visibility approximately 2 metres) people's behaviour changes from normal (but slow) walking, to moving as if in complete darkness, feeling their way along the walls with their hands. Moving in an unfamiliar building in this situation can be very difficult, because the occupant cannot see what obstacles or hazards may be in front of them.

For these reasons it is considered advisable to set limits on smoke obscuration for design purposes. A problem is that there are no obvious absolute tenability limits to set, since the effects on occupants depend on the individuals involved, and the details of the situation they find themselves in. The overall consequences for escape capability are probabilistic, and the detail is missing. One possible approach would be to set a requirement for zero smoke exposure. This is used in practice for design situations such as shopping malls with smoke extraction, where smoke layering is predicted. A common requirement is that the height of the smoke layer above the floor should never be less than 2.5 m, so that

occupants can escape in safety beneath the smoke layer. However, in many fire scenarios in buildings it can be predicted that some smoke exposure is likely to occur. If a zero exposure criterion is applied, then even trivial levels of smoke contamination (for example from a piece of burned toast) could be deemed unacceptable. Alternatively it could be argued that for non-toxic smoke, no design limit is required, since even dense smoke is not directly injurious. This is unacceptable because, as stated, smoke can definitely delay or prevent escape for an extended period, during which fire conditions may become life threatening.

For a situation such as this, the best approach is to consider all the available evidence, from studies of actual incidents and the limited experimental data available, and decide on reasonably practical limits enabling the design of usable buildings while providing an acceptable level of risk. On this basis the smoke tenability limits shown in Table 3.1 have been proposed.[3–5]

A further complication is that smoke from building fires contains irritants, which exert a range of physiological effects on an escaping occupant. Unfortunately experimental data regarding effects on escape capability are more limited than for non-irritant smoke. As for non-irritant smoke, the best approach is to estimate likely effects and set tenability limits based upon such information as is available from a variety of sources as discussed in Chapter 8, including fire incident reports, reports of industrial accidents involving irritant gases, and experimental studies of the effects of individual irritant gases and fire effluent mixtures using humans and a variety of animal species. One set of experimental results on an irritant smoke exists from the work of Jin,[12] as illustrated in Fig. 3.1. In addition to measurements of walking speed in non-irritant smoke, other experiments involved exposure of volunteers to smoke generated from smouldering wood chips decomposed using a bee smoker. Measurements of the smoke OD were made, but no data are available on the composition of the smoke. However, it can be concluded that wood decomposed in this manner involved an element of non-flaming oxidative thermal decomposition, which has been found to produce an effluent mixture containing relatively high yields of partially oxidised organic irritants, and smoke from non-flaming decomposition of wood has been found to be very irritant to exposed primates (see Chapter 8).[5,14] The effects of exposure to this irritant smoke were that for a given smoke OD, the decrease in walking speed was considerably greater than for the non-irritant smoke.[12]

Smoke from building fires is likely to be at least moderately irritant,[11] so based upon these findings, and those regarding smoke densities at which people turned back in incidents, the generic design tenability limits shown in Table 3.1 have been developed. For large public buildings it is considered that occupants may need to be able to see for at least 10 metres in order to find an escape route or exit, and may need to travel some distance to a protected escape route, so a design tenability limit of 10 metres visibility (OD/m 0.08) has been proposed.

Table 3.1 Smoke tenability limits

Smoke density and irritancy OD/m (extinction coefficient)	Approximate visibility diffuse illumination	Reported effects
None	Unaffected	Walking speed 1.2 m/s
0.5 (1.15) non-irritant	2 m	Walking speed 0.3 m/s
0.2 (0.5) irritant	reduced	Walking speed 0.3 m/s
0.33 (0.76) mixed	3 m approx.	30% people turn back rather than enter
Suggested tenability limits for buildings with:		
– small enclosures and travel distances;		OD/m = 0.2 α_k 0.5 (visibility 5 m) *
– large enclosures and travel distances.		OD/m = 0.08 α_k 0.18 (visibility 10 m) *

* Where OD/m is $\log_{10}$ (I_0/I), which is the logarithm to the base 10 of the ratio of the intensities of light transmitted over a path length of 1 m from a light source to a receiver in the absence (I_0) and presence (I) of smoke, respectively. The light extinction coefficient α_k is the natural logarithm of the ratio: ln (I_0/I).
For situations where smoke is expressed in terms of particulate mass concentration, these equate to approximately 0.7 and 0.3 g particulates/m^3 respectively (where particulates g/m^3 $\sim$ 0.356 $\times$ OD/m).

Since the concentration of toxic asphyxiant gases correlates in general with smoke density, such a limit has the added advantage that at this smoke concentration the concentrations of other toxic products are likely to be too low to present a significant hazard over timescales of up to an hour or more. For domestic dwellings, where travel distances to the exits are small and occupants are likely to be familiar with the layout, a visibility distance limit of 5 metres is proposed. Although escape speed may be low in irritant smoke, it is considered that occupants should be able to escape within a few minutes providing this limit is not exceeded.[3]

For a performance-based design case, it would be possible to calculate ASET and RSET for a specific fire scenario to determine if escape should be possible before conditions deteriorate to dangerous levels. For the RSET calculation of travel speed, use can be made of Equations 3.1 and 3.2 (for non-irritant and irritant smoke), which are derived from the data in Fig. 3.1:

$$\text{Walking speed in non-irritant smoke (m/s)} = 1.36 - 1.9 \times \text{smoke optical density (OD/m)} \quad 3.1$$

$$\text{Walking speed in irritant smoke (m/s)} = 2.27 - 9 \times \text{smoke optical density (OD/m)} \quad 3.2$$

These generic expressions and tenability limits may be useful for design purposes, but a further problem with respect to smoke irritancy is the effluent

composition, in terms of the number of irritant chemical species present and their concentrations, which can vary considerably with material and combustion conditions (see Chapters 8 and 14). To assess these hazards it is necessary to predict the toxic (physiological and pathological) effects of each individual irritant chemical species and the mixtures present in different fire effluent atmospheres.

The remainder of this chapter is devoted to consideration of the physiological and pathological effects of irritants in fire effluents and methods for evaluating effects on escaping building occupants.

3.4 Why irritants are an important aspect of fire hazard

- Although asphyxiant gases such as carbon monoxide and hydrogen cyanide and heat are the main ultimate causes of death during and after fires, as stated in the previous section, any aspect of fire effluent that impedes or prevents escape increases the probability that building occupants will remain long enough at the fire scene to encounter fatal conditions.
- Irritants occurring in fire effluents have two main effects, one of which (painful sensory irritation) occurs very rapidly on exposure, during the critical escape 'window', while the second (lung inflammation) occurs over a longer timescale.
- Studies of fire incidents have demonstrated that smoke exposure impedes or prevents escape during fires, and that smoke is usually irritant. In some cases smoke irritancy is described as a specific problem, especially when acid gases are present (for example during electrical fires).
- Common experience of brief human exposure to smoke from sources such as garden bonfires, or barbeques, or to 'sidestream' cigarette smoke (direct exposure to the smoke plume rising from a cigarette when not being puffed) reveals how painfully irritant it is to the eyes and nose, and that the pain causes temporary incapacitation, which will clearly affect travel through the escape routes of a building filled with an irritant smoke.
- Jin's experiments,[12] described in the previous section, demonstrate how walking speed through irritant smoke is much slower than through non-irritant smoke of a similar optical density.
- A number of individual irritant gases occurring in fire effluents are known to cause painful and incapacitating irritancy in industrial exposures and accidents.
- One particular irritant, CS riot control gas (*ortho*-chlorobenzylidene malonitrile), is used specifically in order to incapacitate people at potency levels comparable with those of irritants in fire effluent mixtures.
- Exposure to irritant fire effluents during a fire can lead to fatal lung damage over periods of several hours to days after exposure, or permanent lung

damage in survivors. The main fatal effects are lung inflammation and oedema, bronchiolitis obliterans and bronchopneumonia.[15–18]

3.5 Range of irritant effects and importance of concentration and exposure dose

Irritants affect mainly the cornea of the eyes and the respiratory tract (although skin damp with perspiration is also affected). The physiological and pathological effects of exposure depend upon the extent of exposure at different sites and the normal structure and function of each area affected. The different effects are summarised in Table 3.2, with a comment on the extent to which they are rapidly or slowly developing. The sites of deposition and action of irritants depend upon their physical form and chemical properties. Water-soluble acid gases dissolve preferentially in the fluid or mucous films on the eye corona and upper respiratory tract. Depending upon the proportion removed from an inhaled breath in the upper airways there is also a variable degree of penetration into the lower airways as far as the alveolar region of the lungs. The extent of penetration depends upon the aqueous solubility of the irritant, particle size distribution of the soot and the respiratory physiology and morphology of the respiratory tract, which vary among different species. In all animals, irritants with a relatively low aqueous solubility such as nitrogen dioxide, or carbonyl chloride (phosgene) mainly affect the deep lung, causing lung oedema and inflammation, with relatively minor effects on the upper respiratory tract or eyes. Gases with a high aqueous solubility, such as hydrogen chloride, initially affect the eyes and upper respiratory tract, but in primates and humans,[19] they penetrate more readily into the deep lung than they do in rodents. Other properties such as lipid solubility can also be important. In fire effluents, inorganic and organic irritants are often adsorbed onto the surface of smoke particulates, or present in droplet form. In this case the extent of deposition at different sites and penetration into the lung depends upon the particle size distribution. Fire effluent aerosols contain a high proportion of small particles capable of penetration into the deep lung (0.5–2 μm diameter),[20] and in some cases ultrafine particles capable of penetration into the lung interstitium (see section on polytetrafluorethylene and fluorocarbons in Chapter 8).[21]

Fire effluent mixtures (especially those from non-flaming oxidative decomposition and those containing acid gases) are often potent sensory irritants,[22–24] as are individual irritant species contained in them, including acid gases such as hydrogen halides and organics such as acrolein and formaldehyde.[19] The initial effect, occurring within a few seconds of exposure, is stimulation of the trigeminal nerve irritant (nociceptive) receptors on the cornea, nose and mouth, causing a sensation of irritation or burning pain depending mainly on the exposure concentration.[19,25,26] In addition to the immediate sensation produced, stimulation of these receptors activates a set of reflexes and the gradual release of inflammatory mediators. In the eyes, a rapidly reacting reflex is eye closure (blepharospasm). In

Table 3.2 Effects of irritants on different target sites in the eye and respiratory tract

Target site	Tissue affected	Primary target	Effects	Concentration/dose relationship
Eyes	Cornea	Stimulation of trigeminal nerve pain receptors, followed by corrosive damage to corneal epithelium	1 Sensation ranging from mild irritation to intense pain 2 Blepharospasm (involuntary reflex eye closure) 3 Tearing 4 Difficulty seeing 5 Ocular opacity and ulceration	1–4 Rapidly developing (almost immediate at high concentrations) mainly concentration-related 5 Slower developing (minutes–hours) more dose-related
Upper respiratory tract (nose, mouth, throat-larynx)	Stratified squamous, ciliated respiratory and olfactory epithelium	Stimulation of trigeminal nerve pain receptors, followed by corrosive damage to epithelium, stasis then loss of cilia	1 Sensation ranging from mild irritation to intense burning pain 2 Reflex slow breathing with pause at end inspiration (brief breath holding) (duration depending on animal species and chemical species) 3 Coughing 4 Copious mucus secretion 5 Inflammation and soreness	1–2 Rapidly developing (almost immediate at high concentrations) mainly concentration-related 3–4 Rapidly developing $<$ 1 minute, but increasing with exposure 5 Slower developing (minutes–hours) dose-related
Main airways, trachea, bronchi	Ciliated columnar epithelium	Stimulation of vagal nerve receptors, stimulation of submucosal glands and goblet cells, followed by corrosive damage to epithelium, loss of cilia	1 Sensation ranging from mild irritation to intense burning pain in chest 2 Bronchoconstriction, breathlessness, breathing difficulty 3 Development of rapid breathing (after end of period of slow breathing) after approximately 10 seconds to minutes depending on animal species and chemical species 4 Acute bronchitis and pneumonia	1–3 Rapidly developing $<$ 1 minute, but increasing with exposure 4 Slower developing (minutes–hours–days) dose-related

Table 3.2 Continued

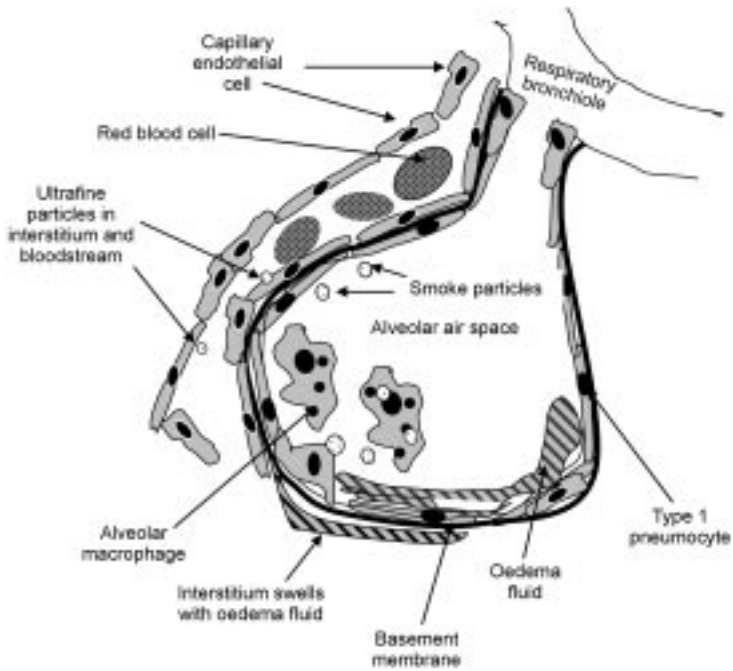
Target site	Tissue affected	Primary target	Effects	Concentration/dose relationship
Bronchioles	Ciliated columnar to cubical epithelium	Corrosive damage with inflammation, development of bronchiolitis obliterans	1 Bronchiolar constriction, breathlessness, breathing difficulty 2 Inflammation and development of brochiolitis	1 Rapidly developing $<\sim$ 1 minute, but increasing with exposure 2 Slow development (hours–days) dose-related
Alveoli	Thin respiratory epithelium, type 1 and type 2 pneumocytes, Clara cells	Corrosive damage starting with oedema followed by inflammation, of interstitium	1 Oedema 2 Inflammation, atelectasis 3 Congestion 4 Pneumonitis	1 Slow development (several hours) dose-related 2–4 Gradual development of other signs (hours–days) dose related

the upper respiratory tract a pattern of slowed breathing occurs, characterised by breath holding at end inspiration between successive breaths. This reflex occurs in all mammals, but is especially well developed in rodents.

Where there is significant penetration of irritants into the airways (large and small bronchi and bronchioles), stimulation of vagal nociceptors occurs. This results in chest pain and activation of further reflexes including coughing (particularly through stimulation of the larynx), and a gradually developing hyperventilation accompanied by bronchoconstriction.[5,22]

In both the upper and lower respiratory tracts, acute exposure to irritants also results in mucus secretion, over a timescale of a minute or so to several hours. Eye exposure results in lachrymation, occurring within a 30 seconds to a minute or so. Where the irritant is corrosive or cytotoxic, tissue damage can occur including corneal opacities in the eyes and ulceration of the cornea and airways.

For irritants penetrating into the deep lung, oedema can begin to occur within a few tens of minutes, but often peaks within a period of 3–4 hours after exposure, accompanied by inflammation, developing over a period of 24 hours or so. In animals and people surviving immediate exposure to heat and asphyxiant gases in fires, lung oedema and inflammation are a major subsequent cause of death. The effects of oedema are swelling of the alveolar interstitium and release of fluid into the alveolar lumen (Fig. 3.2). These result in



3.2 Alveolus and capillary showing site of interstitial and luminal oedema.

lengthening of the diffusion path for gases into and out of the blood, thereby impairing respiratory gas exchange. They also disrupt pulmonary surfactant and alter the mechanical properties of the lung, which further impairs breathing and gas exchange. Because the alveolar lining cells (type 1 pneumocytes) are so thin and delicate they are especially vulnerable to toxic gases and particulates penetrating to this level. The development of oedema is accompanied and followed by inflammation of airway and alveolar tissues with infiltration of inflammatory cells. The development of lung oedema may also be complicated by direct thermal injury to the respiratory tract, or secondary to body surface burns (shock lung).

In human fire victims this can also be associated with, or followed by, a fatal bronchopneumonia. Another serious and sometimes fatal condition arises from inflammation and swelling of the lining of the terminal bronchioles, resulting in complete occlusion (bronchiolitis obliterans) which prevents air exchange in the alveoli leading to suffocation. This may develop over a period of several days or more.[16–18]

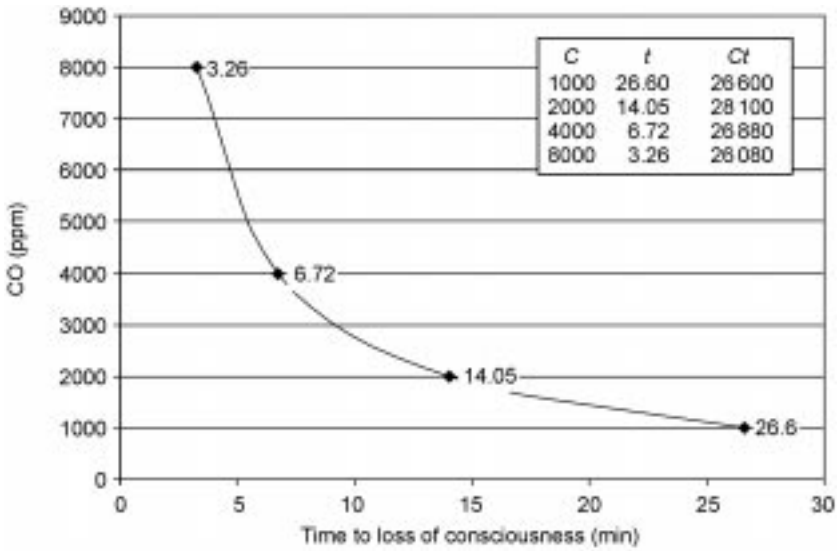
3.6 Concentration and dose–response relationships

3.6.1 Concentration–dose relationships and toxicity mechanisms

An important consideration with respect to the effects of all toxic fire gases is the extent to which their physiological and pathological effects depend upon the concentration rather than the dose of the toxicants, which dictates the calculation models for time to incapacitation, and for setting tenability limits for different exposure times. The simplest situation is that when the rate of uptake of the toxic species is constant, the inhaled dose remains relatively stable in the body. A recognisable toxic end point is reached when a specific exposure dose has been inhaled, irrespective of whether the exposure is to a high concentration of the agent for a short time or an equivalent exposure to a lower concentration for a longer time. Toxic species showing this characteristic are said to comply with Haber's rule.[5,27] For this simple approach exposure dose (k) is expressed as the product of exposure concentration (c) and exposure time (t) so that for any specific toxic end point:

$$C \times t = K \qquad 3.3$$

An example of some experimental data showing agreement with Haber's rule for a specific set of exposure concentrations and exposure times is presented in Fig. 3.3, which shows time to loss of consciousness for active primates exposed to carbon monoxide for periods of up to 30 min. On the resulting hyperbolic curve the Ct product exposure dose for loss of consciousness for each exposure concentration is approximately constant at 27 000 ppm min.



3.3 Example of a toxicological end-point following Haber's rule (loss of consciousness in active primates exposed to carbon monoxide at high concentrations for short periods of up to 30 minutes), showing a constant *Ct* product in the box.

This simple model seems to work reasonably well for the lethal exposure doses (LCt_{50}) of the common irritant gases occurring in fire effluents, for which death in rats occurs mainly due to lung oedema and inflammation after a given exposure dose has been inhaled (for exposure durations from around 10 min to 4 h). Dose–response curves for lung irritation also tend to be relatively steep, so that only relatively minor signs are observed up to a critical lethal dose threshold,[22] and when groups of animals are exposed deaths occur over a narrow dose range.[28] For example the lethal toxicity of hydrogen chloride (LCt_{50} (HCl)) in rats is approximately 114 000 ppm min over a range of exposure periods.

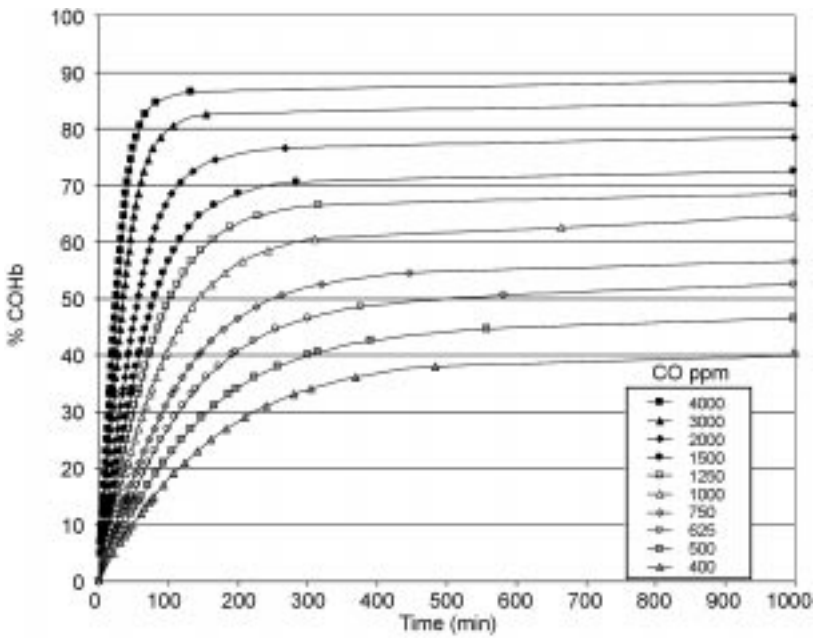
In practice, although the lethal exposure doses of some gases fit this simple model, others deviate significantly from it. For the acute lethal effects of fire gases, the most common form of deviation is that short exposures to high concentrations are more toxic than longer exposures to lower concentrations.[29,30] In such cases the *Ct* exposure doses required for an end point such as death are lower for short exposures than for long exposures. This can occur for a number of reasons; the agent is both inhaled and excreted via the lungs, so that over a period of time the actual dose entering the body each minute decreases as equilibrium is reached; the agent is metabolised and detoxified in the body; or for something stimulating a nociceptor, that the receptor response is in equilibrium. In all such cases, although the nominal *Ct* exposure dose increases linearly with time during an exposure to any particular exposure concentration, the actual dose or concentration at the site of action in the body increases at a

diminishing rate until equilibrium is reached. For the lethal effects of irritant gases, this effect can be compensated for to some extent, in that $C^n t$ can sometimes give a more or less constant value over a useful set of time periods.[29,30]

$$C^n t = k \tag{3.4}$$

Ten Berge *et al.*[30] found that for HCl $n = \sim 1$ so that a reasonable fit is given by the basic $Ct = k$.

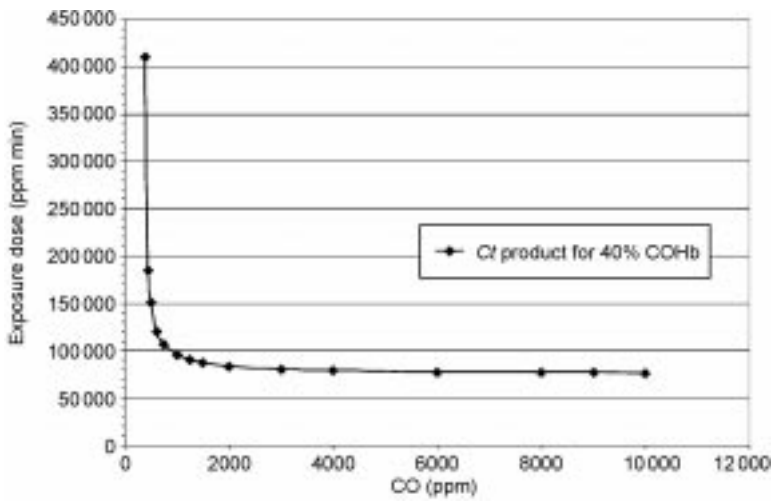
Although it is not an irritant gas, carbon monoxide provides a good example of how these fits and deviations from Haber's rule can occur. The uptake of carbon monoxide into the body can be measured accurately, since most of it remains in the blood in the form of carboxyhaemoglibin, so that the concentration of carboxyhaemoglobin (%COHb) provides a measure of the actual dose in the body at any point in time. The uptake of carbon monoxide in humans has been studied extensively, so that accurate uptake calculation models (the Coburn Foster Kane (CFK) equation) have been developed enabling the %COHb with time in a human subject to be calculated for any given concentration of carbon monoxide inhaled.[31,32] Figure 3.4 shows calculated uptake curves for different carbon monoxide concentrations for a 70 kg man at rest breathing 10 litres of air per minute.



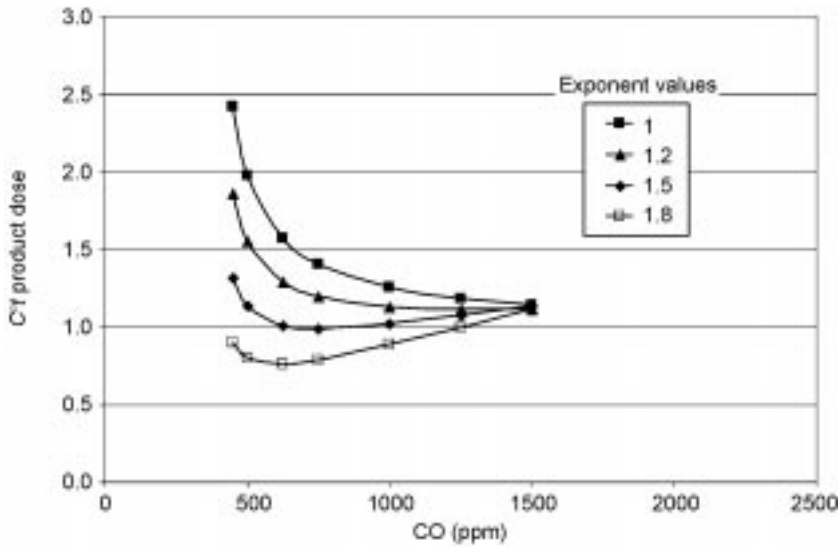
3.4 Uptake curves showing %COHb with time for different inhaled carbon monoxide concentrations for a 70 kg man at rest (calculated using the CFK equation).[31]

In this case the critical end point of interest is a carbon monoxide dose represented by 40% COHb, which is a blood concentration at which incapacitation (loss of consciousness) is predicted in a person at rest. Owing to the high affinity of haemoglobin for carbon monoxide, a certain time is required for an equilibrium to be set up between the concentration of carbon monoxide inhaled and the concentration of free carbon monoxide in the blood, bringing the inhaled and excreted carbon monoxide in the lung into balance so that no further increase in body dose or blood carboxyhaemoglobin concentration occurs. As Fig. 3.4 illustrates, when the inhaled carbon monoxide concentration is well in excess of the equilibrium concentration (which for 40%COHb is 400 ppm carbon monoxide) the rate of uptake at different CO concentrations is approximately linear up to around 40% COHb. The result is that the exposure dose to incapacitation can be represented in terms of Haber's rule as a simple *Ct* product dose without incurring significant error. Figure 3.5 shows a plot of the *Ct* product doses for 40% COHb for the different exposure concentrations in Fig. 3.4. Above approximately 2000 ppm carbon monoxide the *Ct* product is constant at approximately 78 500 ppm min, but at lower inhaled concentrations, closer to the equilibrium concentrations, the uptake becomes non-linear soon after the beginning of the exposure, so that the *Ct* product deviates increasingly from a constant value, especially at concentrations approaching 400 ppm.

Figure 3.6 illustrates an attempt to fit a $C^n t$ model to the data over the range 500–1500 ppm. The data are normalised so that a perfect fit would provide a horizontal line with an ordinate value of 1. The results show that over this range the best fit is given by a model of $C^{1.5} t = k$, although outside this range significant deviations from this model occur.

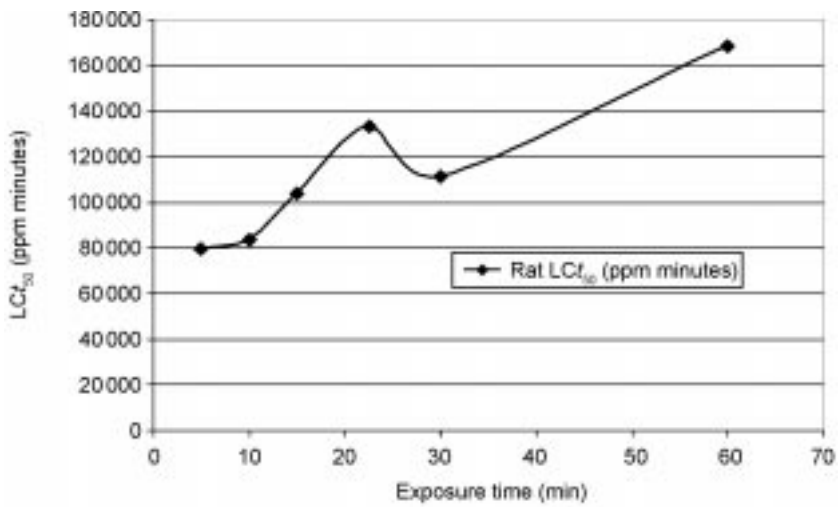


3.5 Ct product carbon monoxide exposure doses to produce 40% COHb plotted from the data in Fig. 3.4.

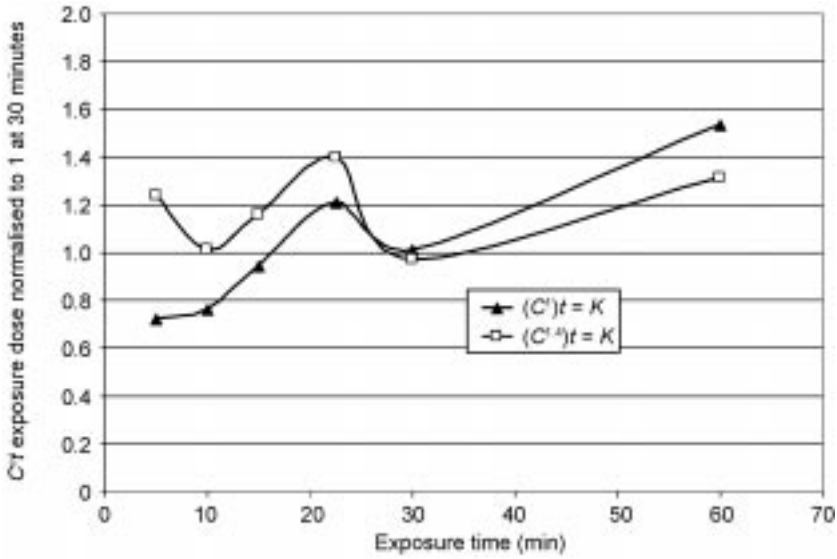


3.6 Fitting $C^n t$ exposure dose models to carbon monoxide uptake data between 450 and 1500 ppm.

Although the lethal exposure dose for hydrogen chloride in rats is regarded as approximately following Haber's rule this is not strictly the case for exposure times common in relation to fires as illustrated in Fig. 3.7, which shows data from Hartzell *et al.*,[28] on the LCt_{50} for hydrogen chloride in rats for different exposure times of from 5 to 30 minutes (plus 14 days post-exposure observation



3.7 *Ct* exposure doses for lethality of HCl in rats for different exposure times. A perfect fit would provide a horizontal line.



3.8 Comparison of normalised Ct and $C^{1.4}t$ exposure dose models for HCl in rats. A perfect fit would provide a horizontal line at an ordinate value of 1.

period). The LCt_{50} for 60 min exposures is approximately twice that for a 5 min exposure. As shown in Fig. 3.8, somewhat better fit is given by $C^{1.4}t = k$. Overall it seems that for the acute lethal effects of irritants on the lung the $Ct = k$ model is reasonable, and an average value for hydrogen chloride over the times measured is approximately 114 000 ppm min.

When considering sensory irritation the situation is somewhat different. As stated, sensory irritant effects tend to be more concentration-related than dose-related, which is to be expected considering the sensory process. Sense organs are designed to provide rapid information to the brain on the presence and intensity of any stimulus. The sensory receptor response is a more or less immediate nerve firing in response to a stimulus (within a few milliseconds), with the strength of the response (nerve firing rate) being proportional to the log of the intensity of the stimulus. The relationship between perceived intensity and applied stimulus intensity tends to follow a power law (according to Steven's law[33]), with the exponent varying somewhat for different sense organs. However, for any sensory response there is an element of 'dose' relationship. Stimulation of a receptor involves a set of physicochemical reactions, so that a small stimulus causes a degree of depolarisation of a sensory nerve fibre, which increases with the intensity and duration of an applied stimulus until the depolarisation becomes sufficient to elicit nerve impulses. Depending upon the stimulus modality, some time may also be required for the stimulus level to accumulate at the receptor site. Thus in order to see a light it is necessary for a sufficient number of photons to impact the pigment in the rods or cones of the

retina. For a sensation of warmth to the skin it is necessary for a sufficient heat flux to flow into the skin for a sufficient time to raise the temperature of the receptors at 0.5 mm depth within the skin.

In general, receptor responses and sensation tend to be 'front loaded', involving both rapidly adapting and slowly adapting neural responses. This means that a strong subjective sensation may be experienced when a stimulus is first applied, which may then continue or abate somewhat, depending upon the sensory response and any reflex reactions, which may require some seconds to take effect. Consider the sensation of jumping into cold water. The time from jumping in to feeling intense cold at the skin is very short, but after around 10 seconds the discomfort lessens as the sensory response adapts and as reflex changes to the skin blood circulation occur. If a bright light is shone into the eyes, a sensation of discomfort occurs immediately, which may induce a rapid eye closure reflex, but the discomfort decreases over a period of seconds, as the pupil constriction reflex takes effect among other adaptive changes.

For a nociceptive chemoreceptor the stimulus depends upon the concentration of the stimulating agent at the receptor site. For an inhaled water-soluble gas the concentration in the fluids around the receptor must increase over time, with some resultant time lag between the concentration in the inhaled air and that at the receptor site. Other relevant factors are any buffering in the epithelial layer, biochemical reactions between tissue components and the agent, and finally the biochemical processes at the receptor itself. However, based upon human experience, at least at concentrations causing strong sensory irritation, the painful sensation in the eyes occurs almost immediately upon exposure (within a second or two), and is immediately followed by the very rapid blepharospasm (eye closure) reflex. Similarly, painful stimulation of the nose occurs as soon as an irritant is inhaled. As experiments involving human exposure to irritants are understandingly not permitted, I will relate my own experiences of exposure. This is certainly my experience from situations in which irritant bonfire smoke or sidestream cigarette smoke has blown into my eyes, or I have inhaled ammonia or acid fumes. I have found the experience painful and temporarily debilitating, being forced to close my eyes and hold my breath, with tears forming within a few seconds. This is also reported from experimental exposure to the potent sensory irritant CS riot control gas.[26] Subjects reported that the immediate sensation was the most painful, and found that although the intensity of the burning sensation was not found to decrease with time, they were able to some extent to get used to it.[26]

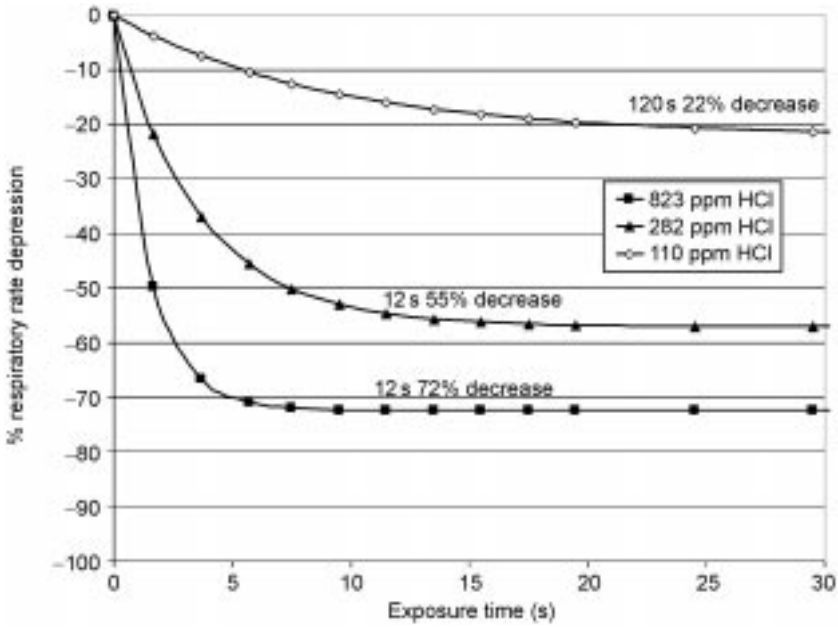
3.6.2 Time–concentration–dose relationships for sensory irritancy

The main function of a sense organ is to detect and measure the intensity of a stimulus. If the stimulus intensity remains constant so does the intensity of the sensation. Thus exposure to light of a constant brightness or sound of a constant

loudness does not result in an increasing sensation of brightness or loudness as exposure continues. In the same way the main effect of a nociceptive stimulation is that the intensity of the response is proportional to the logarithm of the concentration of the irritant (the greater the concentration the smaller the increase in the response). In order for this to be the case, it is evident that stimulation of these sense organs involves rate-related phenomena, providing a concentration–dose effect situation which is somewhat similar to that described for the uptake of carbon monoxide and formation of carboxyhaemoglobin. The intensity of the response depends upon some physical and biochemical factors reaching a dynamic equilibrium between input and removal.

Although detailed measurements of human sensation with time are unavailable, the mouse RD_{50} test provides an indication of the concentration–time dose relationships for different sensory irritants. The mouse RD_{50} test involves measuring the breathing rate of groups of mice before, during and after an exposure to a sensory irritant (see Chapter 8). When exposed to the irritant atmosphere, the breathing rate of the mice decreases, and the percentage decrease is proportional to the log of the exposure concentration. By measuring the percentage decrease in breathing rate (percentage respiratory rate depression) for different exposure concentrations, it is possible to calculate the RD_{50} concentration; the concentration causing a 50% decrease in breathing rate. However, this represents a reflex decrease in breathing rate activated in response to stimulation of the trigeminal nerve by irritants, and as stated, different reflexes require different times for activation. It is therefore likely that the actual sensation of irritancy occurs rapidly to the mouse, some time before the respiratory depression reflex response occurs. Figure 3.9 shows the respiratory rate depression in groups of 4 CD (R)-1 strain mice exposed to three concentrations of hydrogen chloride gas.[24] The exposures were designed to have a 'square wave' time profile, so that the exposure concentration was changed from air to a constant hydrogen chloride concentration within a few seconds. For these exposures, the respiratory rate for each mouse was monitored throughout 10 min pre-exposure, exposure and recovery periods. During the exposures, the time at which the breathing rate settled to a maintained plateau was recorded. Measurements of the average reduced breathing rate were then made during the second 5 min of the exposure period.

In order to generate the curves in Fig. 3.9 a logarithmic model has been fitted to the data for the 282 ppm concentration exposure, to provide a 55% rate depression plateau after 12 seconds of exposure as was observed in practice. The model was then validated against other exposure concentrations, and was found to give a good prediction of both the plateau level and time required to achieve it. The shapes of the curves are similar to an inverse of the carbon monoxide loading curves in Fig. 3.4, but with plateau equilibrium levels attained over much shorter time scales. The calculated RD_{50} concentration from these data was 297 ppm hydrogen chloride (95% confidence levels 227–390), which is



3.9 Time–response curves for percentage respiratory rate depression in mice exposed to hydrogen chloride gas.[24]

very close to that reported by Barrow *et al.* of 309 ppm (219–435).[34] The results show that at concentrations close to and exceeding the RD_{50} concentration (concentration at which sensory irritants are reported to be very painfully irritant to humans), a large decrease in respiratory rate occurs immediately upon exposure, which reaches a 50% decrease after 1.7–7.5 seconds, and maintains this lower level after approximately 12 seconds. However, at the lower concentration exposure level of 110 ppm, the maximum maintained % depression is much less (22%) and the time required to achieve it much longer (120 seconds).

In practice, the time required to reach the maintained respiratory rate reduction plateau varies somewhat with the nature of the specific irritant chemical species. Measuring the time to reach a plateau at the RD_{50} concentration provides a method for comparing different irritant chemical species on a common basis. However, since the respiratory rate depression with time curve is asymptotic, a more accurate method is to compare the time required to reach an intermediate value such as 30% rate depression, which represents a moderate level of irritation to humans. A few examples are compared in Table 3.3, including two individual chemicals, the potent irritant α-chloroacetophenone (phenacyl chloride) and hydrogen chloride gas, and two fire effluent mixtures, involving a plasticised poly(vinyl chloride) (PVC) and low density polyethylene (LDPE), both decomposed under non-flaming oxidative (nf ox) thermal decomposition conditions. For this data set, the time to 30% rate depression

Table 3.3 Mouse RD_{50} concentrations for two individual irritant substances and two thermal decomposition products atmospheres from materials decomposed under non-flaming oxidative conditions in an early version of the ISO 19700 tube furnace

		Time to 30% rate decrease at RD_{50} concentration (seconds)	Time to 50% decrease at RD_{50} concentration (seconds)
α-Chloroacetophenone	8.59 μg/l	40	172
HCl gas	295 ppm	3.2	15.5
PVC nf ox 380 °C	0.26 mg/l	13	56
LDPE nf ox 500 °C	0.06 mg/l	14.9	69

varied from 3.2 seconds for hydrogen chloride to 40 seconds for α-chloroacetophenone. The RD_{50} concentration for α-chloroacetophenone, which was used as a positive control substance, was 8.59 μg/litre, which compares well with a value of 6.4 μg/litre obtained by Alarie *et al.*[35] Thus the painful response to sensory irritants occurs much more rapidly than that to exposure to asphyxiant toxicants such as hydrogen cyanide or carbon monoxide.

3.6.3 Mechanisms of sensory stimulation and pathology

One of the reasons for the variations in the development time and potency of the effects of different chemical irritants may be related to the mechanisms of receptor stimulation. This may also be important when considering interactions between different irritants in mixtures such as fire effluents.

Irritants activate receptors of the sensory nerve endings by a number of different mechanisms depending upon the substance.[19,25] The mechanisms of action have implications for the potency of the irritant and the relationship between concentrations causing sensory irritantcy and the concentrations or doses causing pathological effects on lung tissue. One group of compounds is regarded as acting primarily by physical absorption at the receptor. This includes alkanes and alkylbenzenes, alcohols, saturated ketones, ethers and capsaicin. Alcohols are thought to form hydrogen bonds at the receptor. With the exception of capsaicin, these substances generally have a low sensory irritant potency and relatively low irritant toxic potency. Other groups of compounds act via chemical reactions with the receptor. Sulphur dioxide is considered to act by breaking disulphide bonds. Other substances chemically attack a nucleophilic (thiol) group on the receptor. These include styrene, agent CS, allyl compounds with hydrogen bonding properties such as acrolein and crotonaldehyde, aldehydes, and isocyanates. Isocyanates are unusual in that exposure produces an initial rapid effect, which then slowly increases over period of up to 2 hours. Recovery after short periods is rapid, but much slower after longer exposures.

As well as reacting with thiol groups, these substances react with hydroxy and amino groups to form stable urethanes and ureas, which may explain the slow recovery after prolonged exposure. Oxidising agents such as chlorine are also considered to act by reaction with thiol groups. Acids and bases such as ammonia, amines and inorganic acids are considered to act by acid–base reactions with the receptor.

The potency of action of these compounds depends upon a range of properties related to the reactions at the reactor site, physical properties such as aqueous and lipid solubility and the occurrence of reactions with other tissue components which may compete with the receptor stimulation. Thus isocyanates and oxidising agents react with a range of molecular sites on tissues. The nose has a metabolic capacity considered greater than that of the liver per gram of tissue, so that a range of reactions may occur with irritant compounds, including cytochrome P-450 dependent reactions, alcohol dehydrogenase, hydrolytic enzymes and the glutathione (GSH) system. The general result is that some substances have a high sensory irritant potency at low concentrations, requiring considerably higher concentrations to cause tissue damage. For other substances, such as chlorine, hydrogen chloride or sulphur dioxide, concentrations causing significant sensory irritation can also cause tissue damage at similar concentrations if the exposure is sufficiently prolonged or repeated. This lung tissue damage effect tends to be greater for toxic or corrosive substances with a low aqueous solubility, for which sensory irritant potency may be low due to a limited exposure in the nose, while significant deposition and tissue damage occur in the deep lung.

In addition to the immediate painful sensation, stimulation of the irritant receptors results in the activation of a range of inflammatory responses. Locally, there is a release of substance P, which sets up a neurogenic inflammatory response associated with leuckocyte infiltration and mast cell deregulation. Sensory impulses in the nerve fibres give rise to axon reflexes, causing peripheral vasodilatation, increased vascular permeability, mast cell activation and mucus secretion.[25] This may lead to increased sensitivity to further acute exposures, for example amongst firefighters.

A problem with the assessment of fire effluents is that they contain mixtures of irritant species, so in developing calculation models it is necessary to consider how the different irritants interact to provide the overall irritant potency of the mixture. Based upon the range of different methods by which they stimulate the sensory receptor, it is likely that some irritants would compete for the same receptor site, while others might act simultaneously at different sites. Although this might result in some differences between the degree of stimulation from different mixtures, the greater the aggregate stimulus, the greater the likely extent of stimulation of the receptor nerve, so that the effects of mixtures are likely to be more or less proportionally additive. Thus it seems likely that a mixture of 100 ppm hydrogen chloride and 100 ppm hydrogen bromide would

have approximately the same effect as 200 ppm hydrogen chloride. Where the irritants act at different sites the effect might be more than proportionally additive, since for a single irritant the effects are proportional to the log of the concentration. However, receptors have a range of stimulus intensities over which they are active, so that if one irritant (such as capsaicin) is present at concentrations sufficient to provide a maximal stimulation of a receptor nerve fibre, then additional stimulation with more of the same or with any other irritant produces no further increase in response. Based upon these considerations, currently the best models are the simple fractional effective concentration (FEC) or dose (FED) models commonly used, whereby the concentration or dose present at any time for each individual irritant is expressed as a fraction of the concentration or dose required to produce any specific toxic end point, and the different fractional concentrations or doses for different irritants are then summed to estimate the overall irritant effect as described in Chapter 8.

3.6.4 Conclusions for preferred concentration–dose models

From these studies of irritants it is possible to identify a sequence of acute physiological and pathological effects occurring over a range of timescales:

- Immediate stimulation of trigeminal pain receptors in the eyes and upper respiratory tract and stimulation of vagal receptors in the lower respiratory tract.
- Reflex responses to trigeminal stimulation resulting in eye closure, breath holding and slow breathing, occurring within seconds, sneezing, coughing. Reflex bronchoconstriction and rapid breathing resulting from vagal reflexes, occurring within seconds to minutes. Reflex secretion of tears in the eyes and mucus in the respiratory tract within seconds to minutes.
- Gradually developing inflammatory responses in response to release of inflammatory mediators due to reflex and tissue effects. Gradually accumulating damage to exposed tissues from corrosive or toxic irritants. These processes begin within minutes, increasing over timescales of an hour or more. Acute airway inflammation developing over periods of hours to days.
- Gradually accumulating tissue damage to the alveolar epithelium and interstitium resulting in oedema and inflammation developing over periods of approximately 3–24 hours.
- Bronchopneumonia developing over a period of a few days.

One approach to setting tenability levels for different levels of severity of effects for any particular irritant is to develop a combined exposure dose model, setting different *Ct* exposure doses for different exposure times. This has been done in the context of hazardous industrial chemical releases.[36] Another approach used in the context of fires, is to differentiate between the immediate, mostly concentration-related painful effects of sensory irritant stimulation (and

subsequent rapid reflex responses) and the longer timescale, more dose-related effects of airway and deep lung inflammation and oedema.[5,37]

The reason for making this distinction in relation to fire hazard modelling is that immediate effects of exposure to smoke and sensory irritants are important in delaying or preventing escape during the few minutes often available before conditions become lethal owing to asphyxiant gases or heat. These effects of irritants may therefore determine whether or not an exposed subject escapes and survives or dies at the fire scene. Since the more dose-related effects mostly become significant over timescales of more than an hour, they are generally of minor importance with respect to immediate escape and survival at the fire scene, but are important as a separate issue in relation to longer-term lung injury and survival. For this reason it is important to calculate the accumulating exposure dose of lung irritants as part of an overall hazard assessment. However, the exposure dose of lung irritants accumulates during a fire at the same time as the exposure doses of asphyxiants, and from studies of full-scale experimental fires it is generally found that the exposure doses of asphyxiants (or heat) accumulate to lethal levels before a lethal exposure dose of irritants has been inhaled.[38] For this reason lung irritancy (chemical pneumonitis) is commonly not the main cause of death. Serious chemical pneumonitis does occur in a cohort of fire survivors who have received a serious smoke exposure and most likely been rendered unconscious due to asphxiants, but have been rescued and treated with oxygen at the scene so that they survive the immediate asphyxiant exposure. This group is then at risk from development of fatal lung oedema and inflammation, often complicated by the secondary effects of respiratory tract or skin burns (which can also promote lung congestion and oedema as a result of circulatory changes). For subjects surviving the immediate oedema crisis developing a few hours after exposure, and the risk of bronchopneumonia, recovery from respiratory tract injury can be rapid and complete, but a proportion of subjects may suffer permanent lung injury conditions such as RADS (reactive airways dysfunction syndrome) and sensitisation from effects of substances such as formaldehyde or isocyanates, resulting in allergic asthma.

In order to assess the effects of irritants on the escape capability and survival of humans subjects it is possible to develop several different kinds of calculation models based upon the effects described. The simplest type of model is a FEC model. For this type of model it is assumed that the incapacitating effects of sensory irritation on escape capability occur immediately when exposure to a sufficiently high concentration occurs. The effect at any time during an exposure is expressed as a fraction consisting of the exposure concentration at the time divided by the concentration predicted to cause incapacitation. This kind of model appears to fit quite well with the human data, but does not exactly represent the situation observed in rodents, whereby the RD_{50} response requires a short time to develop to its full extent. If it is assumed that a similar effect occurs in humans it might be useful to apply some form of calculation model designed to allow for this

development time. Alternatively it would be possible to develop a dose–response model for sensory irritancy using some form of $C^n t$ function. For the longer-term effect on the lung a simple Ct model appears to be appropriate as discussed. The choice of model is considered important since it has been the subject of some discussion and may have important implications for hazard assessment methods. In order to examine the effects, benefits and limitations of the different modelling approaches, the three modelling methods have been used to examine the predicted effects of exposure to constant concentration of hydrogen chloride (square-wave concentration–time profile) and a more realistic concentration–time curve similar to those occurring during fires. The results obtained from these different models in terms of calculated time to and severity of sensory and lung irritancy in human fire victims are presented and considered in Appendix A.

Overall it is considered that an incapacitation model based upon exposure concentration rather than some function of exposure dose provides the most useful approach for assessing the incapacitating effects of sensory irritation on escape capability during a fire hazard assessment for the following reasons:

- As data from human exposures demonstrate, at concentrations of irritants causing significant levels of irritancy, severe effects are experienced immediately upon exposure and are concentration-related.
- Sensory irritant effects reported in humans do not increase with exposure duration as do dose-related phenomena.
- Measured effects on respiration in primates and rodents show an immediate, marked decrease in respiratory rate immediately on exposure at significantly irritant concentrations. In mice these develop fully to a plateau level within a short period (15–60 seconds) at the RD_{50} concentration for acid gases and combustion product mixtures. However, since respiratory rate depression is a reflex response it is not possible to determine if it develops as rapidly as the actual irritancy sensation experienced by the animals.
- A complication with exposure during fires is that a person is exposed to concentrations of irritants changing with time, which poses a problem for the application of exposure–dose models for sensory irritancy. An exposure model has been developed which enables calculation of mouse respiratory rate depression with time (or fraction of an incapacitating level of rate depression with time), and different modelling approaches are compared in a later section.

It is considered that for the potentially injurious or lethal effects of irritants on the lung, a simple $Ct = k$ exposure dose model is the most useful.

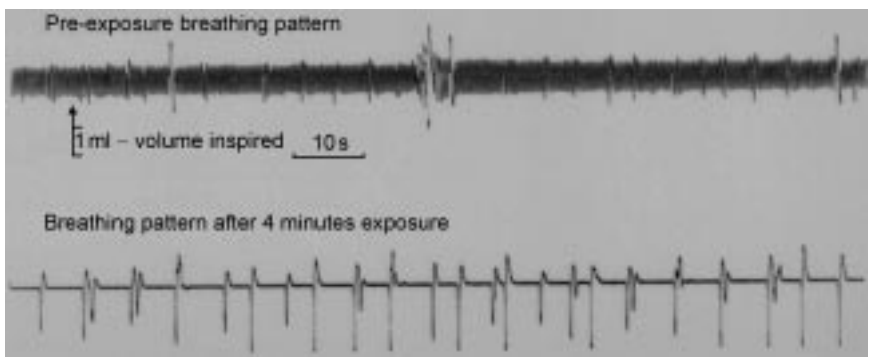
3.7 Similarities and differences between animal species in relation to effects of irritants

The purpose of this chapter is to consider the effects of irritants on humans and the development of models for the prediction of time to, and effects of, exposure

to different irritants at different exposure concentrations and doses. In order to achieve this it is necessary to make use of experimental data from animal exposures, mainly involving rats and mice, plus a limited set of data from experimental exposures of non-human primates and humans. Some of the basic physiological and anatomical similarities and differences between animals species relevant to fire hazard assessments are described in Chapter 8, but it is important to consider here certain aspects relevant to the effects of irritants.

In relation to the physiological and pathological effects of inhaled irritants, the scaling factors between species are relevant. Since the volume of air inhaled each minute per unit body weight is inversely proportional to body size, rodents inhale a proportionally greater volume of air each minute than do primates including humans. It might therefore be expected that they would be more 'sensitive' to the effects of inhaled irritants in terms of inhaled *Ct* exposure doses, since their lungs should be exposed to a proportionately greater dose, per minute of exposure. There is some evidence that this might be true to some extent when comparing rats with mice, but when comparing rodents with primates, other features come into play.

With respect to the effects of irritants, major differences between rodents and primates, including humans, are the relative effects on the upper and lower respiratory tracts. When rats or mice are exposed to most irritant vapours, and especially to irritants with a high aqueous solubility such as hydrogen chloride, the main effects over a range of concentrations and exposure times are on the upper respiratory tract. Thus when mice (or rats) are exposed to an irritant such as hydrogen chloride, the powerful sensory irritant reflex response occurs, consisting of a marked and maintained respiratory rate depression (see Fig. 3.10). The extent of the rate decrease is proportional to the log of the exposure concentration as shown in Chapter 8, Figs 8.5, 8.6 and 8.8, and this reflex is so well developed that a resting mouse can reduce its breathing rate (and hence the minute volume of air

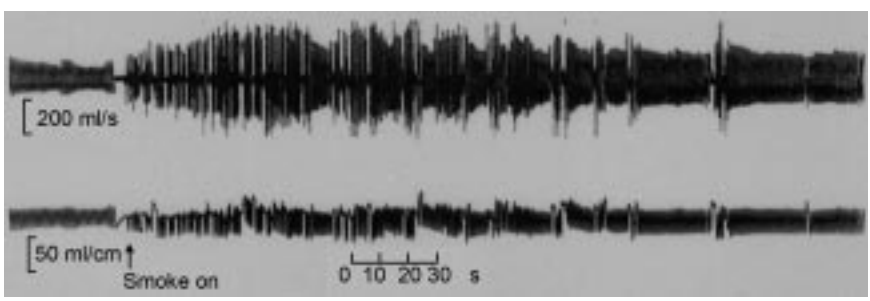


3.10 The effects on the breathing pattern of a rat exposed to a respiratory tract irritant – polytetrafluoroethylene (PTFE) decomposed at 600 °C in the DIN 53436 apparatus – 4.85 mg/litre.

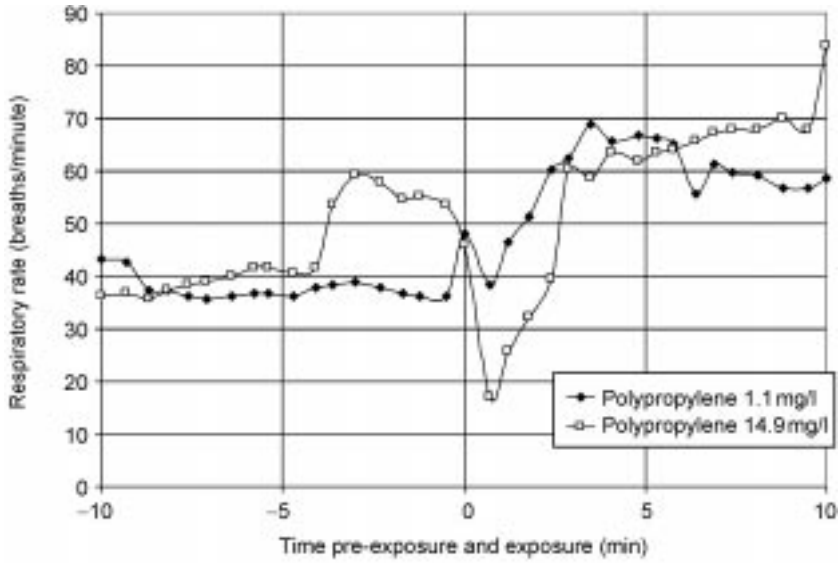
inhaled [V_E]) by up to around 90%, without suffering from serious hypoxia. This reflex thereby considerably reduces the rate of uptake of the toxic irritant into the respiratory tract, protecting the animal from the toxic effects on tissues in the nose and especially in the deeper respiratory tract. The ability to tolerate such a massive decrease in V_E illustrates another difference between rodents and primates – the ability of rodents to tolerate levels of hypoxia that would be almost certainly fatal in primates. When rats or mice are exposed to irritant atmospheres they close down their peripheral blood circulation (becoming pale and cold to the touch), thereby preserving arterial blood oxygen to supply vital organs – a response similar to the diving reflex in marine mammals.

In primates and humans the same reflex reduction in breathing rate occurs initially on inhalation of a sensory irritant, accompanied by a similar respiratory pattern to that observed in rodents, but this soon gives way to a pattern involving a marked increase in respiration, involving increases in both tidal volume and respiratory rate (see Fig. 3.11), or in some cases a rapid but relatively shallow breathing pattern. This results from stimulation of lung vagal receptors and is accompanied by reflex bronchoconstriction. The result of this is illustrated in Figs 3.12, 3.13 and 3.14, which show the effects on a macaque monkey inhaling irritant smoke from the non-flaming oxidative decomposition of polypropylene using an early version of the ISO tube 19700 tube furnace[5,22] to generate the fire affluent. Exposure was via a facemask and pneumotachograph to effluent mixed with air in a chamber. The results for the low exposure concentration show no decrease in respiration on exposure, but a rapidly developing marked increase in respiratory rate and tidal volume, representing an approximate doubling of minute volume. At the higher exposure concentrations, the initial effect is a marked decrease in respiratory rate, accompanied by an increase in tidal volume but a decrease in V_E lasting around 3 minutes, after which hyperventilation supersedes with increases in all three parameters.

Similar effects were obtained in primates exposed to thermal decomposition products from wood and flexible polyurethane foam (although the latter produced only hyperventilation). The same pattern occurs in rodents when

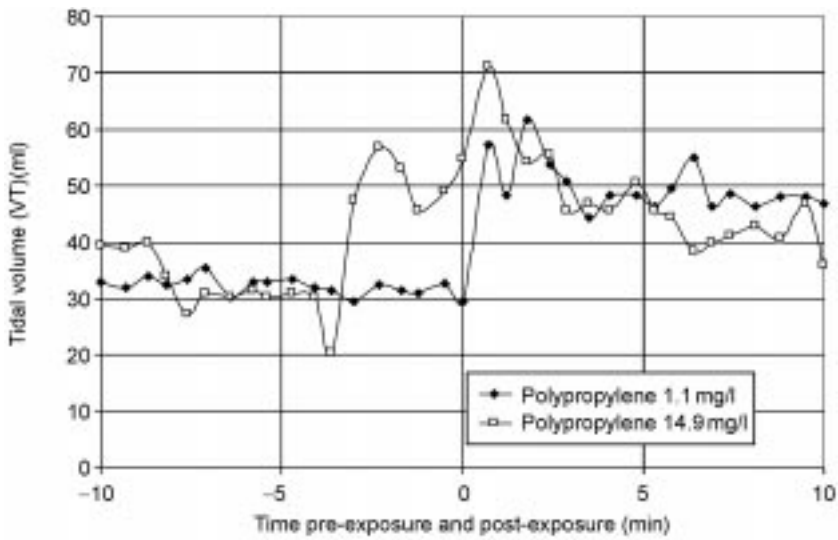


3.11 Effects on respiration pattern of a macaque monkey of exposure to smoke from wood pyrolysed at 300 °C (upper trace flow, lower trace volume).

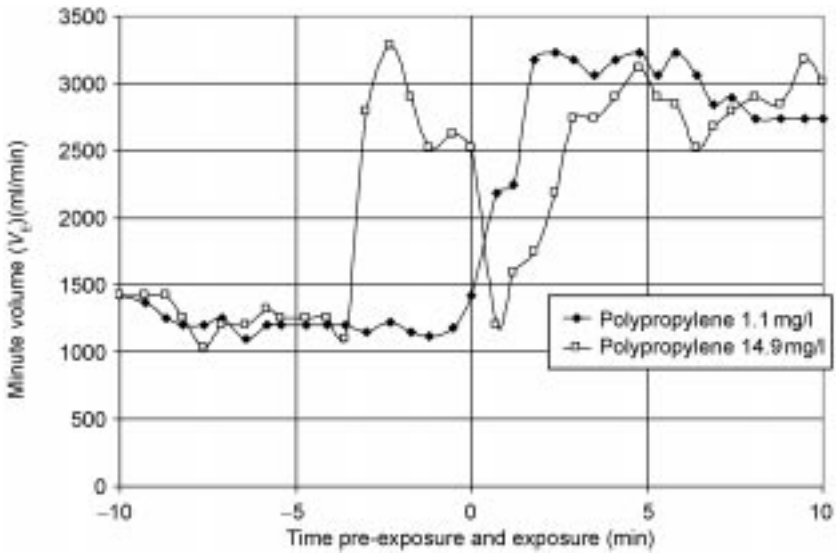


3.12 Respiratory rate in a macaque monkey before and during exposures to irritant thermal decomposition products from non-flaming polypropylene.[5,22]

exposed to lung irritants (gaseous irritants with a low aqueous solubility or in the form of fine particulates, less than ~2 μm diameter). This is illustrated in Fig. 3.15, which shows the respiratory pattern of a rat exposed to an ultrafine fluoropolymer fume.

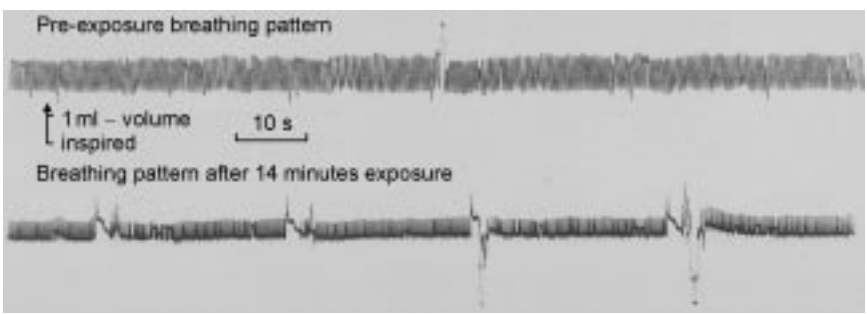


3.13 Tidal volume in a macaque monkey before and during exposures to irritant thermal decomposition products from non-flaming polypropylene.



3.14 Minute volume (V_E) in a macaque monkey before and during exposures to irritant thermal decomposition products from non-flaming polypropylene.

These effects are counterintuitive, since they potentially increase the respiratory tract exposure to irritants and the exposure dose to the lung. In practice there appears to be no increase in overall respiratory gas exchange at the alveolar level, since the rate of uptake of carbon monoxide is not increased (almost certainly due to changes in lung ventilation-perfusion ratio). When Kaplan *et al.*[39] exposed baboons to hydrogen chloride atmospheres they found a similar increase in respiratory rate, but a decrease in tidal volume and in arterial blood oxygen, indicating an actual decrease in gas exchange. The difference in response between the macaques and the baboons may partly reflect the fact that the baboons were heavily sedated while the macaques were not. V_E can be affected by the level of physical activity and other factors. In Fig. 3.14 and to a



3.15 The effect on the breathing pattern of a rat exposed to a lung irritant – PTFE decomposed at 575 °C in the NIST cup furnace – 0.054 mg/litre.

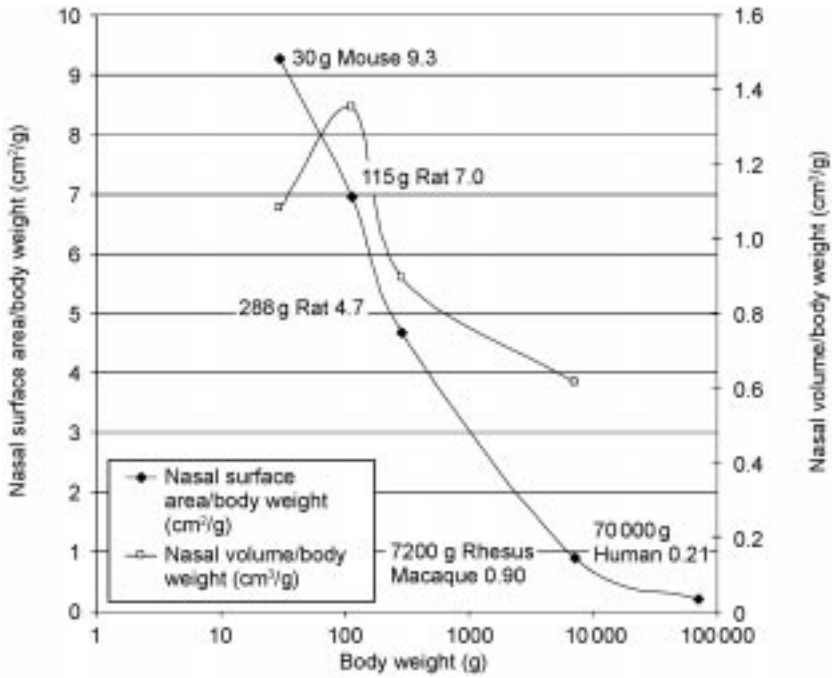
lesser extent in Figs 3.12 and 3.13 it is evident that the animal's V_E increased before the beginning of exposure at the higher concentration, then decreased at the beginning of the exposure period. Such variations are common in active, alert animals and humans, so that the respiratory pattern and V_E is at a minimum in calm, resting subjects, but V_E is increased in active or anxious subjects, depending partly upon physiological factors and partly upon psychological factors. Such variations are especially likely to occur during emergency situations such as fires.

Despite these differences in response, there do not appear to be any fundamental differences between the receptors and reflexes in the upper respiratory tract and lungs of primates and rodents. Nasal stimulation of humans results in a reduced respiratory rate. When rodents are exposed to irritants with a low aqueous solublitity or particle size, resulting in a low degree of deposition in the upper respiratory tract, but with increased deposition in the lung, then the typical respiratory pattern found in primates also occurs in the rodents, with a similar respiratory pattern and increased ventilation. Also, if rats or mice are exposed to water-soluble irritants directly to the lung, bypassing the nasal cavity (for example by introducing the irritant via a tracheal cannula), then a hyperventilation reflex occurs, and fatal lung inflammation results[40,41] from a lower exposure dose than in intact animals.

The implication is that water-soluble irritants are largely scrubbed from the inhaled air in the nasal cavity of rodents, with relatively poor penetration into the deeper lung compared with primates. Also, while rodents are obligate nose-breathers, primates, including humans, resort to mouth breathing following nasal irritation or exercise.

In order to understand why water-soluble irritants are largely removed in the nasal passages in rodents it is useful to compare the anatomy and physiology. Figure 3.16 shows plots of nasal surface area/body weight and nasal volume/body weight against body weights in different species.[42–44] As Fig. 3.16 shows, the surface area of the nasal epithelium of a mouse per unit body weight is 44 times greater than that of a human. Relatively there is a much greater surface area available for absorption of water-soluble acid gases in the mouse nose than in the human nose. For a human, each square centimetre of nasal epithelium is in contact with approximately nine times the volume of air each minute as in a mouse. This means that each millilitre of air spends nine times longer in contact with the nasal epithelium each minute in a mouse than in a human during normal resting breathing (and even longer in the mouse when exposure to an irritant reduces the mouse breathing rate). The relative volume of the nasal cavity is also more than twice as large in rodents.

In addition to the relatively large nasal surface area, another consideration is the much smaller diameter of the upper airways in rodents. The rate of absorption of water-soluble gases from any volume of air into an aqueous surface layer depends partly upon the volume/surface area and the contact time

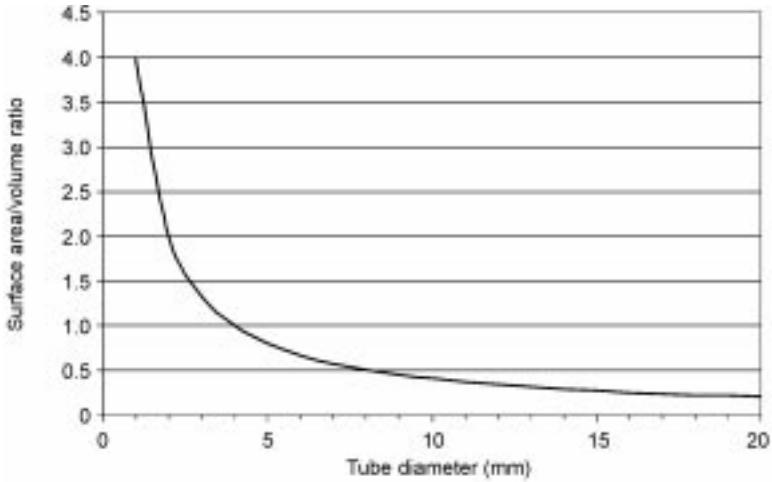


3.16 Nasal surface area/body weight and nasal cavity volume/body weight in different species.

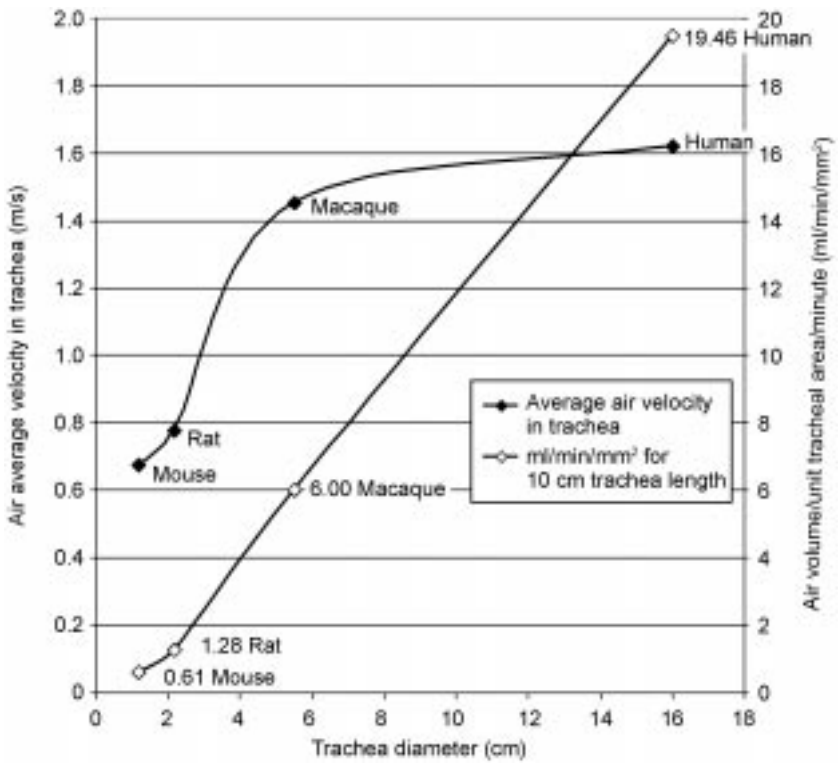
for the gases. Consider air containing a water-soluble gas passing through a tube such as an airway. Figure 3.17 shows a plot of surface/volume against diameter for a 10 mm length tube. For a mouse the diameter of the trachea (and by implication also the larynx and upper airways) is approximately 1.2 mm, while that of a human is around 16 mm. This means that the surface area of a 10 mm length of airway in a mouse presents approximately 16 times the surface area relative to the volume of gas passing through than it does in a human.

Figure 3.18 shows how the species compare when gas flows in the airways are compared. Based upon the minute volumes in the different species, the velocity of the air flowing through a mouse trachea is approximately 2.5 times that through a human trachea when both are breathing at resting rates. When the volume of air coming into contact with a 10 mm length of trachea surface each minute is compared, then the ratio between mouse and humans is 32, which means that 32 times the air volume passes over each square mm of tracheal surface each minute in a human than in a mouse. Again this means that the air spends 32 times longer in contact with the surface in mice than it does in humans.

The results of these comparisons are that even under normal resting breathing conditions, the gases passing through the upper airways of a mouse have a far



3.17 Relationship between surface area/volume ratio and diameter for 10 mm length tubes.



3.18 Average air velocity in the trachea (m/s) and air volume/unit tracheal area per minute in different species under normal resting respiration conditions.

greater opportunity to come into contact with and dissolve in the aqueous fluid surface of the epithelial mucous layer in the both the nasal cavity and upper airways, due to the high relative surface area of the nasal cavity, the surface area/volume scaling factors and the much higher relative residence time of air in the upper airways in rodents. In addition, under laminar flow conditions, the diffusion path between the airway lumen and wall is much shorter in the upper airways of rodents.

It seems likely that these differences may go a long way towards explaining the much greater relative absorbance of acid gases and other irritants in the upper airways of rodents, and also the more powerful upper respiratory tract trigeminal reflex response. When exposure to irritants results in a respiratory rate decrease, this further slows the inhaled air flow, providing even greater opportunity for absorption in the upper respiratory tract. This does not mean that rodents cannot be used as predictive models for the effects of irritants in humans, but that these differences should be considered, especially when considering exposure doses causing lung inflammation. Since the factors described go a long way to protecting rodents from deep lung penetration of irritants, it is to be predicted that humans might be significantly more sensitive to airway and lung inflammation than rodents for a given inhaled irritant concentration.

3.8 Potency ranges for sensory and lung irritancy

The acute sensory irritant potencies of different substances vary over a very wide range of around six orders of magnitude[5,35] (Table 3.4). Concentrations causing severe sensory irritation range from 0.1 to 1.0 ppm for the most potent substances, including riot control agents (CS and CN) and certain isocyanates, to 5000–15 000 ppm for acetone and ethanol. Formaldehyde and chlorine cause severe irritancy in the 1–10 ppm range and acid gases (sulphur dioxide, hydrogen halides and nitrogen dioxide) in the 100–1000 ppm concentration range. The sensory irritant and lung irritant effects of hydrogen chloride have been found to be similar whether exposure was to dry hydrogen chloride gas or a respirable acid mist at comparable hydrogen chloride concentrations.[24] The relationship between concentrations of a particular irritant chemical causing severe sensory irritation and exposure doses causing fatal lung inflammation in rats varies considerably. For toluene diisocyanate and the riot control agents, the ratio between the concentration causing severe sensory irritation and the approximate lethal concentration for a 30 min exposure period is around 500 : 1 and for formaldehyde 250 : 1. For chlorine and hydrogen chloride the ratio is approximately 10 : 1, while for nitrogen dioxide the ratio is 0.4. This means that CS gas is not very hazardous at concentrations causing marked irritation (although it may be at higher concentrations), while nitrogen dioxide can be hazardous even at concentrations where there is little immediate sensation of

Table 3.4 Sensory and pulmonary irritancy of combustion products

Irritant	RD_{50} (ppm) mouse[b]	Severe sensory irritancy in humans (ppm)	30 minute LC_{50} (ppm) mammal	LC_{50}/RD_{50}
	0.1–1.0			
Toluene diisocyanate	0.20	1.0[45]	100	500
o-chlorobenzylidene – malonitrile (CS)*	0.52	0.5[26]	150–400[46,47]	529
α-chloroacetophenone (CN)*	0.96	6–50[26]	300–400[48,49]	365
	1.0–10			
Acrolein	1.7	1–5.5[45,48]	140–170[39,48,49]	91
Formaldehyde	3.1	5–10[45,48]	700–800[40,49]	242
Chlorine[a]	9.3	9–20[48]	100[40]	11
	10–100			
Crotonaldehyde	4.2[50]	4–45[45]	600–1500[45,49,52]	156
Acrylonitrile		>20[45]	4000–4600[49]	
Penteneone			1000[49]	
Phenol	166[51]	>50[45]	400–700[49]	3
	100–1000			
SO_2	117	50–100[45,48]	300–500[40,49]	3
NH_3	303	700–1700[54]	1400–8000[49]	16
HF	151[53]	120[45]	900–3600[40,49]	13
HCl	309	100[45,48]	1600–6000[39,40,49]	12
HBr		100[45]	1600–6000[49]	0.4
NO_2	349	80[45,48]	60–250[40,49]	46
Styrene	980	>700[45]	10 000–80 000[49]	
	1000–10 000			
Acetaldehyde	4946	>1500[45]	20 000–128 000[49]	15
	10 000–100 000			
Ethanol	27 314	>5000[45]	400 000[49]	15
Acetone	77 516	>12 000[45]	128 000–250 000	3

The potential for causing sensory irritation spans six orders of magnitude, while that for causing death spans approximately three orders of magnitude. For substances down to NO_2 death is likely to be due to lung irritation, while for the remainder from styrene to acetone death is likely to be due to asphyxiation.

[a] Substances not detected in combustion atmospheres. [b] RD_{50} concentrations from Alarie[35] except where otherwise indicated.

LC_{50} concentrations have been normalised to a 30 min exposure time according to Haber's rule.

irritancy. For some substances, the irritant effects depend upon chemical changes following deposition. Phosgene (carbonyl chloride) is an organic gas with a low aqueous solubility and sensory irritant potency. It penetrates into the deep lung where it hydrolyses to release hydrogen chloride, resulting in pulmonary oedema and inflammation.

As discussed in Chapters 8 and 14, the most obviously important irritant species in fire atmospheres are the isocyanates and isocyanate-derived chemical species from flexible polyurethane foams, the low molecular weight unsaturated aldehydes (acrolein, formaldehyde and crotonaldehyde), inorganic acid gases, and phenol. High concentrations of isocyanate-derived irritants ('yellow smoke') can be formed during decomposition of flexible polyurethane foams, and toluene di-isocyanate monomer[55] (TDI) has also been detected, although variations in yields are somewhat uncertain. The unsaturated aldehydes are highly potent and are formed at significant yields during non-flaming oxidative decomposition of many organic materials, especially cellulosics such as wood and cotton. However, during flaming combustion their yields are very small. When the measured irritancy in mice (RD_{50}) for fire effluent mixtures generated under non-flaming conditions was compared with the concentration and potencies of the measured individual irritant species present, the observed potency of the mixed irritants was always considerably greater than could be explained in terms of the individual irritants present (assuming a simple additive FEC model). Although the analytical work was semi-quantitative, it was considered that a major contribution was likely from unidentified high potency irritant species (see Chapter 8).

The relationship between the RD_{50} and 30 min LC_{50} also gives an indication of the possible contribution of very acute inflammatory reactions (in addition to sensory irritation) to incapacitation during exposure at a fire scene. For TDI, and the unsaturated aldehydes, the ratio between the concentration causing severe sensory irritation (RD_{50}) and the 30 min lethal concentration varies by factors of approximately 100–500, which means that the exposure concentrations would most likely need to be considerably higher than the RD_{50} concentration for inflammatory reactions to contribute significantly to the painful incapacitating effects suffered during exposure. Among the acid gases, the ratio for the hydrogen halides is around 12. Assuming that significant inflammatory effects might occur at around a third of the lethal dose, it is possible that although painful sensory irritation would be the major effect during exposures, there might be some contribution from inflammation, and this is more likely for sulphur dioxide and phenol. For nitrogen dioxide, sensory irritancy and fatal inflammation occur at similar exposure concentrations, although the lung irritant effects require some time to develop. For fluorocarbons, the most important 'normal' toxic irritants are carbonyl fluoride (which hydrolyses to hydrogen fluoride partly in the air and partly in the lung), perfluoroisobutylene and ultrafine fluoropolymer particulates. Hydrogen fluoride is both a sensory and

lung irritant, while the other compounds are potent lung irritants. These are discussed in Chapter 8 and in Purser.[21]

3.9 Setting tenability limits for concentration and dose-related irritant effects

3.9.1 Identification of end points and consideration of inter- and intraspecies differences

In order to assess the toxic hazard in fires, it is necessary to set physiological end points for different irritant effects. The end points considered important are:

- concentrations likely to impair the efficiency of escape attempts due to painful sensory eye and respiratory tract irritation;
- concentrations likely to cause incapacitation (cessation of effective escape attempts), due to painful sensory eye and respiratory tract pain, blepharospasm, bronchoconstriction, lachrymation and mucus secretion, respiratory distress and hypoxia;
- exposure doses resulting in significant post-exposure eye and respiratory tract inflammation, oedema and pathology;
- exposure doses resulting in post-exposure lethality due to lung oedema and inflammation.

With respect to the sensory irritant effects, clearly defined end points are problematic since the painful effects are on a continuum, increasing in severity with the exposure concentration. Concentrations at which significant impairment or prevention of effective escape behaviour is likely to occur are the most appropriate for hazard assessments. In setting such tenability limits it is useful to distinguish between the severity of effects likely to occur to the average person, and limits designed to allow for ranges in sensitivity within the exposed human population. In setting such limits it is also necessary to consider uncertainties in extrapolating from the available data (especially interspecies differences) to predict effects in humans. Similarly, with respect to exposure doses causing lung damage and lethality, it is necessary to consider uncertainties within the data and for extrapolation to average humans (particularly interspecies differences), and for variations in susceptibility within the human population, especially for those with impaired respiratory function. In contrast to the effects of sensory irritancy, the dose-related effects on the lungs tend to have a threshold below which effects are relatively minor, but above which severe injury and death become probable.

Owing to these uncertainties the setting of tenability levels for different chemical species and different effects inevitably requires the application of consensus estimates, and this has resulted in quite widely differing recommendations. In order to consider the data, rationale, approaches and conclusions

of some different experts to this problem, the effects of two irritants, CS riot control gas and hydrogen chloride have been examined in some detail. Both are potent upper respiratory tract irritants, with important concentration-related effects.

3.9.2 CS (*o*-chlorobenzilidene malonitrile)

Although CS is not normally released in fires, it is useful to consider its effects as an example of a potent sensory irritant that has been selected for riot control purposes specifically because the ratio between the concentration causing incapacitating sensory irritation and that causing any pathological damage to the respiratory tract or death from other causes is so large. CS is also the only sensory irritant for which reasonably detailed data exist on experimental human exposures at incapacitating concentrations, in addition to reports of effects on the general public during incidents, and effects on animals. The justification for considering the sensory irritant effects of CS as an example is that the basic effects of all sensory irritants are similar and that at the mouse RD_{50} concentration (or different fractions of the RD_{50} concentration) almost all sensory irritants are reported to have effects of similar severity in both mice and humans (see discussion in Chapter 8). This relationship is used as a basis for setting industrial hygiene levels for sensory irritants by different authorities and the validity of the mouse RD_{50} as a metric for predicting effects at different levels of severity in humans has been confirmed by a number of studies (Table 3.5).[19,35,56,57]

The effects described during volunteer human exposures[26,46,58] consist of an almost instantaneous severe inflammation of the eyes, accompanied by pain, excessive lachrymation (tears) and blepharospasm (involuntary closure of the eyes due to spasm of the eyelids). There is irritation and running of the nose with a burning sensation in the nose, mouth and throat, and a feeling of intense discomfort during which the subjects cough, often violently. If the exposure continues, the discomfort spreads to the chest and there is difficulty in breathing. Many subjects describe a tightness of the chest or chest pain as the worst symptom. The breathing is irregular and the breath is held for short periods. Attempts to avoid the irritation by breath holding, followed eventually by fairly deep breaths, are reported as being extremely unpleasant. At this stage most individuals were acutely apprehensive and highly motivated to escape from the smoke (the subjects were military personnel).

The basic findings from the CS work are that for this substance with a high irritant potency, but otherwise low toxic potency, the sensory irritant effects on humans are severe at any concentration above around one-fifth the mouse RD_{50} concentration, and are reported as being most unpleasant and disruptive immediately on exposure. At 0.26 ppm (approximately half the mouse RD_{50} concentration) the effects were so bad that five of six exposed subjects were forced to

Table 3.5 Sensory irritant effects of agent CS (*o*-chlorobenzilidene malonitrile)

Species	Concentration (ppm)	Effect
Mouse	0.52	RD_{50}
Rat	150–400	30 min LC_{50}
Human[58]	2.6	Almost immediate eye pain, blepharospasm, severe lachrymation, nasal irritation and running, chest pain, coughing.
	0.19	As above.
	0 to 0.8 over 10 min	As above, 3 of 4 subjects had to leave chamber.
Human[26]	0.1	Immediate symptoms as above very unpleasant; however, after 4–5 min more tolerable and could play cards, symptoms same intensity but got used to them.
	0.26	Immediate symptoms intolerable – forced to leave chamber.
Incidents[59,60]	–	Crush injuries and deaths on stairs during extreme escape behaviour in Chicago, USA. Descriptions of collapse onto floor following exposure in an incident in Manchester, UK.

leave the chamber within 30 seconds, and the sixth after 1 min. However, subjects reported that when the exposure concentration was maintained constant at lower concentrations, although the severity of the symptoms remained approximately constant, they gradually developed some tolerance and were able to perform simple tasks. They were even able to tolerate gradually increasing exposure concentrations over a 1 hour exposure period, and seven of eight exposed subjects were able to tolerate the same high concentration (0.27 ppm) when achieved gradually over an hour, that they were forced to leave immediately when suddenly exposed from 0 to 0.27 ppm.

It also seems that over this range from one-fifth of the mouse RD_{50} concentration, severe concentration-related sensory irritant effects occur immediately on exposure, at least as rapidly as the time required for full development of the mouse respiratory rate depression at the RD_{50} concentration, and most likely even more rapidly.

Accepting that similar effects, at a similar level of severity, occur in humans exposed to any of the common smoke irritants (acid gases and unsaturated aldehydes) as discussed in Chapter 8, it seems likely that in a fire scenario, sudden exposure to irritant smoke at around the mouse RD_{50} concentration is likely to be extremely disruptive to escape behaviour, with the following predicted effects:

- pain and visual difficulties resulting in slow walking speeds;
- for subjects immersed in irritant smoke, very strong motivation to escape, presenting hazards of exit blocking and crush injuries in crowded situations;
- for subjects attempting to enter and move through irritant smoke, strong motivation to turn back and seek refuge or alternative escape routes;
- incapacitation (lack of effective escape movements) at higher concentrations (around three times the RD_{50} concentration) or at around the RD_{50} concentration in more sensitive individuals, especially for more corrosive or tissue-damaging irritants, due to pain, vision and breathing difficulties.

3.9.3 Hydrogen chloride

For hydrogen chloride there are no modern experimental human studies on irritant effects except at very low concentrations (around 1.8 ppm). In order to set tenability levels it is necessary to make use of human incident data and attempt extrapolation from experimental data obtained from primates and rodents. The situation for hydrogen chloride and similar irritants causing tissue pathology is that it is necessary to consider both sensory irritant effects on escape capability and pathological effects on the eyes and respiratory tract resulting in post-exposure injury and death. The kind of data available and the approaches used by some different experts and expert groups to set tenability levels for different hazardous effects are illustrated in Table 3.6.

Consideration is given only to single acute exposures and effects likely to be significant in industrial emergency situations or fires, for different exposure times of up to 1 hour. The basic situations are that for very low concentrations and for short exposure times (up to around 10 min), the main concerns are sensory irritancy, since for hydrogen chloride, with a *Ct* product exposure dose following Haber's rule, the concentrations required to cause pathological damage over short exposure periods are significantly higher than those required to cause very painful sensory irritancy.[30] The longer the exposure period the more likely that injury can occur at concentrations also causing painful sensory irritancy.

Starting from low concentrations, the lower levels at which significant sensory irritant effects occur that might disrupt human escape attempts are around 50–100 ppm. The frequently conflicting claims relating to safe levels of hydrogen chloride have recently been reviewed.[61] Reports of early investigators (based upon industrial workplace experience) suggest that work becomes impossible at around these concentrations. I have also spoken to two individuals who briefly exposed themselves to an atmosphere containing 100 ppm hydrogen chloride (one deliberately and one accidentally), and both reported that the experience was devastatingly painful and incapacitating. Exercising guinea pigs were reported as being incapacitated at 140 ppm,[62] and the mouse RD_{50} concentration is 309 ppm,[24,34] so this is also predicted to be very painfully irritating

Table 3.6 Irritants effects of exposure to hydrogen chloride

ppm	Effect
1.8	AEGL-1[63]
3	ERPG-1 Maximum concentration human exposure up to one hour without experiencing other than mild transient health effects of a clearly defined objectionable odour[64]
<5	Minor nasal irritation can be detected below 5 ppm (the occupational exposure limit, OEL)
20	ERPG-2 Maximum concentration human exposure up to one hour without impairing ability to take protective action or develop serious health effects
43	AEGL-2 for 30 min exposure
50	IDLH (immediately dangerous to life and health)[65]
10–50	Perceived as irritant, but work is possible at up to approximately 50 ppm
50–100	Strongly irritant, and some people (personal communications) report exposure to 100 ppm as being excruciatingly painful to the eyes and respiratory tract
100	ERGP-3 Maximum concentration human exposure up to one hour exposure not life threatening Also AEGL-2 for 10 min exposure and AEGL-3 for 1 hour
140	Incapacitation in guinea pigs after 16.5 min
190	No obvious signs in baboons during 5 min exposure
200	Purser, *SFPE Handbook* – predicted to impair escape in average person[5]
210	AEGL-3 (lethal) human 30 min
300	ISO-13571 maximum concentration to prevent human incapacitation (allowing for sensitivity variations in the population)[37]
309	Mouse RD_{50}[34]
500	Hyperventilation (lung irritation) in sedated baboons and post-exposure chronic lung injury after 15 min exposure[39]
620	AEGL-3 (lethal) human 10 min
700	Severe upper respiratory tract and eye cornea damage following 15 min exposure rats[24,66]
900	Purser, *SFPE Handbook* – predicted to cause incapacitation average person[5]
800–1000	Signs of severe irritancy in baboons during 5 min exposure including eye rubbing, profuse salivation and blinking. Able to perform shuttle box escape[39]
1000	ISO-13571 maximum concentration to prevent human incapacitation in average person
1000–2000	Brief exposure regarded as being dangerous to lethal to humans[49]
1095	30 min LC_{50} tracheal cannulated mice[40]
1293	30 min rat exposure (nose or mouth breathing) severe necrotizing rhinitis, turbinate necrosis, pseudomembrane formation, ulcerative tracheitis, necrosis, polymorhonuclear leucocyte infiltration down to alveoli[40]
2810	60 min rat LC_{50}[28]
3800	30 min rat LC_{50} (representing an exposure dose of 114 000 ppm min)[28]
5000	40% decrease in arterial blood oxygen in sedated baboons[39]
15 000	5 min lethal exposure concentration in rats and baboons is around 15 000 ppm but baboons able to perform shuttle box escape from a chamber after 5 min exposure[39]

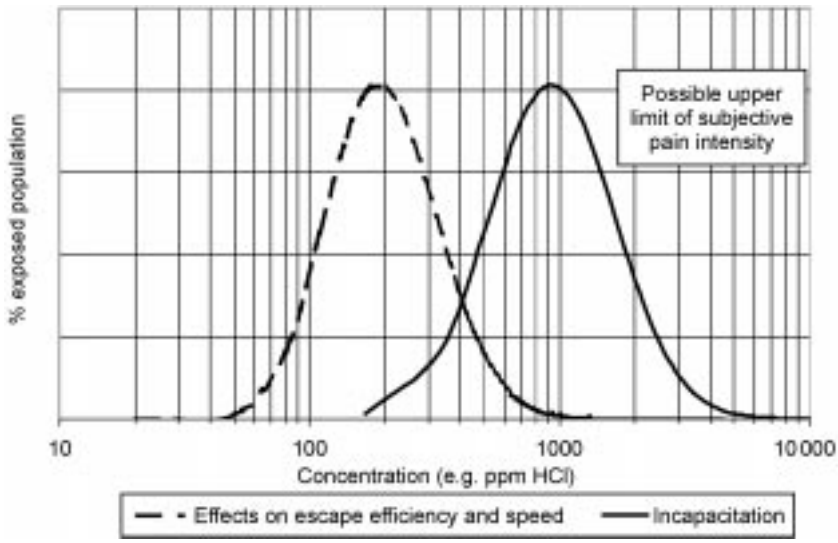
to humans. Baboons exposed to 190 ppm for 5 min showed no obvious signs of distress and were capable of performing a shuttle box escape.[39]

Above around 500 ppm, the picture of sensory irritancy starts to become complicated by signs of tissue damage even after fairly short exposure periods. Thus baboons showed signs of lung irritation and post-exposure lung damage after 15 min at 500 ppm,[67] and signs of severe sensory irritancy at concentrations above 800 ppm for 5 min exposures. Although they were able to perform their escape test up to the exceptionally high concentration of around 15 000 ppm, even a 5 min exposure resulted in fatal post-exposure lung damage at this concentration.[39]

Historically, brief human exposure at 1000–2000 ppm has been regarded as potentially lethal[49] and 30 min exposures in rodents at around 1000 ppm result in severe respiratory tract tissue damage and even deaths, although the 30 min LC_{50} concentration in rats is 3800 ppm, representing a lethal *Ct* product dose of 114 000 ppm min.[28,41]

3.9.4 Sensitivity distribution issues

The range of susceptibility in the human population must be adequately addressed. Some individuals, particularly those with respiratory diseases, are likely to be more susceptible than others, while other, especially fit individuals or those used to working in irritant environments, are likely to be more resistant. Based upon the data reviewed, it is also likely that the subjective irritancy of an exposure is on a logarithmic scale or power scale of sensitivity for humans, as it is in rodents. Figure 3.19 illustrates a likely distribution of sensitivity for a human population for hydrogen chloride, in terms of the proportion of the population to suffer irritancy likely to impair escape at different concentrations, and the proportion of the population likely to suffer incapacitation. This is based upon existing human and animal data and the judgement of the author. While the escape capability of most individuals is considered likely to be affected at around 200 ppm, more sensitive individuals may be affected by lower concentrations of around 70 ppm or less, while some may be able to tolerate exposure to very high concentrations of over 500 ppm without impairing escape. Similarly, while it is considered that the average person is likely to be incapacitated and incapable of effective escape movements at around 900 ppm, some more robust individuals may be able to resist incapacitation at concentrations of up to several thousand ppm, as did the baboons. It is also likely that with respect to sensory irritation, there is an upper limit to pain receptor performance above which further increases in concentration may have little additional effect over short exposure periods. This may partly explain why the baboons were still able to perform a simple escape test at the exceptionally high concentrations of around 10 000+ ppm hydrogen chloride.[5,65]



3.19 Approximate estimated sensitivity distribution to hydrogen chloride exposure for human population.

3.9.5 Setting tenability limits for hydrogen chloride and other irritants

In addition to summarising the available data, Table 3.6 shows tenability limits set by different experts in relation to emergency situations. Two sets of limits are for fires and two for industrial emergencies. As stated, there are differences between the needs for limits with respect to fires and those for industrial emergencies, in that for fires the main requirement is to ensure a rapid evacuation before conditions become untenable due to heat or asphyxiant gases. For industrial accidents only one irritant substance is usually under consideration at any one time, so that for emergency planning it is necessary to consider levels that might impair escape or be life threatening following exposure at the scene, and lower concentrations that might endanger the health or survival of surrounding populations after a release.

As described for CS and hydrogen chloride there are issues with regard to setting tenability limits for sensory and pulmonary effects of irritants for humans in relation to the limitations of the available data for humans, the relevance of experimental data from animals and scaling issues to predict effects in humans. Also relevant is the purpose of the tenability limits set (the extent to which they should or should not be conservative for design purposes and to allow for uncertainties in predicted effects in humans). Owing to the importance of resolving these issues for development of hazard calculation models, the tenability limits developed by different expert groups and the rationales used to arrive at them are discussed in Appendix B.

In the next section calculation models are derived for calculating time at which exposure is predicted to cause incapacitation due to sensory irritancy and time to inhale potentially lethal doses.

3.10 ASET FED calculation models for time to incapacitation and lethal dose of irritants

During fires, the concentrations of irritants to which people are exposed vary with time. The fire effluent also includes a mixture of several different irritant chemical species, the relative concentrations of which may also vary with time. In order to estimate time to incapacitation it is therefore necessary to develop calculation models taking into the account the effects of changing concentrations and exposure doses of irritant mixtures. As stated, the main concerns with respect to irritants in ASET and RSET calculations are:

- concentrations causing impairment of escape capability due to sensory irritancy;
- concentrations causing incapacitation due to sensory irritancy;
- concentrations contributing to asphyxia during exposure;
- relationship between exposure concentrations and evacuation walking speeds;
- exposure doses resulting in post-exposure injury or death due to lung inflammation and oedema in persons surviving the immediate fire exposure.

These may be used as potential tenability end points for ASET calculations and the effects on walking speed may also be used for egress (RSET) calculations. A design may be considered to have failed if an occupant is predicted to be exposed to conditions producing these end points (during design fire scenarios) while attempting to escape. In such a case, using the first end point would present a more conservative approach than using the second end point, or for a probabilistic analysis would present a lower probability of occupants experiencing serious injury or death.

They are calculated using the FEC method applied to irritants, whereby the concentration of any individual irritant gas at any time during a fire is expressed as a fraction of the concentration predicted to result in either escape impairment or incapacitation. The FECs of each individual irritant present are then summed to provide an overall FIC for sensory irritancy as follows:

$$\begin{aligned} \text{FEC} = {} & \text{FEC}_{\text{HCl}} + \text{FEC}_{\text{HBr}} + \text{FEC}_{\text{HF}} + \text{FEC}_{\text{SO}_2} + \text{FEC}_{\text{NO}_2} \\ & + \text{FEC}_{\text{CH}_2\text{CHO}} + \text{FEC}_{\text{CH}_2\text{O}} + \Sigma\text{FEC}_x \end{aligned} \qquad 3.5$$

where FEC = overall fractional irritant concentration for the mixed irritants present, and ΣFEC_x = FECs for any other irritants present.

The denominators for the FECs or each individual gas are those shown in Table 3.7, either for escape impairment or incapacitation depending upon the

Table 3.7 Exposure concentrations and exposure doses for escape impairment, incapacitation and lethal lung damage (*SFPE Handbook*[5] and BS7999-2[68])

Gas	Concentration predicted to impair escape in the average person (ppm)	Concentration predicted to cause incapacitation in the average person (ppm)	Exposure doses predicted to be lethal to half the population (ppm min)
HCl	200	900	114 000
HBr	200	900	114 000
HF	200	900	87 000
SO_2	24	120	12 000
NO_2	70	350	1 900
NO	–	>1 000	~30 000
CH_2CHO (acrolein)*	4	20	4 500
HCHO (formaldehyde)*	6	30	22 500

*Where the concentrations of acrolein and formaldehyde (or other important irritants) are unknown, a term derived from smoke density 0.5 OD/m may be used as an indication of irritancy likely to impair escape efficiency, and 90 OD/m min may be used as an indication of lethal organic irritant exposure dose.

end point desired. An end point is reached if the overall FEC reaches one at any time during the fire. If the FEC decreases below 1 at any time then escape is no longer impaired. As shown in Appendix B, Table B.6, the result of applying this expression for incapacitation is similar to that in ISO 13571.

For lung irritants the effects depend upon an exposure dose, which accumulates throughout exposure in the fire. In order to calculate this effect, the fractional lethal dose (FLD), the special case of the FED referring to lethality, of each irritant is calculated for each short period of time during the fire (for example every 10 seconds). The *Ct* exposure dose inhaled each time period is then expressed as a fraction of the lethal exposure dose, and the exposure doses of each of the irritant gases present during that time period are then summed to provide an overall FLD. The FLD equation for the lethal effects of inhaled irritants is then:

$$\begin{aligned} \mathrm{FLD_{irr}} = {} & \mathrm{FLD_{HCl}} + \mathrm{FLD_{HBr}} + \mathrm{FLD_{HF}} + \mathrm{FLD_{SO_2}} + \mathrm{FLD_{NO_2}} \\ & + \mathrm{FLD_{CH_2CHO}} + \mathrm{FLD_{HCHO}} + \Sigma \mathrm{FLD}_x \end{aligned} \quad 3.6$$

The FLDs for each small time period are then integrated to provide an overall FLD with time during the fire. When FLD = 1 it is predicted that a subject has inhaled a sufficient exposure dose of irritant to result in death from lung inflammation some hours after exposure. The threshold concentrations shown in Table 3.7 are proposed for common fire irritants likely to severely affect escape capability in most humans. In order to allow for more sensitive individuals it is recommended that design limit threshold of 0.3 times these levels might be used.

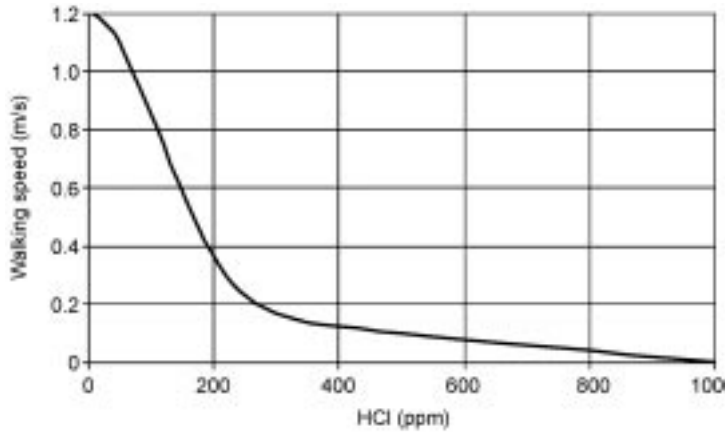
With respect to lung irritancy the FLD makes no allowances for uncertainties related to the data available or interspecies differences. It also does not allow for the possibility of significant sublethal lung injury. Based upon the data discussed in the previous section a further factor of 3 might be used to reduce the probability of significant post-exposure lung injury and another factor of 3 to allow for interspecies differences (rounded to a total factor of 10). Since rodents have been shown to be much more sensitive to lung irritation when the nasal cavity is bypassed (as occurs in primates including humans during mouth breathing), it is reasonable to assume that a human may be somewhat more prone to lung irritation than a rat.

3.11 Calculating the effects of sensory irritancy on walking speed

Near the beginning of this chapter the experientially determined effects of optically dense non-irritant and irritant smoke on walking speed in humans were described, with Equations 3.1 and 3.2 derived for calculation of walking speed at any specific smoke density. Equation 3.2 was for irritant smoke produced using a bee smoker, most likely containing smouldering wood chips. Although this may be quite useful as a default, generic, method for estimating walking speed in smoke, a problem with the prediction of effects for different fires is that the irritant composition, and hence the level of irritancy, is very dependent upon the composition of the fuel and the decomposition conditions. For this reason a calculation model has been developed which can be applied to any individual irritant fire gas of mixture of known irritants.

The basis of the model is that above certain concentrations, it is considered that exposure to irritant gases in smoke will severely impair and even prevent escape. For the majority of flaming fires, it is considered that the concentrations of mixed smoke irritants will be below this level provided the smoke optical density does not exceed OD/m = 0.2. Exceptions could be smouldering fires, for which the organic irritant yields tend to be high, and fires involving fuels giving off significant yields of inorganic acid gases (HCl, HBr, HF, SO_2, NO_x). Between zero and the concentration causing incapacitation there will be a relationship between the irritancy of the smoke and walking speed (as demonstrated by Jin[12]). In order to provide some indication of possible effects on walking speed between these limits, expressions have been developed for any irritant based upon the concentration estimated to be very painfully irritant.

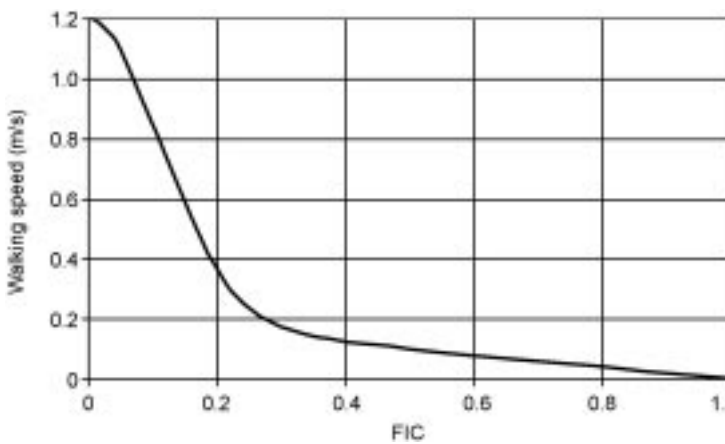
The model is based upon a concept that at low concentrations an increase in irritancy will have a relatively minor effect, as does smoke (for example walking speed in 10 m visibility smoke should be the same as in 100 m visibility smoke). There is then a middle range, over which an increase in irritancy is likely to have large effect on walking speed, and then a point where walking is slow and further increases in irritant concentration have less incremental effect. This



3.20 Estimated relationship between hydrogen chloride concentration and walking speed (average person).

concept is illustrated in Fig. 3.20, which shows predicted unimpeded walking speed as a function of hydrogen chloride concentration. Unlike the situation for non-irritant smoke, the curve reaches a fractional speed of zero at 900–1000 ppm hydrogen chloride. This is because painful effects on vision and breathing are predicted to be of sufficient severity to cause incapacitation and cessation of effective escape movements at this concentration. As discussed it is considered that this will occur at an exposure concentration of around 300 ppm for sensitive members of the population.

Figure 3.21 shows a general case for the effect of exposure to any irritant gas or mixture or irritant gases on walking speed (assuming an unaffected average walking speed of 1.2 m/s). The abscissa show the fractional irritant concen-



3.21 Estimated relationship between fractional walking speed and FIC for any sensory irritant.

tration (FIC), a special case of the FEC describing incapacitation from irritants, where FIC = 1 represents incapacitation (e.g. 900 ppm hydrogen chloride).

An equation for the curve in Fig. 3.21 which can be applied to any individual irritant compound, or to the fractional irritant concentrations for a mixture of compounds, is given by:

$$W_{\text{irr}} = \mathrm{e}^{-(1000x/b)^2} + (-0.2x + 0.2) \tag{3.7}$$

where W_{irr} = walking speed, $b = 160$ and x = FIC. The overall effect of exposure to an irritant smoke on walking speed (W_{sirr}) would then be given by:

$$W_{\text{sirr}} = 1.2 - (1.2 - W_{\text{s}}) - (1.2 - W_{\text{virr}}) \tag{3.8}$$

where W_{sirr} = overall walking speed in irritant smoke, W_{s} = walking speed adjusted for smoke visibility effects and W_{virr} = walking speed adjusted for effects for irritant compounds 1 to n.

3.12 Conclusions

Based upon the irritancy data examined, calculation models investigated and discussions in this chapter and in Chapter 8, it is concluded that irritant acid and organic gases and particulates in fire effluents present significant hazards to fire victims by causing immediate, concentration-related sensory irritancy of the eyes and respiratory tract, resulting in escape impairment or incapacitation if a sufficiently high concentration is inhaled. Exposure to irritants can also cause injury to the eyes and respiratory tract, resulting in oedema and lung inflammation, usually some hours after exposure, which can be fatal. Lung irritant effects occur when a specific exposure dose has been inhaled, with the severity of the inflammation and probability of death increasing with exposure dose.

Although there are uncertainties in the precise exposure concentrations causing escape impairment or incapacitation and the precise exposure doses causing fatal lung inflammation, in human fire victims, the effects are sufficiently serious that they should be considered in safety and hazard evaluations. From a combination of human incident data and experimental data from low level human exposures, and higher level exposures of primates and rodents, it is possible to develop practical hazard calculation models for times to incapacitation and lethality for application to fire hazard assessments. Considerable similarities exist between the effects of inhaled irritants in animals (including primates and rodents) and humans. However, it is important to recognise and make allowances for both inter-species difference, and intra-species variations in susceptibility within the exposed human population.

Based upon these findings with respect to data and model development it is concluded (as stated by Shusterman *et al.*[57]) that for sensory irritant effects, the concentration-related FEC model provides the simplest and most effective method for estimated sensory irritant potency and incapacitating effects for

humans exposed in fire scenarios, while a simple FLD Ct model (or $C^n t$ model) provides the best method for estimating the hazards from post-exposure lung inflammation.

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Appendix A: Comparison of FEC, $C^n t$ and RD models for calculating time to and severity of sensory irritancy in human fire victims during fires

A.1 Different modelling approaches

The purpose of calculation models for sensory irritancy is to provide an estimate of the time during a fire at which an exposed subject is predicted to suffer escape impairment or incapacitation due to eye and respiratory tract pain, visual and breathing difficulties. In previous sections three different possible modelling approaches have been described.

A.1.1 FEC model

The simplest model is the FEC model, whereby sensory irritant effects are assumed to occur immediately upon exposure, with irritant severity expressed in terms of the fraction of the concentration for any individual irritant (or irritant mixtures) considered to cause either escape impairment or incapacitation.

The advantages of this method are:

- Calculation are simple and easy to apply to time-varying fire conditions.
- Used by the ISO for fires and by AEGL for short exposure periods (10 min).
- Provides a good representation of reported human symptoms whereby maximum pain and distress are reported immediately upon exposure to irritants, with severity concentration-related.
- Provides a constant level of irritant potency for a maintained constant irritant concentration, not an increasing degree of incapacitation, as would a $C^n t$ exposure dose model. This also corresponds with human experience and findings in animal experiments including the mouse respiratory rate measurements.
- The calculated irritancy reduces if the irritant concentration decreases, as occurs in practice.
- The model may be slightly conservative in terms of time to effect, since in practice sensation may not be instantaneous, but require a few seconds to develop to the full extent in human subjects.

The possible disadvantage of the model is that it does not allow for any dose-related effects. In practice sensory response to exposure to any constant concentration of an irritant is not instantaneous, but requires a few seconds to develop to its full extent. At low exposure concentrations (less than around a third of the mouse RD_{50} concentration), a longer period (up to a few tens of seconds) may be required for effects to develop to their full extent owing to rate-related phenomena affecting the sensory response. This is evident with the mouse respiratory rate depression reflex as discussed.

A.1.2 $C^n t$ model

The $C^n t$ model is particularly useful for estimating effects that have a dose-related component. For irritants it provides a good fit with rodent data for tissue injury and lethal lung irritant effects over timescales from a few minutes up to several hours. It is not very useful for modelling sensory irritancy because of the following:

- It is somewhat non-conservative during the early stages, since some time is required for a dose to build up for any particular exposure concentration before a Ct exposure dose end point is reached, while in practice irritant effects begin to occur almost immediately.
- For a continued exposure it results in a dose increasing continuously as the exposure continues, implying an increasing severity of effect, which does not occur with sensory irritancy.
- The fit of $C^n t$ models with irritancy data is problematic, as described.

The method is therefore difficult to apply to fire hazard evaluations with respect to sensory irritant effects, although it is recommended for lung irritant effects.

A.1.3 RD models

It is possible to develop RD calculation models to predict respiratory rate depression in mice as shown in Figure A.1. The model used to generate the figure is a logarithmic model typically representing processes in which the time to, and intensity of, a response is determined by rate-related uptake and removal processes. The advantages of applying a model such as this are as follows:

- The model can be used to calculate the percentage mouse respiratory rate depression with time for any constant exposure concentration of an irritant.
- If human sensory response to irritants is assumed to follow exactly the mouse response, in terms of timing and severity, this could in principle be used to predict human sensory response.
- The intensity of effect is on a logarithmic scale, which probably reflects human sensory response.

- The effect plateaus for any specific exposure concentration, as occurs in the mice and as is reported in humans. It does not increase continuously with time as does the $C^n t$ model.

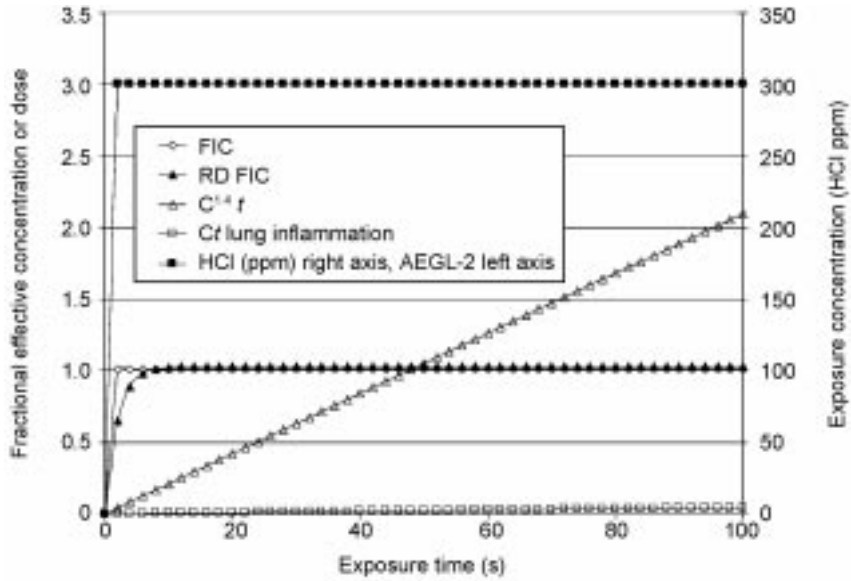
The disadvantages of this approach are as follows:

- The RD response is a reflex, with a specific time-response pattern; this may not reflect either a mouse or human sensory response, which is reported to be very rapid.
- The percentage respiratory rate depression plateaus at a maximum level for any specific irritant, typically between 70 and 85%. This means that as the exposure concentration, and hence the severity of the insult, increases, above a certain concentration this is not reflected by an increase in the mouse response. There are two ways of looking at this. It may be that this reflects the reality of the subjective sensation – in that the intensity of pain and reflex response has a maximum level above which further increases in exposure concentration have no additional effect. Or it may be only that this particular reflex response has a maximum level, since obviously the animal will die if respiration is reduced below a critical level, but that other aspects, such as intensity of subjective pain and other physiological effects continue to increase with exposure concentration. If this is the case, while the respiratory rate depression profile may be useful as an indication of early sensation development, and the RD_{50} concentration may be a useful indicator of exposure concentrations intensely irritant to humans, it may be less useful as an indicator of effects of greater severity at high exposure concentrations.
- Although it is relatively simple to develop algebraic models for predicting time to and extent of rate depression during exposures to different constant concentrations of an irritant, such models do not lend themselves readily to situations with constantly changing exposure concentrations such as occur during fires.

Figures A.1 and A.2 have been prepared in an attempt to illustrate the application of each of these approaches to modelling effects on human subjects in fires.

A.2 Application of models to example case involving exposure to a constant hydrogen chloride concentration

Figure A.1 illustrates a theoretical case involving sudden continuing exposure to hydrogen chloride at a concentration of 300 ppm (approximately the mouse RD_{50} concentration and a concentration predicted to cause escape impairment in the average person or incapacitation of sensitive human subjects). The concentration and effects are calculated assuming they are monitored at 2 second intervals though the exposure. The exposure concentration changes from zero to a plateau of 300 ppm hydrogen chloride at 2 seconds. The FIC also reaches a



A.1 Application of three different models for the prediction of the development and severity of sensory irritation, and one model for lung irritation, for a sudden continuing exposure to 300 ppm hydrogen chloride (HCl on right hand axis).

plateau value of 1 after 2 seconds, indicating immediate and maintained sensory irritancy.

The RD FIC represents the predicted human response, assuming it develops with the same timescale as the mouse respiratory rate depression response. This is achieved by calculating the predicted mouse respiratory rate depression with time and expressing the percentage depression as a fraction of 50. This results in an RD FIC of one at approximately 300 ppm hydrogen chloride. The resulting curve illustrates differences in time to effect of the human response if it were to develop at the same rate as the mouse response, rather than instantaneously as for the FIC model. The results show that the human end point is predicted after 4–8 seconds using the RD FIC model, compared with 2 seconds using the FIC model. Both models then show a continuous maintained degree of irritancy for the remainder of the exposure.

The open triangles show the result of applying the $C^n t$ exposure dose model. This relies on finding a $C^n t$ exposure dose that is relatively constant for a given end point (such as an RD_{50} response or equivalent pain end point) for different exposure concentrations and exposure doses. For hydrogen chloride the best fit to the mouse experimental data was found to be a model using $C^{1.4}t$. This model was then applied to calculate an FED value for the 300 ppm hydrogen chloride exposure concentration. As Fig. A.1 shows, this method provides a poor fit to human experience and the mouse response curve, in that severe irritancy (FED = 1) is predicted only after a delay of 50 seconds. Also, because it is a

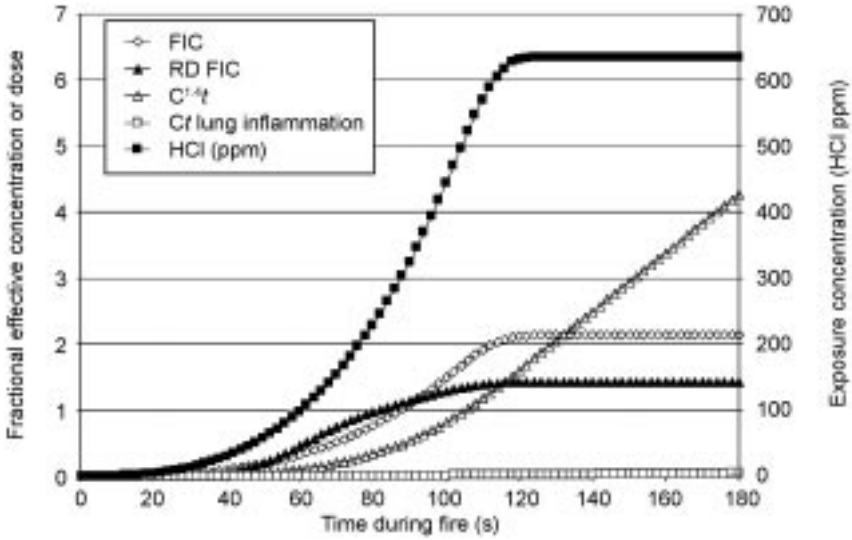
dose-related method, the exposure dose continues to increase throughout the exposure, indicating that the effects would be twice the severity after 100 seconds as they would have been at 50 seconds (FED = 2). In practice, as shown by the mouse experimental data and the human CS exposures, this does not occur.

However, an exposure dose of hydrogen chloride is building up in the lung. This is illustrated as *Ct* exposure dose for lung inflammation (open squares). If this exceeds a threshold exposure dose (FLD) of 1, then there is an increasing probability of post-exposure lung damage and death, and the severity of injury and probability of death really do increase with increasing exposure dose. For this calculation a threshold FLD level is represented by one-tenth of the rat LCt_{50} exposure dose for hydrogen chloride of 114 000 ppm min. This is estimated to be an exposure dose below which death or serious lung injury is unlikely in the average human. In this case a value of $n = 1$, as has been found approximately to fit the experimental rat lethality data. The resulting curve rises at a much slower rate than the $C^{1.4}t$ model curve, but would rise more steeply if a more conservative end point was used (for example a factor of 30 to protect sensitive humans).

It is useful to compare the results for this FLD model with the FEC model. The modelling predicts that for this 'square wave' exposure profile an exposed human subject would experience intense pain and distress within approximately 2 seconds, and a potentially hazardous exposure dose after 38 minutes. It is considered that an approach such as this is superior to the AEGL approach because it shows the timing of these two very different effects on exposed subjects and provides a better basis for estimating time to different hazards, particularly in a fire exposure where other additional hazards occur over different timescales.

A.3 Application of models to a fire case involving exposure to changing hydrogen chloride concentrations

Figure A.2 represents an attempt to illustrate the way hazards develop in a typical fire incident. For this hypothetical example it was assumed that a flaming fire involving PVC grew with a medium scale t^2 fire curve ($Q = 0.011\,72t^2$) in an enclosed room with a volume of 750 m^3. After a period of growth the fire becomes ventilation controlled and then self-extinguishes when the oxygen concentration in the fire room decreases sufficiently. From that time the concentration of fire effluents in the room remains approximately constant. The model shown in Fig. A.2 is a very simple hypothetical representation of such a fire, but the basic profile is similar to those frequently measured in experimental compartment fires (see Chapter 14). For this example the only constituent considered is the hydrogen chloride concentration with time during the fire and the irritant effects on an exposed subject in the room.



A.2 Application of three different models for the prediction of the development and severity of sensory irritation, and one model for lung irritation, for a gradually increasing concentration of hydrogen chloride following a medium t^2 fire curve.

The essential difference between Figs A.1 and A.2 is that in Fig. A.2 the concentration of hydrogen chloride increases in line with the t^2 fire curve and then settles to a steady maintained concentration, as opposed to the step function hydrogen chloride Ct curve in Fig. A.1. As in Fig. A.1, the FIC term in Fig. A.2 increases in the same pattern as the hydrogen chloride Ct curve, with a continuously increasing degree of irritant severity until an FIC of 1 is reached after 88 seconds, at which point significant escape impairment or incapacitation is predicted. The pattern of development of the RD FIC differs somewhat, showing a logarithmic curve, so that an RD FIC of 1 is reached after 82 seconds, which is slightly in advance of the FIC. The reason for this is that since respiratory rate depression is proportional to the logarithm of the exposure concentration, lower concentrations exert a more potent effect than they do for a linear relationship such as that used to calculate the FIC.

This finding is important because it means that in actual fire exposures involving a gradually increasing exposure concentration, the lack of a dose-related element in the FIC calculation does not result in a slightly earlier prediction of time to incapacitation as it does for a step function concentration profile, which means that in practice the FIC method is not overly conservative in terms of calculating time to effect. As in Fig. A.1 the $C^{1.4}t$ curve in Fig. A.2 also lags significantly behind the FIC and RD FIC curves, and then continues to provide an increasing and exaggerated estimate of the irritancy severity even after the hydrogen chloride concentration becomes constant.

The *Ct* lung irritancy curve predicts inhalation of a minimal exposure dose after 180 seconds, from which time the exposure dose correctly continues to increase as the exposure is prolonged, indicating an increasing probability of lung injury and death. Based upon these findings it is concluded (as stated by Shusterman *et al.*[57]) that for sensory irritant effects, the concentration-related FEC model provides the simplest and most effective method for estimating sensory irritant potency and incapacitating effects for humans exposed in fire scenarios, while a simple *Ct* model (or $C^n t$ model) provides the best method for estimating the hazards from post-exposure lung inflammation.

A.4 Basis of RD FIC model

The RD FIC model is a spreadsheet calculation model, which has been developed using the following features:

- The model calculates the respiratory rate depression with exposure time for mice. FIC is then expressed as the percentage respiratory rate depression divided by 50, so that FIC = 1 at the RD_{50} concentration.
- The model is based upon a concept that when mice are exposed to any constant concentration of an irritant, after a finite time an equilibrium is set up between the rate of inhalation of the irritant and the rate of detoxification or removal from the receptor sites (primarily in the nasal cavity). This results in a constant respiratory rate at a maintained level proportional to the log of the exposure concentration (as is observed in practice).
- From the start of the exposure there is a gradual decrease in respiratory rate proportional to the increasing concentration of irritant at the receptor site, which depends upon the same relationship between the rate of uptake and removal.
- The rate of intake is proportional to an exposure dose inhaled over successive short time periods (in this example 2 second periods), which depends upon the exposure concentration and a correction to the volume of air inhaled (V_E) proportional to the fractional decrease in respiration rate (i.e. at 50% respiratory rate depression the rate of uptake is half that at 0% respiratory rate depression).
- The rate of removal/detoxification is proportional to the concentration at the receptor site.
- The concentration at the receptor site is a function of the rate of uptake minus the rate of removal/detoxification.

A spreadsheet model has been set up with these features and used to produce respiratory rate depression curves such as those illustrated in Fig. A.1 for exposures of groups of mice to constant concentrations of individual irritants. A set of constants was then applied to the basic model until a curve was obtained that fitted the experimental respiratory rate depression curve for a group of mice

at a concentration close to the RD_{50} concentration. The calculation model curve was then validated by comparison with the experimental curves obtained for groups of mice at several different constant exposure concentrations of the irritant, and found to provide a good fit in terms of both the predicted steady state percentage respiratory rate depression and the time curve for its development. For the final form of the model the only input variable required is the input *Ct* curve for the irritant gas or fire effluent mixture, while the constants applied vary for each individual irritant species. The version for hydrogen chloride was then used to generate the curves for RD FIC in Figs A.1 and A.2.

Appendix B: Setting tenability limits for irritants

B.1 Setting tenability limits for hydrogen chloride and other irritants

One set of limits developed for dangerous acute exposures in an industrial context by the American Industrial Hygiene Association is the *Emergency Response Planning Guidelines* (ERPG).[64] These are expressed in terms of three limit levels of which two are relevant to survival in emergencies such as fires. These are:

- ERPG-2: maximum levels below which nearly all individuals could be exposed for up to 1 hour without experiencing or developing irreversible or other serious health effects or symptoms that could impair an individual's ability to take protective action
- ERPG-3: maximum levels designed to prevent death

For example with respect to hydrogen chloride:

- ERPG-2 is set at 20 ppm on the basis that >20 ppm would be expected to cause serious eye and respiratory tract irritation (which might impair an individual's ability to take protective action). This reflects the immediate effect of exposure concentration.
- ERPG-3 is set at 100 ppm on the basis that exposure exceeding this level for 1 hour may be expected to produce severe health effects such as pulmonary oedema and possibly death in a heterogeneous human population. This reflects the effect of an exposure dose. The same principle applies to the other irritant gases.

In the context of ability to escape from a fire, the ERPG-2 level of 20 ppm would therefore represent the appropriate tenability limit. This is in fact an order of magnitude more stringent than the design tenability limit proposed here for fire engineering design. It is considered that although 20 ppm hydrogen chloride would be unpleasantly irritant, it would be unlikely to prevent escape from a fire. On this basis the higher concentration of 200 ppm is proposed as a design

Table B.1 Emergency Response Planning Guidelines for common fire irritants

Definition	HCN	HCl	HF	Acrolein	Form-aldehyde
ERPG-3 (ppm) The maximum airborne concentration below which it is believed that nearly all individuals could be exposed for up to 1 hour without experiencing or developing life threatening health effects	25	100	50	3	25
ERPG-2 (ppm) The maximum airborne concentration below which it is believed that nearly all individuals could be exposed for up to 1 hour without experiencing or developing irreversible health effects of other serious health symptoms that could impair an individual's ability to take protective action	10	20	20	0.5	10
ERPG-1 (ppm) The maximum airborne concentration below which it is believed that nearly all individuals could be exposed for up to 1 hour without experiencing or developing other than mild, transient adverse health effects or without perceiving a clearly defined objectionable odour	na	3	3	0.1	1

tenability limit, although it is likely that a proportion of the population might suffer some degree or impairment at lower concentrations as indicated in Fig. 3.19. Table B.1 shows the ERPG levels for some sensory irritants commonly occurring in fire atmospheres.

A more recent set of emergency guidelines has been published between 2004 and 2006 by the US Environmental Protection Agency under the AEGL scheme (Acute Exposure Guideline Levels of Hazardous Substances).[63] In an similar way to the ERPG system, three levels are set, but different exposure durations are also taken into account. The definitions of the different threshold effect levels are shown in Table B.2.

In the context of fire exposures both the AEGL-2 and AEGL-3 could be considered relevant. The AEGL-2 is important with respect to short exposure periods because it predicts impairment of escape capability (sensory irritant effects over short exposure periods), while the AEGL-3 is relevant to the exposure doses that may cause post-exposure injury or death. The AEGL values for different exposure times for hydrogen chloride of up to 1 hour are shown in Table B.3.

Table B.2 Acute Exposure Guideline Levels of Hazardous Substances (AEGL)

AEGL-1 is the airborne concentration of a substance above which it is predicted that the general population, including susceptible individuals, could experience notable discomfort, irritation, or certain asymptomatic nonsensory effects. However, the effects are not disabling and are transient and reversible upon cessation of exposure.

AEGL-2 is the airborne concentration of a substance above which it is predicted that the general population, including susceptible individuals, could experience irreversible or other serious, long-lasting adverse health effects or an impaired ability to escape.

AEGL-3 is the airborne concentration of a substance above which it is predicted that the general population, including susceptible individuals, could experience life-threatening adverse health effects or death.

Table B.3 Acute Exposure Guideline Levels for hydrogen chloride

Classification	10 minutes	30 minutes	60 minutes
AEGL-1 non-disabling	1.8	1.8	1.8
AEGL-2 disabling	100	43	22
AEGL-3 lethal	620	210	100

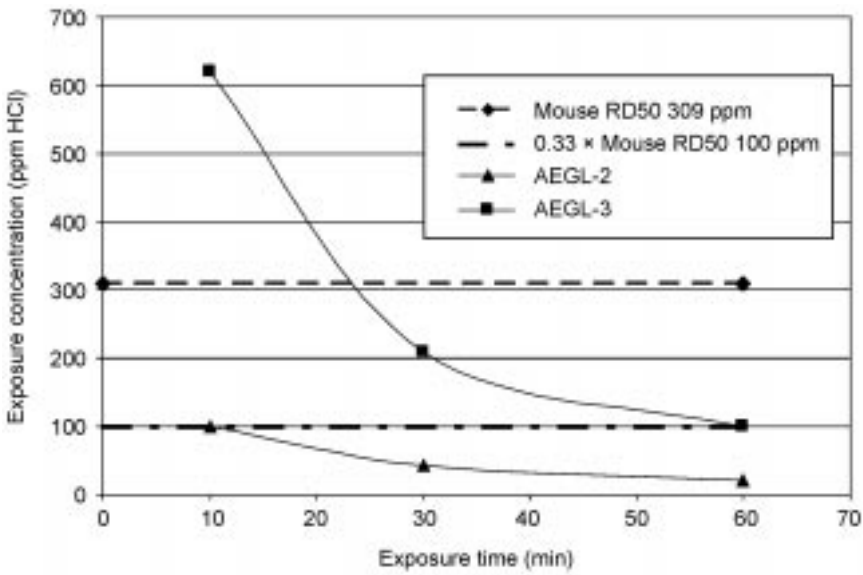
It is useful to consider the rationale used by the expert committee in order to set the AEGL-2 levels for different exposure times.[61] For the longer exposure times of 30 minutes and above the levels were based mainly on evidence of severe pulmonary and nasal histopathology in rats exposed at 1300 ppm for 30 minutes.[41] To these data, the committee then applied several factors to allow for uncertainties in extrapolating to predicted AEGL-2 effects on humans. This therefore represents the application of the precautionary principle – in that they could not be sure that humans would not be severely adversely affected at concentrations above the levels they decided to set. First a factor of 3 was applied to account for the relatively sparse database describing effects defined by the AEGL-2 criteria. Then a further factor of 10 was applied, based upon a factor of 3 to allow for intra-species variability (this would normally be a factor of 10 but only a factor of 3 was used due to the steepness of the concentration response curve), and a further factor of 3 to allow for interspecies variability – rounded to a total factor of 10. For timescaling between 30 minutes and 1 hour a $C^n t$ dose was assumed with $n = 1$, as reported by Ten Berge *et al.*[30] The 10 min level was based not upon dose considerations, but upon the measured RD_{50} concentrations, since over timescales of up to 10 minutes it is the concentration-related sensory irritancy that dominates rather than the dose-related pathological effects. The measured mouse RD_{50} was divided by 3 to obtain a concentration causing irritation,[34] and citing the established relationship between human

irritancy and mouse RD_{50} concentrations.[35] Attention was also drawn to the fact that one-third of the mouse RD_{50} concentration for hydrogen chloride corresponds to an approximate decrease in respiratory rate of 30%, and that decreases in the range 20–50% correspond to moderate irritation.[69]

Other data considered in relation to the AEGL-2 included the baboon escape and pulmonary function studies,[39,67] and the exercising guinea pig studies,[66] the results of which were considered consistent with the AEGL-2 values. Other studies were considered to have produced effects more severe than that defined by AEGL-2 (see page 103 of reference 63).

The AEGL-3 (lethal) values were based upon a 1 hour rat LC_{50} concentration of 3124 ppm,[70] with a factor of 3 used to estimate a concentration causing no deaths. It is stated that this is considered conservative, since no deaths were observed in the studies at 1813 ppm, indicating that the lethality curve is steep, with relatively little variation between animals. An uncertainty factor of 10 was then applied based upon a factor of 3 for interspecies variation and a factor of 3 to protect vulnerable individuals. The values of 10 and 30 minutes were then based upon a $C^n t$ dose model with $n = 1$ as for the AEGL-2.

The effects of the AEGL system are illustrated in Fig. B.1. For disabling concentrations (AEGL-2) the upper limit of 100 ppm is based upon moderate sensory irritation ($0.33 \times RD_{50}$) likely to affect escape capability, which is the dominant effect for periods of up to 10 minutes. For longer exposure periods, the exposure dose posing a danger of lung tissue damage is lower than that causing



B.1 Comparison of AEGL-2 and AEGL-3 and mouse RD_{50} concentrations for hydrogen chloride over timescales of up to 1 hour.

sensory irritancy, so the maximum exposure dose then decreases with increasing exposure time. For the AEGL-3, lethal effects occur for short exposures at concentrations considerably higher than the RD_{50} of 309 ppm, but for exposure times exceeding around 20 minutes potential lethality is predicted at progressively lower concentrations, so that for a 1 hour exposure the predicted lethal risk occurs at 0.33 times the RD_{50} concentration.

Another emergency response level is the IDLH standard of the NIOSH.[65] This represents the maximum concentration from which one could escape within 30 minutes without any escape-impairing symptoms or irreversible health effects, and the IDLH value for HCl is 50 ppm. This is based not upon extrapolation from animal data but reported acute effects on humans.

Table B.4 compares the lethal and incapacitating concentrations for the different emergency guidelines for different exposure times from the three authorities. Also shown is the guidance for application to ASET calculations for fire hazard analysis and fire engineering design. The first set, developed by Purser, is in the *SFPE Handbook of Fire Safety Engineering*[5] and in British Standard BS7972 part 2.[68] For this method, guidance for application to ASET calculations is presented separately for effects causing sensory irritancy and effects causing post-exposure pathology and death. For most fires there is a critical period of a few minutes available for escape, so that immediate effects

Table B.4 Comparison of ERPG, AEGL, IDLH, SFPE and ISO guideline for different emergency threshold levels

Emergency planning level or end point	Human population considered	Exposure period (minutes)		
		10	30	60
ERPG-3 lethal	Includes susceptible			150
AEGL-3 lethal	Includes susceptible	620	210	100
SFPE lethal	Average	11 400	3800	1900
SFPE lethal	Includes susceptible	3 762	1254	627
ERPG-2 escape impaired/ health effects	Includes susceptible			20
AEGL-2 escape impaired/ health effects	Includes susceptible	100	43	22
IDLH escape impairment/ health effects	Includes susceptible		50	
SFPE/BS7899-2[61] incapacitation	Average	900	900	900
SFPE incapacitation	Includes susceptible	300	300	300
SFPE escape impaired	Average	200	200	200
SFPE escape impaired	Includes susceptible	66	66	66
ISO/13571 incapacitation	Average	1000	1000	1000
ISO/13571 incapacitation	Includes susceptible	330	330	330

on escape capability are considered especially important, although exposures over periods of up to an hour or more can occur in trapped victims. Dose-related respiratory tract damage normally occurs after exposure, as discussed.

For sensory irritancy, two FEC threshold levels are distinguished: concentrations considered capable of causing significant impairment of escape capability and concentrations considered capable of causing incapacitation (effective cessation of escape movements). For hydrogen chloride it is proposed that 200 ppm (chosen as two-thirds of the mouse RD_{50} concentration, but also taking into account the baboon data) is likely to cause significant impairment of escape capability in the average person, while 900 ppm is likely to result in incapacitation. These sensory irritant effects remain approximately constant throughout the exposures, so there is no change with exposure time. It is also recommended that in order to allow for variations in sensitivity in the human population a factor of three should be used, providing design limits of 66 ppm for escape impairment and 300 ppm for incapacitation. The figures of 200 ppm and 66 ppm for escape impairment are therefore comparable with the AEGL-2 10 min escape impairment value of 100 ppm, but somewhat higher than AEGL-2, ERPG-2 and IDLH values designed to cover longer exposure times of up to 60 min, all of which bring in elements designed to protect from lung injury, which is not addressed in the SFPE FEC value.

The SFPE FLD of 114 000 ppm min is the rat LCt_{50} (representing 3800 ppm for a 30 min exposure). This uses the same basic method of derivation as the AEGL-3, but does not provide any adjustment for uncertainty or interspecies differences. As with the FEC, a factor of 3 would be applied to allow for variation within the human population. The FLD approach is therefore considerably less conservative than the AEGL-3 and ERPG-3 levels, and was originally intended more to predict likely outcomes than to set a safety level for prevention of post-exposure lethality due to lung damage. It is notable that the approximate lethal exposure dose of hydrogen chloride for baboons was around 80 000 ppm min for a 5 min exposure.

In order to allow for threshold levels in rats a factor of 3 might be applied, with a further factor of three to allow for interspecies differences. Rounding this to a factor of 10 and applying to the SFPE LCt_{50} would give a maximum design exposure dose of 11 400 ppm min for the average person and 3800 ppm min allowing for the range of sensitivity within the human population. This then gives a maximum exposure concentration of 127 ppm for a 30 min exposure or 760 ppm for 5 min. The SFPE method also recognises the likely contribution of inhaled irritants to overall asphyxiant hypoxia during exposure to fire effluents, so the FLD value is applied as an additive factor with the effects of asphyxiant gases such as carbon monoxide and hydrogen cyanide (see Chapter 4). The hypoxic effects of irritants are demonstrated by the reductions in arterial P_{O_2} in baboons observed by Kaplan *et al.* during hydrogen chloride inhalation.[67]

ISO 13571 is also designed for application to fire hazard assessment ASET calculations. The concentration predicted to cause incapacitation in the average person is 1000 ppm, which is similar to that of 900 ppm in the SFPE method, but this is intended as the sole criterion for escape impairment, so is therefore considerably less conservative than the SFPE, or AEGL-2 values. Since the intention of the standard is to cover escape capability only, potential post-exposure lung inflammatory effects are considered beyond its scope.

Overall it is considered that examination of the available data and approaches used by different authorities is supportive of the position adopted for the SFPE, such that hydrogen chloride concentrations in the 66–200 ppm range are likely to cause significant impairment of human escape attempts, while 300–900 ppm are likely to result in incapacitation. Although it is recognised that baboons were able to escape from an exposure chamber at much higher concentrations, it is considered that this task was much simpler than that involved in the evacuation of large and crowded buildings, and also that the training and repeated exposures involved are likely to have improved performance and induced a degree of tolerance.

B.2 Setting tenability levels for irritants commonly found in fire effluents

The general effects and considerations applying to HCl are considered also to apply to other water-soluble acid gases commonly found in fire effluents (HF, HBr, SO_2, H_3PO_4) and also to organic irritants such as acrolein and formaldehyde. An example of a data set and treatment of acrolein is shown in Table B.5.

Acrolein has a considerably greater sensory irritant potency than hydrogen chloride, with a mouse RD_{50} concentration of 1.7 ppm.[35] The ratio between the concentration causing severe irritation and the exposure concentration causing lung oedema and inflammation is higher at a ratio of 91, so that short exposures to painfully irritant concentrations should be less damaging to the respiratory tract than equivalent concentrations of hydrogen chloride.[39,48,49] Concentrations reported as being strongly irritant to humans are in the range 0.4–1 ppm, with around 5.5 ppm being reported as severely painful.[45,48] On the basis of the human and mouse data, the SFPE concentration predicted to cause escape impairment in fire victims has been set at 4 ppm for the average person (1.33 to protect susceptible individuals),[5,68] which is higher than the proposed AEGL-2 of 0.44 ppm,[71] while incapacitation is predicted at around 20 ppm for the average person. This compares with an ISO 13571 value of 30 ppm for incapacitation/escape impairment, which is much less conservative.[37] As with hydrogen chloride, a complication with acrolein is the results of baboon escape experiments following 5 min exposures, with animals performing successful escapes at up to 1025 ppm and no pulmonary damage post-exposure at 505 ppm.

Table B.5 Irritant effects of exposure to acrolein

ppm	Effect
0.1	Odour threshold and OEL
0.44	AEGL-2 escape impairment and health effects – susceptible person[71]
1	Strongly irritant to the eyes and nose in humans[45,49]
1.7	Mouse RD_{50} concentration[35]
2.5	AEGL-3 30 min
4	SFPE escape impairment (average person)
5.5	Severely painful eye and respiratory tract irritation
>10	Suggested as being potentially lethal to humans after a short exposure
20	SFPE incapacitation (average person)
30	ISO/13571 incapacitation (average person)
135	30 min rat LC_{50}
505	Baboon: no pulmonary effects following 5 min exposure[39,67]
1025	Baboon: death occurring following 5 min exposure[67]

As for hydrogen chloride, the baboon data were taken into account when setting the SFPE and ISO levels, but these experiments were considered unrepresentative of escape hazards encountered by people during building fires.[39]

Table B.6 shows the concentrations for different irritant gases for predicted escape impairment, incapacitation and death after 30 min for the average person recommended for fire hazard ASET analysis in the *SFPE Handbook*.[5] The 10 min AEGL-2 and 30 min AEGL-3 values are shown for comparison.[36] As with hydrogen chloride and acrolein, the escape impairment levels (corrected for susceptible persons by a application of a factor of 3) are generally comparable

Table B.6 SFPE/BS7899-2, ISO13571 and AEGL guidelines for escape impairment and incapacitation

	SFPE escape impaired	SFPE	ISO 13571	SFPE 30 min lethal	AEGL-2 10 min escape impairment	AEGL-3 30 min life threatening
		Incapacitation				
HCl	200	900	1000	3800	100	210
HBr	200	900	1000	3800	100	250
HF	200	900	500	2900	95	62
SO_2	24	120	150	400–1400	0.75	30
NO_2	70	350	250	63	20	25
NO	–	>1000	–	~1000	–	–
CH_2CHO (acrolein)	4	20	30	150	0.44	2.5
HCHO (formaldehyde)	6	30	250	750	14	70

with the AEGL-2 values, while the 30 min lethal values are considerably less conservative.

B.3 Irritant effect of exposure to fire effluents

The SFPE concentrations for individual irritant gases in Table B.7 are used in the fire hazard FED ASET calculation model. However, it is also relevant to consider the irritant effects of exposures of mice and macaque monkeys to actual irritant fire effluent mixtures. The mouse RD_{50} concentrations for fire effluent mixtures from a range of materials decomposed under oxidative thermal decomposition conditions, and the effects on physiological and behavioural effects on primates are described in a previous section of this chapter and in Chapter 8. In this section the implications for tenability limits for the irritant effects of exposure to thermal decomposition products from polypropylene are considered.

The data are summarised in Table B.7. Primates were exposed in a chair by facemask while their respiration was measured, or in a behavioural chamber where their ability to perform an operant conditioned task was measured during exposure.[5] The basic finding was that the behavioural performance disruption and effects of respiration were relatively minor at effluent concentrations of up to 10 times the mouse RD_{50} concentration, although as the concentration was increased over the range 1–8 mg polypropylene/litre the signs of respiratory tract irritancy became much more severe, with signs of lung oedema and a fatality occurring at 6 and 8 mg/l.[22] Similarly, in another study Potts and Lederer[72] exposed mice and humans simultaneously to smoke from the pyrolysis of red oak (mouse RD_{50} 0.37 mg/l). At this concentration the smoke was barely visible and all human subjects reported that although the smoke was unpleasant and

Table B.7 Comparison of irritant effects of thermal decomposition products from non-flaming oxidative decomposition of polypropylene[5,22]

Species	Concentration (mg/l)	Effect
Mouse	0.1	RD_{50}
Macaque	0.9	Slight disruption of behavioural task performance
30 min	1.1	Pulmonary irritation – hyperventilation
exposures	1.85	Eye irritation and mild behavioural task performance disruption
	4.0	Lung irritation preceded by hypoventilation
	6.0	Stronger irritancy, nasal and pulmonary inflammation some hours later
	8.0	Strong irritancy during exposure – died from lung inflammation overnight

irritating in no sense were they physically incapacitated, and they were quite capable of performing tasks such as threading together nuts and bolts of various sizes.

These polypropylene and wood atmospheres are rich in irritant organic species, including a range of aldehydes, so it is to be expected that human exposure would be most unpleasant at the mouse RD_{50} concentration. Based upon the findings of these studies it seems that for some thermal decomposition product atmospheres containing organic irritants, mice may be somewhat more sensitive to the irritant effects than primates including humans.

B.4 Concentration–effect and dose–effect levels for sensory and lung irritants

As stated, for sensory irritancy, the severity of the signs and symptoms increase continuously as a function of concentration, the best fit is apparently that severity is proportional to the logarithm of the exposure concentration, possibly with an upper limit beyond which further increases in concentration may result in little or no further increase in pain sensation. With regard to the lethal dose-related effects of respiratory tract and lung inflammation, two considerations are the threshold for serious injury compared with that for deaths, and the steepness of the mortality curve for groups of animals (the extent to which sensitivity to lethality is spread over a range of dose levels). For rats, severe histopathological damage was found following 1300 ppm hydrogen chloride over 30 min,[41] while 10% mortality occurs at around 2600 ppm and the LC_{50} is 3715 ppm.[28] There appears to be a relatively high threshold for histopathological damage and a steep lethal dose-response curve. In another study, Anderson and Alarie[73] reported a 30 min LC_{50} value of 10 137 ppm for normal mice and a value of 1095 ppm for trachea-cannulated mice. Similarly, when baboons were exposed for 5 min to 11 400 ppm no serious post-exposure effects were reported, while exposures at 16 570 and 17 290 resulted in deaths.[39] When baboons were exposed to 5000 and 10 000 ppm for 15 min (approximately equivalent to 15 000 and 30 000 ppm for 5 min), all survived, with relatively minor lung damage following 5000 ppm exposures and more severe effects following 10 000 ppm.[39] When macaque monkeys were exposed for 30 min to non-flaming thermal oxidation products from polypropylene, post-exposure signs were minor up to 6.3 mg/l, more severe following 6.9 and 7.3 mg/l and fatal flowing 8 mg/l.[22]

These data indicate that for lung inflammation and oedema, effects tend to be relatively minor up to a threshold concentration above which there is a narrow range between exposure doses resulting in significant injury and lethal exposure doses, so that serious injury and death may be a low probability at exposure concentrations approximately 3 times lower than the LC_{50} concentration for a particular irritant.

4

Asphyxiant components of fire effluents

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Abstract: Asphyxiant gases are the main causes of incapacitation (loss of consciousness) and death in fires, inducing tissue hypoxia by inhibiting the supply or use of oxygen in the tissues. The main fire asphyxiants are carbon monoxide and hydrogen cyanide, with contributions from oxygen depletion and minor asphyxiant effects from nitrogen oxides and irritants. In this chapter the mechanisms of uptake of oxygen and asphyxiant gases from the lungs, their carriage and effects on the blood, causative mechanisms of hypoxia, and effects on different target organs are described. Methods are described for calculating the effects of each gas in terms of time and doses to incapacitation and death individually and when present in mixtures in sedentary and active subjects, as well as post-exposure effects and washout calculation methods for forensic applications.

Key words: asphyxiant, fire gases, carbon monoxide and hydrogen cyanide in fire victims, hypoxia, carbon dioxide and hyperventilation, mechanisms of toxicity of cyanide and carbon monoxide, blood cyanide and methaemoglobin.

4.1 Introduction

The main cause of death in fires is exposure to asphyxiant gases. These gases cause incapacitation (loss of consciousness) due to tissue hypoxia, in that there is insufficient oxygen in the body tissues to maintain normal function. The most important asphyxiant gases in fire effluents are carbon monoxide and hydrogen cyanide, while hypoxia from oxygen-depleted atmospheres can also be important, especially during later stages of exposure. Carbon dioxide (CO_2) stimulates breathing, which increases the rate of uptake of other toxic gases, although at concentrations above approximately 7% CO_2, it also causes direct narcotic effects which can lead to loss of consciousness. Other gases having a minor influence are nitrogen oxides and irritants.

In this chapter the mechanisms of uptake of oxygen and asphyxiant gases from the lungs, their carriage and effects on the blood, causative mechanisms of hypoxia, and effects on different target organs are described. Methods are described for calculating the effects of each gas in terms of time and doses to incapacitation and death. The physiological interactions between the different gases in mixtures are then considered, and methods for calculating the overall effects of gas mixtures.

4.2 Asphyxia, hypoxia and asphyxiant fire gases

4.2.1 General

The toxic fire gases that cause death directly are usually the asphyxiant gases:[1] carbon monoxide (CO), hydrogen cyanide (HCN) and carbon dioxide (CO_2), combined with a reduction in oxygen (O_2) concentration. To a lesser extent nitrogen oxides (nitric oxide NO and nitrogen dioxide NO_2) and irritant gases may also contribute to asphyxia.

Asphyxia represents a cessation of breathing, or in more general terms any state in which the body tissues become deprived of oxygen. The main effect of inhalation of these gases is to cause tissue hypoxia, which, when it develops to a sufficient degree, results in loss of consciousness followed by death. Asphyxia (or hypoxia) is the main direct cause of death in fire victims. Sometimes these fire gases are described as narcotic gases since their effects include a state of narcosis (a condition of deep stupor or unconsciousness produced by a drug or other chemical substance).

The major functions of the lungs and blood circulation system are to obtain and carry sufficient oxygen to the tissues to support tissue respiration and remove carbon dioxide. Each of these gases interferes with these processes by different mechanisms, resulting in tissue hypoxia and/or hypercapnia (an elevated blood CO_2 partial pressure [P_{CO_2}]).

The main purpose of this chapter is to consider the development of fractional effective dose (FED) calculation models for evaluation of hazards from asphyxiant fire gases in terms of time to incapacitation or death. In order to achieve this it is necessary to understand the effects of each asphyxiant gas individually and the interactions between the different gases in fire effluent mixtures.

Tables 4.1, 4.2 and 4.3 summarise the main sites of action and effects resulting in hypoxia during exposure to fire effluent mixtures. The first considerations with respect to the uptake and effects of asphyxiant gases and development of hypoxia are effects on the lung and breathing, in particular effects on the volume of air inhaled each minute (minute volume, V_E). Anything that tends to increase the volume of air inhaled each minute during a fire increases the rate of uptake of any asphyxiant gases present and shortens the time to incapacitation. People tend to increase their respiration somewhat when anxious, but the major factors increasing respiration are the level of physical activity and the inhaled carbon dioxide concentration. Respiration is driven by the arterial partial pressures of carbon dioxide, oxygen and pH. The main parameter is the pH in the blood and cells of the peripheral chemoreceptors (carotid and aortic bodies) and the central chemoreceptors in the brain's medulla (responsible for 78% of the response to carbon dioxide).[2] Increases in P_{CO_2} or decreases in P_{O_2} lead to decreases in extracellular and intracellular pH, which stimulates respiration. The main driver for respiration is P_{CO_2}. Increases in

Table 4.1 Effects of anxiety, exercise and inhaled fire gases on gas exchange in the lungs

	Primary effect	Consequence	Effect on oxygen uptake in lungs
Anxiety	Increases V_E	Increased uptake of all gases	**Improved:** oxygen uptake
Exercise	Increases V_E	Increased uptake of all gases	**Improved:** oxygen uptake
Inhaled CO_2	Increases V_E	Increased uptake of all gases	**Improved:** displaces oxygen so reduced oxygen partial pressure, but improved oxygen uptake due to hyperventilation
Lower % O_2 in inhaled air	Some increase in V_E	Increased uptake of all gases	**Reduced:** decreased oxygen uptake, direct hypoxia sudden exposure to very low levels actually removes oxygen from venous blood
Inhaled CO	No immediate effect	CO uptake depends on V_E, CO ppm and %COHb	**None at first then reduced**: no effect until loss of consciousness reduces V_E
Inhaled HCN	Increases V_E after a few minutes depending on inhaled concentration	HCN uptake depends on V_E and HCN ppm	**Increased-reduced**: increased initially, then decreased
Inhaled NO	No immediate effect	Uptake depends on V_E and NO ppm	**No significant effect:** at low levels opens airways[3]
Inhaled irritants	Breath holding then increases in V_E: in primates transient decrease in V_E followed by an increase after a few seconds. In rodents maintained decrease during exposure to sensory irritants	Broncho-constriction, ventilation–perfusion imbalances. In primates no increase in uptake of gases, can be some direct hypoxia due to adverse effects on gas exchange. In rodents reduced V_E reduces uptake of all gases	**Reduced:** reduced V_E in rodents induces tolerated hypoxia and reduced uptake of other gases. In primates increased V_E, but inefficient gas exchange reduces oxygen uptake

Table 4.2 Blood gas parameters: normal and minimal for cerebral oxygen supply to prevent loss of consciousness

Respiratory parameter	Normal values/ranges	Minimal conditions for adequate cerebral oxygen supply
Arterial		
pH	7.40	
P_{CO_2} mmHg[a]	40.0 (36–44) 80 maximum	
P_{O_2} mmHg[a]	100 (80–100)	29
Haemoglobin saturation %	97.5	57.0
Cerebral venous		
pH	7.367	
P_{CO2} mmHg[a]	46.0	
P_{O2} mmHg[a]	33	20
Haemoglobin saturation %	63.0	32
O_2 capacity ml/100 ml	20	
O_2 consumption ml/min	46	
Cerebral blood flow ml/min	620	868
O_2 arterial/venous difference ml/100 ml	7.4	5.3

[a] Atmosphere pressure = 760 mmHg

physical activity increase the amount of carbon dioxide produced in the body, which increases P_{CO_2} and stimulates respiration (respiratory acidosis). Anaerobic respiration (especially in voluntary muscles) releases lactic acid, which further stimulates respiration (metabolic acidosis).

Table 4.2 illustrates some blood gas parameters. Under normal resting conditions the arterial P_{CO_2} is 40 mmHg (which can rise to 50 mmHg during breath holding) and pH 7.40. Inhaled oxygen concentration in dry air is 20.95% (P_{O_2} is 159 mmHg) but as it enters the lungs the partial pressure decreases due to humidification (saturation at 37 ºC, partial pressure of water vapour 47 mmHg) and mixture with residual oxygen-depleted air in the lungs. There is also a small gradient between the alveolar gas and the maximum concentration in the lung capillaries. The resulting maximum oxygen partial pressure in the blood leaving the lungs is 100 mmHg, resulting in 97.5% haemoglobin saturation (i.e. 97.5% of haemoglobin in the form of oxyhaemoglobin). The level of saturation varies somewhat depending upon factors such as age, health status and level of physical activity, with a minimum of around 80 mmHg in young adults (or 70 mmHg above age 60). The P_{CO_2} of 40.0 represents a concentration of 5.51% in dried end-expiratory alveolar air (the portion of exhaled air from the alveolae, after removal of water) (~3.8% in mixed expired air, containing both unexchanged air exhaled first and alveolar air subsequently exhaled). The maximum tolerable P_{CO_2} level is approximately 80 mmHg, above which severe

Table 4.3 Effects of inhaled fire gases on gas exchange in the blood and oxygen delivery to the tissues

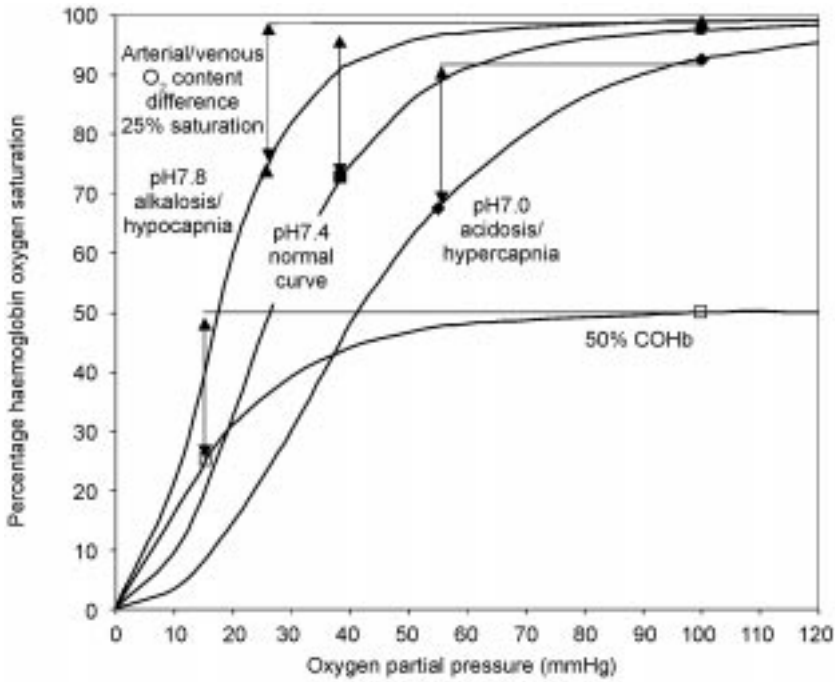
Gas	Blood effects	Mechanism	Effect on oxygen delivery to tissues
Oxygen	Blood oxygen rapidly in equilibrium between inhaled partial pressure, air volume and rate of consumption in tissue	Haemoglobin: high affinity for oxygen, stores and transports from lungs to release in tissues; oxygen dissociation curve ensures efficient delivery to tissues unless inhaled O_2 less than around 10–12% O_2	Normal: arterial P_{O2} 100 mmHg, cerebral venous P_{O2} 33 mmHg Minimal: arterial P_{O2} 36 mmHg cerebral venous P_{O2} 20 mmHg
CO_2	Reduces blood pH	Right shift of oxygen dissociation curve and reduces blood pH (respiratory acidosis) Normal arterial blood P_{CO2} 40 mmHg, pH 7.40 Normal venous blood 46 mmHg, pH 7.367	Main effect is to increase tissue O_2 and decrease hypoxia, increased cerebral blood flow, but increased acidosis toxic at high concentrations
CO	Takes minutes–hours to reach equilibrium with inhaled CO partial pressure Forms carboxyhaemoglobin: 200–250 times more affinity for Hb than oxygen	Left shift of Hb dissociation curve Haemoglobin: much higher affinity for CO than for oxygen, so oxygen displaced Metabolic acidosis at high exposure doses	CO causes hypoxia by two main mechanisms: 1. Displaces oxygen from HbO_2 forming COHb, so reduces amount of oxygen carried in the blood 2. Reduces ability of Hb to release remaining O_2 in tissues (left shift of oxygen dissociation curve)
HCN	Accumulates in blood plasma, extracellular and intracellular fluid spaces but also combines weakly with haemoglobin and partly detoxified by reaction with methaemoglobin forming cyanomethaemoglobin	Plasma concentration depends upon interactions between rate of uptake from lungs, binding with haemoglobin and dispersal in to different body fluid compartments	Carried in blood plasma to tissues. Has no direct effect on oxygen carriage in the blood, but prevents consumption of oxygen in the tissues, so oxygen accumulates in the blood
NO_x	Inhaled NO and NO_2 react with haemoglobin to form methaemoglobin 1500 times greater affinity for Hb than oxygen	Methaemoglobin cannot carry oxygen so the oxygen-carrying capacity of the blood decreases in proportion to the % methaemoglobin	Direct hypoxic effect by reducing the amount of oxygen carried in the blood.

adverse effects occur on a range of physiological parameters including impaired cerebral function.

The concentrations of gases in the body tissues in the case illustrated, the cerebral tissues, are best represented by the venous blood which, under normal conditions is maintained with a P_{O_2} of 33 mmHg representing a saturation level of 63%, while the P_{CO_2} is increased to 46.0 and the pH decreases to 7.367.

The normal venous blood oxygen saturation of 63% illustrates an important point, that body physiology is very resistant to hypoxia and that there are a number of reserves and compensatory mechanisms available to resist it. The result of this is that as the oxygen supply becomes reduced for any reason, the effects on normal function are generally minor until the compensatory mechanisms are overcome, whereupon a sudden dramatic decline in function occurs. The organ most sensitive to hypoxia is normally the brain, which unlike other organs has minimal metabolic reserves and must function normally at all times if consciousness is to be maintained. If the oxygen supply to the brain decreases below minimum levels, loss of consciousness can occur within seconds. The minimum conditions required to maintain normal cerebral function are shown in Table 4.2. The key parameter is the cellular oxygen partial pressure (P_{O_2}) (which is almost identical to the venous oxygen partial pressure), for which the minimum level required to maintain consciousness is 20 mmHg oxygen. In addition to the reserves of oxygen in the blood, a major compensatory mechanism during hypoxia is an approximately 40% reflex increase in cerebral blood flow. In order to maintain the 46 ml/min of oxygen required for cerebral function at an increased cerebral blood flow of around 868 ml/min, the minimum arterial oxygen partial pressure is 29 mmHg (representing 57% oxygen saturation). This means that most people can tolerate hypoxia due to low inhaled oxygen concentrations down to around 11% inspired oxygen without suffering serious effects, or even lower in some situations. Table 4.3 summarises the effects of the different asphyxiant gases on the blood and on oxygen delivery and consumption in the tissues.

A complication with regard to oxygen carriage and delivery of oxygen in the blood is the effect of carbon dioxide on the oxygen dissociation curve. This is illustrated in Fig. 4.1. A decrease in blood pH due to the presence of CO_2 causes a rightward shift in the dissociation curve and increases in pH a leftward shift. Under normal conditions this slightly enhances oxygen delivery to the tissues, since the pH is lower in venous blood than in arterial blood. When air containing a low oxygen concentration is inhaled, resulting in hyperventilation, the excretion of carbon dioxide via the lungs is increased, causing respiratory alkalosis (increased blood pH), which results in a leftward shift in the dissociation curve and a lower venous P_{O_2}. This thereby worsens the hypoxia so that subjects inhaling 10% oxygen suffer significant impairment of consciousness. Certain fire suppression systems flood the fire with inert gas. In some cases carbon dioxide is added to provide 5% CO_2 in combination with approximately 10% O_2 in the inhaled air to prevent asphyxiation to anyone inhaling the fire suppression



4.1 Haemoglobin–oxygen dissociation curve showing the effects of differences in pH resulting from hypocapnia or hypercapnia (or metabolic acidosis), and the effects of 50% COHb saturation. Assuming an arterial–venous difference of 25% oxygen saturation for each case, the normal curve at pH 7.4 provides a venous P_{O_2} of 40 mmHg. A respiratory alkalosis (pH 7.8) provides a left shift venous P_{O_2} of 25.7 mmHg and a respiratory acidosis a right shift venous P_{O_2} of 55 mmHg. At 50% COHb a venous P_{O_2} of 15 mmHg is required to deliver a 25% oxygen saturation decrease. The acidosis and 50% COHb cases therefore provide inadequate levels of oxygen partial pressure to support normal cerebral function (data from Nunn[2]).

gas during accidental releases. This results both in an increased degree of hyperventilation and in acidosis, providing a rightward shift of the dissociation curve, with the result that exposed subjects were able to perform normally with no significant impairment of cerebral function.[4,5] During fires, any decrease in inhaled oxygen is replaced by an approximately equivalent increase in carbon dioxide. This inhaled carbon dioxide therefore improves the uptake and delivery of available oxygen during exposure to fire effluents.

The haemoglobin oxygen dissociation curve and some parameters affecting it are shown in Fig. 4.1. The curve is designed to maximise delivery of oxygen to the tissues at lower oxygen partial pressures. Under normal conditions the decrease in saturation between arterial and venous blood is around 25%, which delivers 5 ml oxygen to the tissues per 100 ml blood. This results in a venous oxygen partial pressure of around 40 mmHg. If the blood pH increases to 7.8 due

to hyperventilation and respiratory alkalosis, resulting in a left shift of the dissociation curve, the venous partial pressure must decrease to around 25.7 mmHg to deliver the same volume of oxygen. This partial pressure is below the minimum required for normal cerebral function. A respiratory or metabolic acidosis shifts the curve to the right, resulting in a higher venous P_{O_2}. At 50% COHb the maximum blood oxygen saturation is 50%, so if this decreases to 25% oxygen saturation, the venous P_{O_2} will be around 15 mmHg, which is much too low to support normal cerebral function (see Section 4.4).

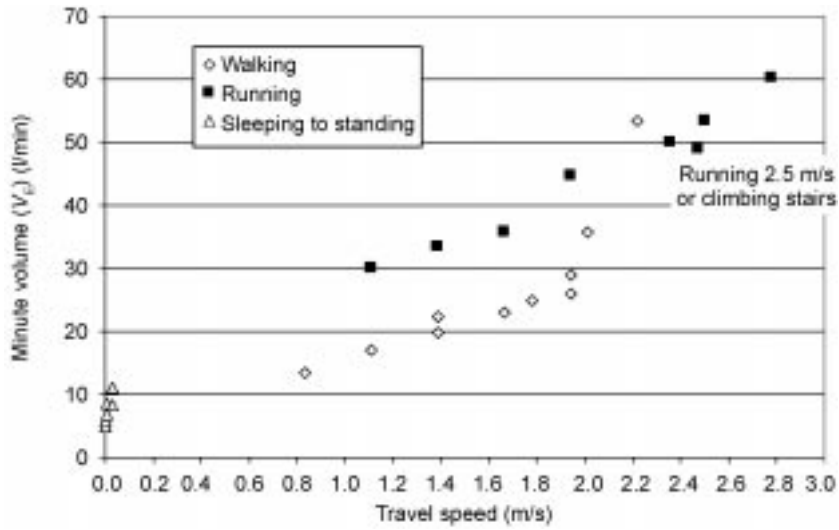
4.2.2 Effects of exercise

During exposure to fire effluent the level of physical activity has a significant effect on the respiratory ventilation (and hence the rate of uptake of toxic fire gases) and the sensitivity to hypoxia. This is illustrated in Table 4.4, which shows the rate of oxygen consumption (V_{O_2}) and minute volume (V_E) for various activities and physical work rates.[6–8]

Table 4.4 Work rate, oxygen consumption and minute ventilation for different activities (for ~70 kg body weight)

Activity	Speed (km/h)	Work (kcal/min)	Work (watts)	V_{O_2} (l/min STPD[a])	V_E (l/m ATPS[b])
Sleeping and lying, includes turning over, getting up	0	1.1	77	0.22	4.9
Resting	0	1.26	88	0.252	5.6
Sitting, includes reading, eating, desk work	0	1.5	105	0.3	6.7
Sitting	0	1.9	133	0.38	8.5
Standing	0	1.875	131	0.375	8.4
Standing, includes activities such as moving between rooms	0	2.5	174	0.5	11.2
Walking, outdoors, and other activities	3	3	209	0.6	13.4
Walking	4	3.8	265	0.76	17.0
Walking	5	4.45	311	0.89	19.9
Light industry	5	5	349	1	22.3
Walking	6	5.15	359	1.03	23.0
Walking	6.4	5.6	391	1.12	25.0
Walking	7	5.8	405	1.16	25.9
Manual labour	7.24	8	558	1.6	35.7
Running	5.6	11.2	782	2.24	49.9
Running, climbing stairs, heavy manual work	8.9	11	768	2.2	49.0

[a]STPD = Standard temperature (0 °C) and pressure (760 mmHg) dry
[b]ATPS = Ambient temperature and pressure saturated

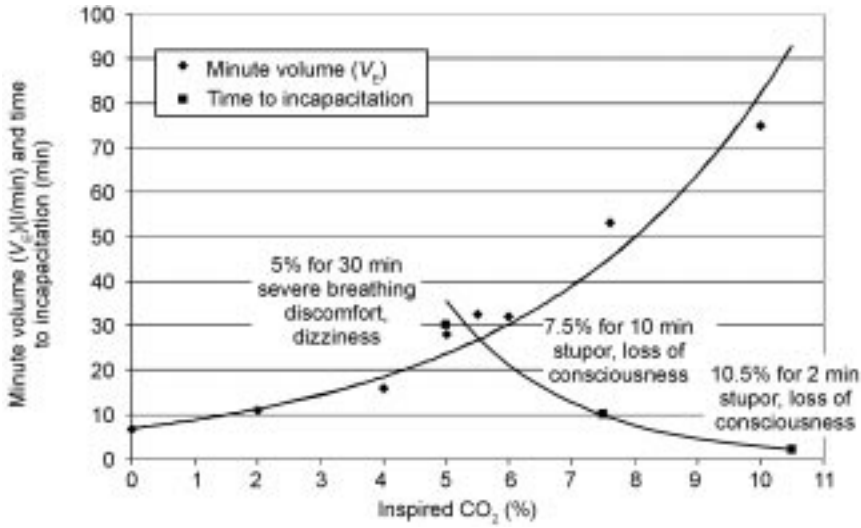


4.2 Relationship between travel speed and respiratory minute volume.

The general effects are illustrated in Fig. 4.2. For a stationary adult person (~70 kg body weight) V_E varies between approximately 5 and 5.5 l/min while sleeping or resting to 11 while standing (including activities such as moving occasionally between adjacent rooms in a dwelling). Average unrestricted travel speed for evacuating building occupants is approximately 1.2 m/s, and at this walking speed ventilation is increased to approximately 19 l/min, which is more than three times that of a resting person. Under conditions involving heavier physical work such as climbing stairs, the ventilation is increased to around 50 l/min. These differences will obviously have a significant effect on a fire victim. During early stages of exposure, perhaps while asleep, the ventilation may be at resting levels. Once a subject responds to an alarm and starts to evacuate the building, the combination of anxiety and increased physical exercise results in a considerable increase in ventilation and therefore an equivalent increase in the rate of uptake of toxic gases such as carbon monoxide. Since resting V_E is inversely proportional to body size, V_E per kg body mass is greater for children than for adults, which results in even greater rates of uptake of toxic gases, approximately in proportion to the relative body surface area/body mass ratios.

4.2.3 Effects of inhaled carbon dioxide

Similarly, the presence of inhaled carbon dioxide can provide a considerable stimulus to ventilation. This is illustrated in Fig. 4.3, which shows the relationship between inhaled carbon dioxide concentration and V_E. The equation for this relationship is as follows:



4.3 Ventilatory response to inhaled carbon dioxide.[9–12]

$$V_E \text{ (l/min)} = 6.744\, e^{0.2495[CO_2]} \quad 4.1$$

where $[CO_2] = \%CO_2$. In order to reflect the effect of carbon dioxide on the rate of uptake of other gases in FED hazard calculations a multiplication factor V_{CO_2} is used, which is the ratio between the enhanced level of ventilation and the resting level. Allowing for certain inefficiencies in gas exchange at high ventilation levels a simplified factor for the effect on uptake is:

$$V_{CO_2} = e^{([CO_2]/4)} \quad 4.2$$

Although the main hazard presented by inhaled carbon dioxide in fires is enhancement of the rate of uptake of other toxic fire gases, it does itself cause incapacitation when inhaled at high concentrations. From approximately 3% up to 6% there is a gradually increasing degree of respiratory distress. This becomes severe at approximately 5–6%, with comments from subjects such as 'breathing fails to satisfy intense longing for air' or 'much discomfort, severe symptoms impending[12] with headache and vomiting also occurring. These effects worsen due to the gradual equilibrium process and other physiological changes, so that around 30 min is regarded as an endurance limit. At concentrations in the 7–10% range a further set of signs consisting of dizziness, drowsiness and unconsciousness is superimposed on the severe respiratory effects.[12–15] These severe effects occur progressively earlier with increasing exposure concentrations approaching 10% CO_2 as shown in Fig. 4.3, and an expression for time to incapacitation due to asphyxia and loss of consciousness is:

$$t_{I_{CO2}} = 474.52e^{-0.519[\%CO_2]} \quad 4.3$$

This may be applied to hazard calculations but in practice it has been found that incapacitation due to the effects of other fire gases occurs before incapacitation due to the direct toxic effects of carbon dioxide. For this reason it is usually omitted from hazard calculations as a toxicant in its own right, although it is important to include effects of carbon dioxide on the uptake of other toxic fire gases.

4.2.4 Other effects on lung function

Hydrogen cyanide also causes a brief period of hyperventilation which is considered in this chapter. Irritant fire gases, described in Chapter 3, also affect lung function. In humans, and other primates, the initial effect of inhaling most irritants is a brief period of breath-holding, with a subsequent pattern of pauses at end inspiration between successive breaths. This therefore represents a transient period of hypoventilation lasting a few seconds, during which the rate of uptake of oxygen and other fire gases is decreased. This is then followed by an increase in breathing rate and possibly tidal volume, resulting in a continuing hyperventilation (see Chapter 3, Figs 3.12 and 3.13). This pattern of respiration is accompanied by bronchoconstriction and ventilation–perfusion changes, which result in an impairment of gas exchange. Ventilation–perfusion mismatches occur in the lung when a region of the lung well ventilated with air is poorly supplied with blood, while other regions well supplied with blood are poorly ventilated. Anaesthetised baboons inhaling hydrogen chloride air mixtures[16] showed a decrease in arterial P_{O_2}. For this reason it is considered that inhalation of irritant fire gases, while having little effect on the rate of uptake of other fire gases, may exert some additive effect on overall level of hypoxia. A term for the effects of irritants is therefore included in the FED calculations for time to incapacitation due to effects of asphyxiant gases.

4.2.5 Asphyxiant gases affecting the blood and tissues

Table 4.3 summarises the effects and interactions of asphyxiant gases in the blood and Table 4.5 summarises the effects on tissue respiration. Carbon monoxide exerts its hypoxic effects partly by displacing oxygen from haemoglobin, to form carboxyhaemoglobin (COHb). The stability constant for carboxyhaemoglobin is 200–250 times that for oxyhaemoglobin (O_2Hb), so that an inhaled carbon monoxide concentration of approximately 640 ppm will eventually reach an equilibrium level of 50% COHb after an exposure period of approximately 13 hours at a low level of activity (V_E 10 l/min). At 50% COHb the amount of oxygen carried in the arterial blood is halved from 20 ml oxygen/100 ml blood to 10 ml oxygen/100 ml blood. If this were the only effect of carbon monoxide it would reduce the venous P_{O_2} to 27 mmHg, as does simple anaemia involving a 50% decrease in total haemoglobin. Since this is above the

Table 4.5 Effects of asphyxiant gases on tissue respiration or function

Gas	Effect on tissue respiration or function		Contribution to hypoxia
CO_2	High concentrations cause respiratory acidosis, reducing both extracellular and intracellular pH	Venous P_{CO_2} 90–120 mmHg CO_2 causes loss of consciousness,[2] with impairment after 30 min at 5% inhaled or a few minutes at 10%[12]	Can cause seizures, release of catecholamines
CO	Some degree or impairment of tissue respiration through inhibition of mitochondrial cytochrome[17]	Some inhibition of oxygen cellular oxygen metabolism	Minor contribution to hypoxia
HCN	Main toxic effect due to inhibition of cytochrome oxidation reactions[18]	Severe inhibition of cellular oxygen metabolism	Major contribution to hypoxia

minimum of 20 mmHg required to maintain normal cerebral function, the consequences would not be too serious. However, because the release of oxygen at lower P_{O_2} is impaired by the left shift in the oxyhaemoglobin dissociation curve, the actual venous P_{O_2} decreases to around 15 mmHg, which is why 50% COHb is usually fatal.

The main effects of carbon monoxide are therefore on carriage and delivery of oxygen in the blood, but it also combines with myoglobin in muscle tissue, thereby further impairing the oxygen supply to active muscles. In addition, carbon monoxide penetrates into cells and mitochondria, resulting in some impairment of tissue respiration (electron transport inhibition) by combining with cytochromes *b* and *aa*3.[17] Nitric oxide and nitrogen dioxide also affect the carriage of oxygen in the blood, forming nitrosylhaemoglobin with rapid oxidation to methaemoglobin (MetHb),[18–20] in which the haem iron changes from ferrous to ferric, in which form it does not carry oxygen. Nitric oxide forms nitrous acid in water:

$$4NO + 2H_2O + O_2 \rightarrow 4HNO_2$$

Nitrogen dioxide forms nitrous and nitric acid:

$$H_2O + 2NO_2 \rightarrow HNO_2 + HNO_3$$

The nitrite ion (NO_2^-) reacts with haemoglobin:

$$2H^+ + 3NO_2^- + 2O_2Hb(Fe^{2+}) \rightarrow 2MetHb(Fe^{3+}) + 3NO_3^- + H_2O$$

The normal concentration of methaemoglobin in blood is 0.01–0.5 g/100 ml.[21]

The effects of nitrite are similar to those of carbon monoxide in that the amount of oxygen carried in the blood is reduced in relation to the proportion of haemoglobin converted to methaemoglobin, and also that the oxygen dissociation curve is left shifted, although not by as much as that caused by carbon monoxide. The affinity of nitrite with haemoglobin is 1500 times greater than that of carbon monoxide. The overall effect is to cause tissue hypoxia by reducing venous P_{O_2} and oxygen delivery to the tissues. The effects are therefore additive with those of carbon monoxide. Although nitric oxide and nitrogen dioxide convert some Hb to MetHb they not normally are present in sufficient concentration to have a significant asphyxiant effect in fires.

The main effect of hydrogen cyanide is inhibition of mitochondrial electron transport by binding with cytochrome *ass*3 and *c*+*c*1.[18,22] This results in strong inhibition of tissue oxygen consumption and oxidative phosphorylation (the interconversion of ATP ↔ ADP ↔ AMP). The resultant hypoxia therefore relates to an inability to use oxygen rather than its absence, so that the blood remains highly oxygenated, giving venous blood an appearance and oxygen content close to that of arterial blood.[23] The active agent is free cyanide (CN^- and HCN) in plasma and tissue fluids (both extracellular and intracellular fluids), but in the blood, cyanide is also loosely bound to haemoglobin in the erythrocytes and to plasma proteins. Depending upon the exact conditions, the greatest proportion of whole blood cyanide is bound in the erythrocytes, so that whole blood cyanide provides a poor indication of the concentration of cyanide in solution in the plasma and tissues. Also important is the proportion of haemoglobin in the form of methaemoglobin. Methaemoglobin combines strongly with cyanide to form cyanomethaemoglobin, in which form the cyanide is more strongly bound than it is with mitochondrial cytochromes. This results in the effective detoxification of the proportion of cyanide in the form of cyanomethaemoglobin.[18]

Under normal conditions the methaemoglobin content of blood is small, but can be increased by introducing nitrite into the bloodstream, which indeed has been used as a cyanide antidote.[18] During the early stages of fires involving materials containing nitrogen, a small proportion of fuel nitrogen is released as NO_x, mainly in the form of NO. This nitric oxide will somewhat increase the methaemoglobin content of the blood, contributing slightly to hypoxia as described. As compartment fires grow, they tend to become vitiated (underventilated), so that a significant proportion of fuel nitrogen is released in the form of hydrogen cyanide (see Chapter 14), but very little as NO_x.[24] Under these conditions, the methaemoglobin formed as a result of the initial NO_x exposure will remove a small proportion of the inhaled cyanide from circulation, somewhat offsetting the inhaled cyanide toxicity.

4.3 Dose–effect relationships and uptake rate calculation methods for individual gases and interactions

In the following sections the toxic effects and uptake dynamics of each gas are considered individually and their interactions when present as mixtures, in order to evaluate the overall asphyxiant effects of the mixed gases in fire effluents. For each gas the following aspects are considered:

- The nature and severity of physiological effects at different concentration and dose levels.
- Concentration–time relationships for the effects, whether they occur immediately or some time after exposure, and the extent to which the effects of a short, high concentration exposure are the same as those of a longer, low level exposure.
- Quantification of the parameters determining rate of uptake, dispersal within the body and detoxification or excretion.
- Relationships between inhaled exposure doses and blood concentrations.
- Development of calculation methods for time to incapacitation for application to fire hazard assessment.

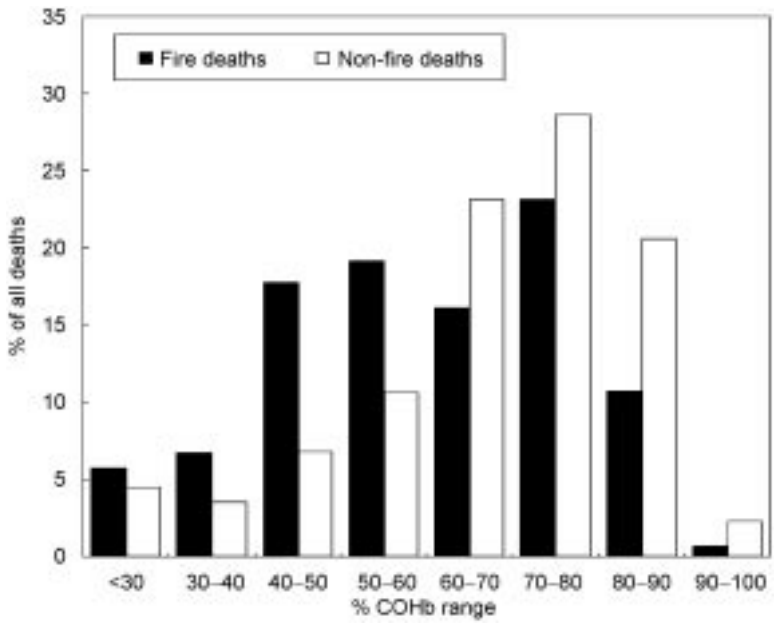
4.4 Carbon monoxide

There is little doubt that carbon monoxide is the most important asphyxiant agent formed in fires, being one of the main causes of incapacitation of victims at a fire scene and probably the main ultimate causes of death[1,25–27] of fire victims (see Chapter 1).

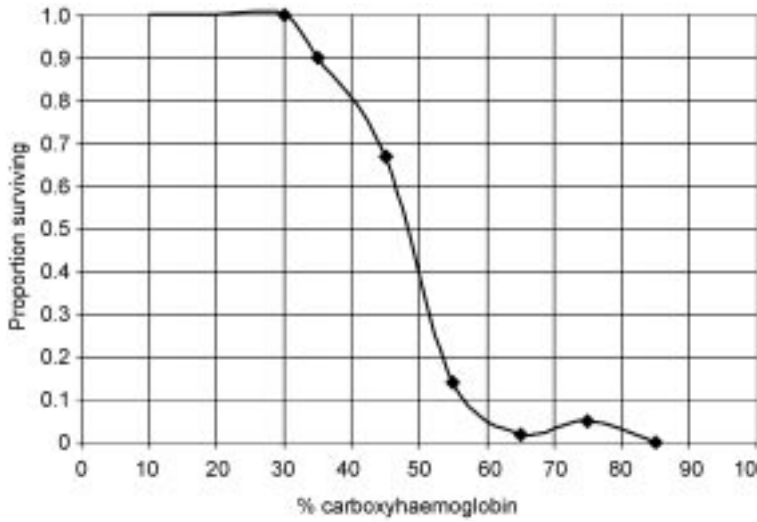
In a detailed pathology study carried out in Scotland,[25] lethal levels of carboxyhaemoglobin (>50% COHb) were found in 54% of all fatalities, while some 69% had carboxyhaemoglobin levels capable of causing incapacitation (>30% COHb). Incapacitating levels are also common in victims surviving immediate fire exposure.[28] Carboxyhaemoglobin is stable in cadavers and stored blood samples, providing a good indication of the overall exposure to toxic smoke. In building fires carboxyhaemoglobin concentrations can vary across a wide range from a few per cent to over 90% in victims found in the fire enclosure, but are rarely less than approximately 40% in victims discovered in locations more remote from the fire enclosure. This indicates that the majority of non-burn victims remote from the fire source are exposed to sufficient carbon monoxide to cause incapacitation or death. For victims in the fire enclosure, while a high proportion also have carboxyhaemoglobin concentrations sufficient to cause incapacitation or death, other factors, including heat and burns, are involved in a proportion of ‘room of origin’ deaths. Fire survivors also often have significant carboxyhaemoglobin blood concentrations, but once they are removed from the fire scene, the carbon monoxide is gradually ‘washed out’ of

the body via the lungs as fresh air is inhaled. It is also normal practice to treat fire survivors at the fire scene with oxygen, which increases the rate of carbon monoxide washout. For these reasons, the %COHb amounts measured in blood samples taken after arrival at hospital are likely to be considerably lower than those at the time of rescue. However, if the time between exposure and that when blood samples are taken is recorded, and the treatment regime over the intervening period is known, then it is possible to back-calculate the %COHb concentration at the time of exposure.

Evidence of the extent to which carbon monoxide contributes to fire smoke deaths is provided from a study by Nelson,[27] of the distribution of %COHb levels in non-burned fire fatalities and non-fire fatalities from carbon monoxide poisoning in a US database. The results summarised in Fig. 4.4 show a distribution of concentrations measured in decedents, with the mode in the 70–80% COHb range for both carbon monoxide poisonings (mostly from faulty space heaters and suicides in young males using vehicle exhaust fumes) and from fire fatalities. Although there is considerable similarity between carbon monoxide and fire deaths, the fatality distribution for fire deaths is somewhat shifted towards lower %COHb concentrations than the carbon monoxide deaths, indicating that although carbon monoxide appears to be the main cause of death in the fire victims, the contribution from other factors is significant, probably involving hydrogen cyanide and low oxygen hypoxia. Also, the 'carbon



4.4 Distribution of fatal %COHb in non-burned fire victims and non-fire carbon monoxide poisoning cases (after Nelson[27]).



4.5 Proportions of survivors and fatalities in different COHb ranges from a sample of 260 carbon monoxide poisoning cases (after Pach[29]).

monoxide' deaths have not resulted from exposure to carbon monoxide alone, but to fumes containing other combustion effluents, although carbon monoxide is considered to be the dominant toxicant present in such cases.

A further consideration with the carbon monoxide lethality data is that in practice few people survive an exposure of more than 50% COHb even if rescued and treated, although much higher levels are found in the bodies of decedents. This is because once a subject collapses and becomes comatose due to carbon monoxide intoxication, carbon monoxide uptake continues until the point is reached at which respiration and circulation cease. This is illustrated by comparing Nelson's data with those from a study by Pach *et al.*[29] (Fig. 4.5), which shows the proportions of survivors from a sample of 260 carbon monoxide poisoning cases. The data show that survival is rare above 50% COHb, increasing to around 0.67 in the 40–50% COHb range.

4.4.1 Variations in susceptibility within the human population

Figures 4.4 and 4.5 also demonstrate that both for fire and non-fire deaths there is a considerable range in %COHb levels at death within the human population, indicating that there is a range of susceptibility to fatal carbon monoxide poisoning. Various factors may contribute to this range of susceptibility including alcohol, other prescription and non-prescription drugs, age and health status. Fire victims are often found to have elevated blood alcohol levels, and alcohol is considered to interact to some extent with carbon monoxide intoxication. Age is a known factor, since the average %COHb concentrations in

fatalities of very young children and persons over 60 years of age are somewhat lower than those in young adults.[27] However, even elderly subjects with cardiovascular or respiratory disease are sometimes found to have fatal levels in the 80% plus range. Nevertheless, on average it is likely that the more sensitive subpopulations include the approximately 15% of children and 5% or adults who are asthmatic and the elderly. The elderly, and particularly those with impaired cardiac perfusion, are particularly susceptible to asphyxiant gases. It has been shown in experimental studies that as little as 2–4% COHb reduces the time to onset of chest pain in an exercise test for angina suffers, which could be of importance during escape attempts from a fire, especially in high rise buildings.[30] Asthmatics, and sufferers from other lung conditions such as chronic bronchitis (chronic obstructive pulmonary disease) and reactive airways dysfunction syndrome (RADS), are particularly susceptible to bronchoconstriction upon even a brief exposure to low concentrations of irritants, which may increase susceptibility to carbon monoxide asphyxiation.[31] A further complication of both fire and non-fire carbon monoxide poisoning is that both kinds of atmospheres contain fine particulates, which have been shown to enter the bloodstream and stimulate clot formation, resulting in coronary artery obstruction and strokes in some cases following exposure to fire effluents.

The range in Fig. 4.4 also emphasises the need to accommodate more sensitive proportions of the population when setting design tenability limits for exposure to any toxic substance. As discussed in Chapter 3 with regard to the incapacitating effects of exposure to irritants, it is considered advisable to set tenability limits to at least a third of the mean toxic end point concentration or exposure dose, and for some applications (for example when designing residential homes or hospitals) to a tenth of the average exposure dose or concentration for any specific limiting effect in order to protect the most susceptible persons.

4.4.2 Relationship between carbon monoxide exposure dose, carboxyhaemoglobin concentration and symptoms during acute experimental exposures in humans and animals

As with most toxic substances, the toxic effects of carbon monoxide show some relationship with the dose taken into the body and the concentration in key target organs.[32–37] The simplest situation is that when the rate of uptake of the toxic species is constant, the inhaled dose remains relatively stable in the body and a recognisable toxic end point is reached when a specific exposure dose has been inhaled, irrespective of whether the exposure is to a high concentration of the agent for a short time or an equivalent exposure to a lower concentration for a longer time. Toxic species showing this characteristic are said to comply with Haber's rule[1,38] (see Chapter 3). For this simple approach exposure dose is

expressed as the product of exposure concentration and exposure time so that for any specific toxic end point:

$$C \times t = K \qquad 4.4$$

The simplest method for assessing carbon monoxide exposure dose and effects in experimental situations, or for fire modelling exposure calculations, is in terms of the *Ct* product exposure dose. However the actual 'dose' or body burden of carbon monoxide in a subject at any point in time can deviate from the theoretical exposure dose for a number of reasons, but is relatively simple to assess directly. The blood contains 85–90% of the body burden of carbon monoxide, almost all of which is combined with haemoglobin in the form of carboxyhaemoglobin.[39] Most of the remaining 10–15% of carbon monoxide is bound to myoglobin.[39,40] The main route of uptake of carbon monoxide is through external exposure, a small amount resulting from endogenous metabolism, and the main route of excretion is via the lungs.[41] In cadavers, the concentration of carboxyhaemoglobin in blood remains remarkably constant over periods of weeks in blood or tissues stored at room temperature or under refrigeration.[42] Blood or tissue carbon monoxide levels can be analysed relatively simply.[35,42,43]

The result of these physiological features of carbon monoxide is that the true 'dose' or body burden of carbon monoxide in a subject at any point in time expressed in terms of %COHb is simple to assess, and can be compared with the clinical signs and symptoms exhibited by the subject.[1,35] The classic signs and symptoms of carbon monoxide intoxication described in the literature show a clear relationship with carboxyhaemoglobin concentration, as shown in Table 4.6.[1,35–37,44] However, an important consideration with regard to these data, particularly those related to exposure concentrations up to 50% COHb, is that they mostly relate to acute, short duration (up to around 30 min) experimental exposures of healthy young men or animals.[27,36,45] Under these conditions, there is a good agreement between the findings of different investigators.

Up to around 20% COHb, the only significant effects in most subjects are headache, effects on exercise tolerance and minimal neurophysiological changes. The exceptions are subjects with heart conditions, who suffer angina pain on mild exercise. Above 20% COHb subjects begin to feel unwell, often reporting flu-like symptoms including headaches. Neurophysiological investigations show abnormal visual evoked responses and tunnel vision. At around 30–40% more severe signs and symptoms occur, depending upon the susceptibility of the subject and the extent of physical activity.[46] Nausea and vomiting may occur and collapse with loss of consciousness (syncope). Some subjects maintaining a low level of physical activity, such as lying down, may be able to avoid serious effects up to around 50% COHb. Human volunteers at rest have been able to function normally at COHb concentrations (able to converse and write) even as high as 55% acute experimental exposures, but collapsed

Table 4.6 Classical relationship between carboxyhaemoglobin concentration and signs exhibited in humans and non-human primates

Blood saturation %COHb	After Stewart[37]	After Sayers and Davenport[44]	After Purser and co-workers[1,26,35,36] (non-human primates)
0.3–0.7	Normal range due to endogenous production		
1–5	Increase in cardiac output to compensate for reduction in oxygen carrying capacity of blood (heart patient may lack sufficient cardiac reserve)		
5–9	Exercise tolerance reduced, visual light threshold increased, less exercise required to induce chest pains in angina patients	Minimal symptoms $< 10\%$	
16–20	Headache, abnormal visual evoked response, may be lethal for patients with compromised cardiac function	Tightness across forehead and headache experienced 10–20%	
20–30	Throbbing headache; nausea; abnormal fine manual dexterity	Throbbing headache	
30–40	Severe headache; nausea and vomiting; syncope (fainting)	Severe headache; generalised weakness, visual changes; dizziness, nausea, vomiting, and ultimate collapse	30% caused confusion, collapse and coma in active animals during 30 min exposures with nausea after
40–50		Syncope, tachycardia (rapid heartbeat) and tachypnoea (rapid breathing)	40% caused coma, bradycardia (slow heartbeat), arrhythmias, EEG changes, in resting animals during 30 min exposures
50+	Coma; convulsions	Coma and convulsions	
60–70	Lethal if not treated	Death from cardiac depression and respiratory failure	

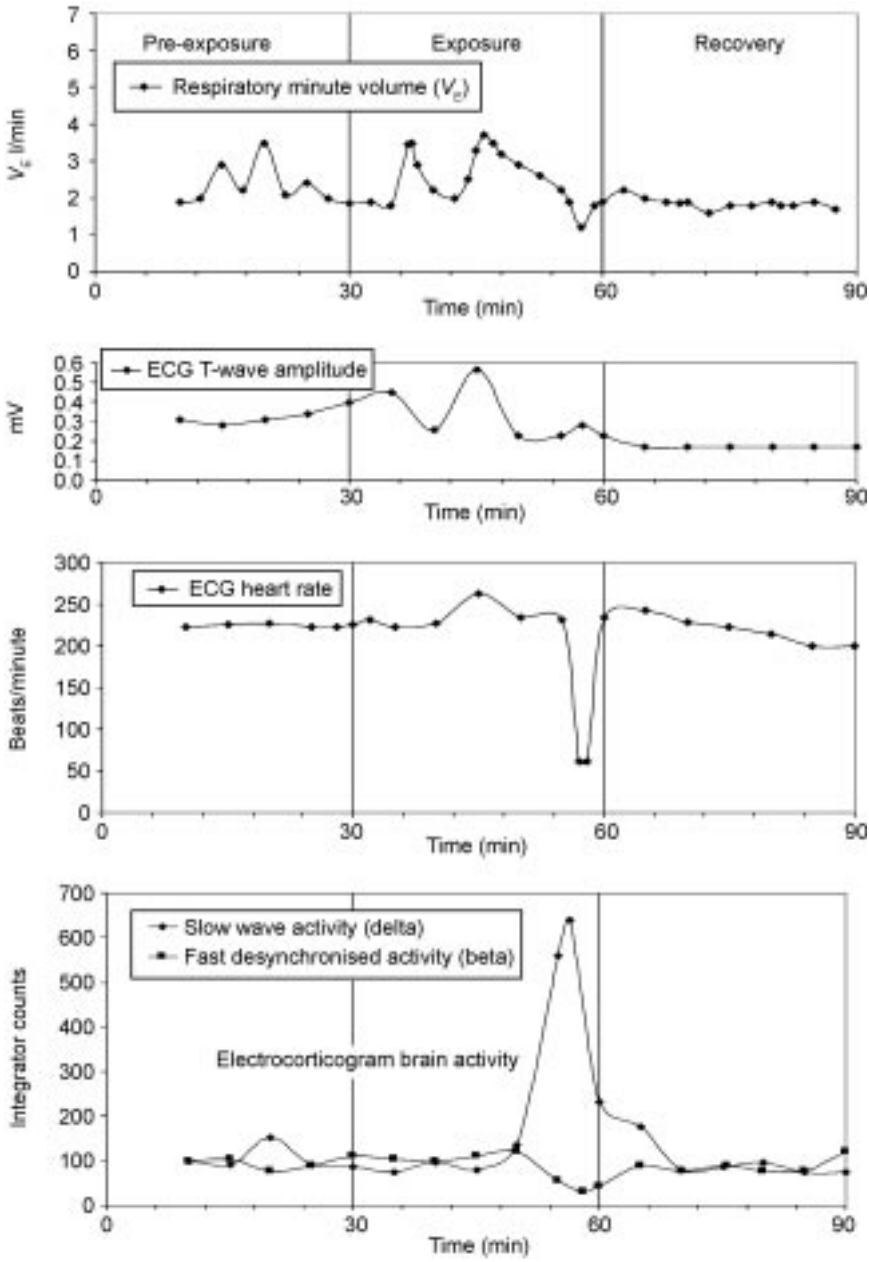
immediately when attempting to stand up and move.[47] As shown in Fig. 4.5 death is likely to occur at 50% COHb and above.

An important consideration in relation to effects on humans attempting to escape during fires is the extent to which incapacitating effects develop gradually as the exposure dose (or %COHb) increases, or whether effects are very minor until a critical dose is inhaled, at which point severe incapacitating effects occur. Based upon the effects described and summarised in Table 4.6 it is evident that the latter is more likely to be the case. Body physiology is designed to maintain adequate oxygen supply to vital organs, especially the brain, under conditions when oxygen uptake and dispersal within the body are reduced. The general effect is that normal function is maintained up to a point where compensatory systems are no longer sufficient, when severe effects occur.

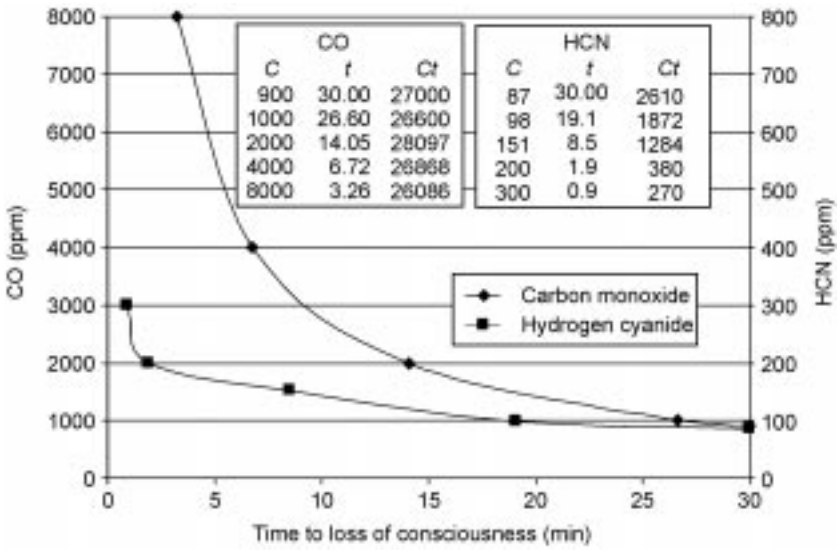
These effects were studied in some detail in a series of carbon monoxide exposure experiments in primates. For one set of experiments macaque monkeys at rest in chairs were exposed to carbon monoxide via a face mask while a set of physiological variables were measured, including respiratory tidal volume and frequency, electrocardiogram (ECG), electrocorticogram (similar to electroencephalogram but measured directly from the brain surface), auditory evoked potentials and peripheral nerve conduction velocity.[26,36] The results for a typical exposure are illustrated in Fig. 4.6.

For these experiments the effects on physiological parameters were minor until close to the end of the exposure period, when the carboxyhaemoglobin concentration was approximately 40%. At this point a dramatic change occurred as an animal passed suddenly from a near normal state to one of unconsciousness. At this point there was a sudden decrease in heart rate and breathing, and electrocorticogram changes indicated severe cerebral depression, consisting of a large increase in delta wave activity accompanied by a large decrease in beta activity. This was accompanied by a decrease in peripheral nerve conduction velocity and auditory evoked potential changes.

In other experiments macaque monkeys were trained to perform a behavioural task using operant conditioning.[35] The animals were trained on a sound signal to press a lever at one end of a chamber and then run to the other end to obtain a confectionary reward, which was presented for a brief period. The test was repeated at 3–5 min intervals throughout exposure periods of up to 30 min during exposures to different concentrations of carbon monoxide. The aim of the experiments was to keep the animals physically active, while measuring their physical performance and ability to perform a task involving abilities similar to a person escaping from a building. The results were that for any individual exposure there was little or no effect on performance until a point was reached where the animals showed signs of intoxication, consisting of reduced spontaneous movements and a slow response to the signal, followed by a slowing of reaction times to press the lever and to obtain the reward, often with unsteady walking (similar to a person with severe alcohol intoxication). Once



4.6 Physiological effects of an atmosphere containing CO (1850 ppm) – wood pyrolysed at 900 °C.



4.7 Comparison of the relationship between time to incapacitation and concentration for carbon monoxide and hydrogen cyanide exposures in primates. Time and concentration are equivalent for carbon monoxide, but for hydrogen cyanide a small increase in concentration causes a large decrease in time to incapacitation (see Section 4.4.5).

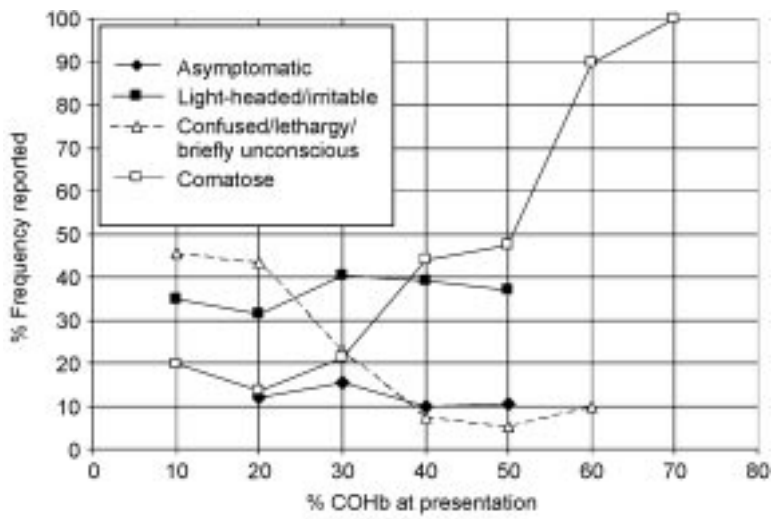
these signs occurred, collapse and loss of consciousness followed within a few seconds. During the recovery period (exposed to air) the animals recovered consciousness within a few minutes and gradually resumed performance of the conditioned task. At the time of loss of consciousness the measured caboxyhaemoglobin concentrations were 25–35%. These experiments therefore gave similar findings to those involving physiological measurements, in that the intoxication effects were minor up to a point just prior to collapse, but that for active animals the exposure dose causing incapacitation was lower at around 30% COHb compared with approximately 40% COHb for sedentary animals.

Another finding from this work was that over these short timescales the effects of carbon monoxide followed Haber's rule, in that incapacitation occurred at a fixed exposure dose of approximately 27 000 ppm min, for different exposure concentrations between 900 and 8000 ppm carbon monoxide, as shown in Fig. 4.7. The finding on %COHb required for incapacitation are in general agreement with those reported for humans, as shown in Table 4.6. For similar experiments using baboons trained to escape from an exposure chamber after 5 min exposures to carbon monoxide, the incapacitating carbon monoxide concentration was found to be 6850 ppm, representing a *Ct* product exposure dose of 34 350 ppm min.[16] This is similar to but slightly higher than the exposure dose required for the macaques, which is consistent with the larger body weights of the baboons.

4.4.3 Clinical experience of the relationship between carboxyhaemoglobin concentration and symptoms

Based upon experimental exposures, the %COHb concentration is a good indicator of a subject's exposure, and an important measure in predicting the effects of exposure and the prognosis. However, the clinical experience relating carboxyhaemoglobin concentrations in patients with the degree of carbon monoxide intoxication when they present at a hospital is rather different. In this situation the relationship between %COHb, symptoms and prognosis is much more complex. Figure 4.8 summarises the frequency of occurrence of signs and symptoms show by 191 patients admitted to the Maryland Shock-Trauma Unit compared with carboxyhaemoglobin levels taken at the scene.[40]

There is some general relationship with %COHb in that the proportion of comatose patients increased with %COHb, especially at 40% COHb and above, and above 50% COHb all patients were either comatose or seriously affected. However, 5 asymptomatic patients had %COHb levels above 30% (one 50% COHb), 9 comatose patients had COHb levels of <20% and 21 patients with confusion and lethargy had %COHb levels <20%. So more than half of patients reporting with serious signs had relatively low %COHb concentrations (<30% COHb), while at high concentrations in the 40–50% COHb concentration range about half were either asymptomatic or showed relatively minor signs, although all those above 50% COHb were seriously affected.



4.8 Frequency of occurrence of symptoms of various levels of severity in patients presenting with different carboxyhaemoglobin concentrations (after Meyers and Thom[40]).

4.4.4 Possible reasons for differences between experimental and clinical symptoms of carbon monoxide poisoning and % COHb

The apparent discrepancy between %COHb and the severity of signs and symptoms in clinical cases of carbon monoxide poisoning calls into the question the classical findings in this area. It is important to understand why this discrepancy might occur in order to determine the role of exposure dose in carbon monoxide poisoning and to determine the value of establishing the %COHb concentration in relation to exposure conditions, the severity of symptoms and the prognosis for patients.

There are several factors that might contribute to this apparent discrepancy. One possibility is differences between the health status and vulnerability of the general population to carbon monoxide poisoning compared with the subjects used to establish the effects of acute exposures in laboratory experiments. The general population includes the young and elderly, and in particular, subjects with cardiovascular and respiratory health problems, all of whom have been shown to be more vulnerable to the effects of carbon monoxide poisoning.[36,37,40,48] This is particularly true of subjects with cardiovascular disease, who suffer symptoms and may die at considerably lower %COHb levels than healthy individuals.[40] Another important factor may be that the exposure included other toxic gases in addition to carbon monoxide. This is particularly true of fire victims, for whom exposure to hydrogen cyanide, high concentrations of carbon dioxide, low oxygen hypoxia and range of irritant gases and particulates occurs at the same time as exposure to carbon monoxide. The effects of these additional toxins may partly explain the somewhat lower %COHb ranges in the frequency distribution of fire deaths compared with non-fire deaths in Fig. 4.4.[27,49,50]

A third and probably more important reason for apparent discrepancies between experimental and clinical data probably relates to differences between the exposure history and initial treatment of carbon monoxide poisoning cases and experimental carbon monoxide exposure subjects. As stated, the classical symptoms of carbon monoxide poisoning and their relationship with %COHb have largely been derived from acute exposures under experimental conditions at rest, especially for the effects of %COHb below 50%. Exposures are normally carried out over periods of a few minutes (sometimes up to around 30 minutes) and the %COHb is usually the maximum attained, i.e. the symptoms reported are displayed as the subject attains the reported level. In cases of clinical poisoning, subjects presenting with acute symptoms may have been exposed for periods of between a few minutes (as in some fire cases) and many hours, or for many hours on a daily repeated basis (as in cases involving faulty space heaters). They may also have been engaged in various levels of physical activity while being exposed, a factor shown to be important during primate experiments.[35] There is evidence that the severity of symptoms is somewhat related to the

duration of exposure, and in particular that neuropathological effects are intensified by prolonged cerebral hypoxia and related factors induced by prolonged periods at elevated %COHb levels.[40]

Another consideration is that the time will vary between the peak of the exposure and the time when a blood sample is taken in the emergency room. Often subjects will be given oxygen during this period by the emergency services. The %COHb declines exponentially when a subject is removed from the exposure as the carbon monoxide is excreted via the lungs.[41] The rate of decrease and half-life depend on a range of factors including body size, pulmonary ventilation and inhaled oxygen concentration. The result is that the %COHb measured on arrival at the emergency room can be considerably less than that at the time of exposure. In general it is to be expected that a subject would recover in proportion to the %COHb remaining in the blood, and in general terms this is the case, but there is now clear clinical evidence that symptoms persist for some time after carbon monoxide is removed from the body, and that the extent of permanent health effects, particularly cardiovascular and neurological effects, depend upon the severity and duration of exposure, as well as immediate and subsequent treatment (in particular the administration of air, or normobaric or hyperbaric oxygen).[40]

In order to evaluate the effects of exposure in a particular subject, to predict the likely sequelae and determine appropriate treatment regimes, it is therefore important to establish the history and severity of the exposure. In particular it is important to assess as far as possible the duration of the exposure and the maximum %COHb attained. It is likely that when this can be established and related to additional factors such as pre-existing health status, a clearer relationship between carbon monoxide exposure dose, duration of exposure and severity of symptoms will be established.

For this reason it is considered important to ascertain the peak %COHB to which the subject was exposed, and as far as possible the time–%COHb history. In the following sections calculation methods are described which can be used to estimate exposure history from the %COHb measured in the emergency room and the reported exposure conditions. In particular a method is described for estimating the %COHb at the time of rescue by calculating the rate of washout of carbon monoxide for different individuals, including children, under different emergency treatment regimes.

4.4.5 Calculating uptake and excretion rates and time to incapacitation for carbon monoxide

Applications for carbon monoxide uptake and excretion calculations

For application to fire hazard analysis it is important to be able to calculate both uptake and excretion (washout) rates for carbon monoxide in humans to

determine the increasing dose from exposure to calculated or measured fire atmospheres for which time–concentration curves for carbon monoxide (and other fire gases) are available. In this way the time to incapacitation or inhalation of a lethal exposure dose can be calculated. This can also be applied to actual fire incidents if the fire conditions are determined using fire modelling or full-scale reconstruction experiments, but an additional source of data from incidents is the carboxyhaemoglobin concentrations in the blood of decedents and fire survivors. Since carboxyhaemoglobin is stable in post-mortem blood it is possible to compare the carbon monoxide dose actually inhaled with that predicted by calculating uptake from the forward-modelled fire, providing the period of exposure of the decedent is known. For fire survivors, carboxyhaemoglobin concentrations are usually measured on arrival at the emergency room, and if the time from rescue is known it is possible to back-calculate the %COHb in the subject at the time of rescue from a knowledge of carbon monoxide washout curves and half-life. Such %COHb estimates can be valuable not only in understanding the exposure history of the subjects, but also in validating the fire modelling or full-scale fire testing carried out to replicate the conditions in the incident. In this context the bodies of persons exposed during the fire contain a measure of the *Ct* exposure dose of carbon monoxide present in the fire. If the forward-modelled or measured fire carbon monoxide exposure dose agrees with the back-calculated carbon monoxide exposure dose from exposed subjects, this provides independent verification that the modelled fire conditions are similar to those that actually occurred during the incident.

Different approaches to calculating carbon monoxide uptake and exposure dose

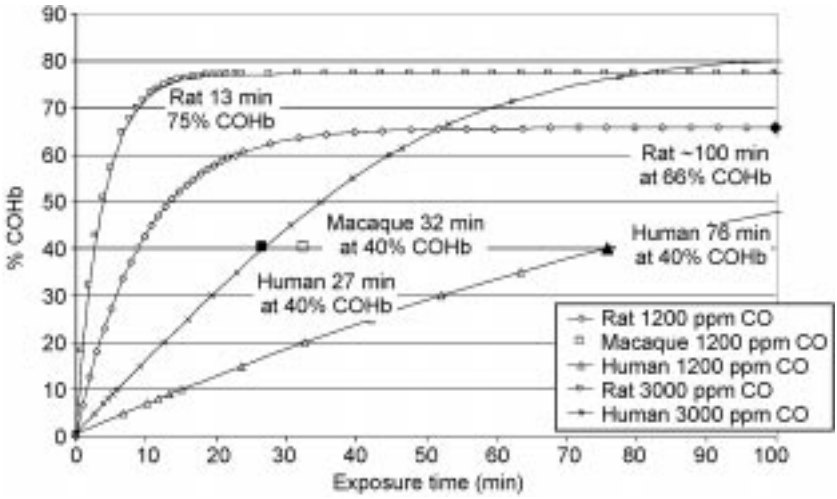
It is possible to estimate carbon monoxide uptake in terms of exposure dose (expressed in ppm min). However, for most applications carbon monoxide uptake is estimated in terms of %COHb. Early studies of the uptake and excretion dynamics of carbon monoxide and its interaction with haemoglobin were carried out by Haldane[51] and later by Roughton[52] and Forbes and co-workers.[33,53] More recently a physiological calculation model for uptake and excretion of carbon monoxide was developed by Coburn, Forster and Kane[41] (the CFK model), which took into account a number of important variables. This model, originally developed to study endogenous carbon monoxide production, was later applied to the uptake and excretion of exogenously inhaled carbon monoxide by Peterson and Stewart.[54,55] The model was validated for carbon monoxide uptake against experimental exposures of human volunteer subjects. The model takes into account a range of important physiological variables including body size, blood volume, ventilation rate, haemoglobin concentration, inhaled oxygen concentration and barometric pressure. It can be used to predict uptake of carbon monoxide in adults and children in a wide range of situations. In addition to the CFK model, which derives carbon monoxide uptake and

excretion using fundamental physiological parameters, a simpler, empirically derived model developed by Stewart *et al.*[45] is useful in defined situations. The Stewart *et al.* model was derived by fitting a regression curve to data obtained by exposing adult male volunteers to a range of carbon monoxide concentrations for short periods. It can be applied to adults in situations where the concentration of carbon monoxide in the blood is well below equilibrium levels with the inhaled carbon monoxide concentration, so that uptake is essentially linear. Under these conditions it has been found to give a reasonably good agreement with the CFK equation applied to adult males.[1]

Parameters affecting carbon monoxide uptake and %COHb formation

A number of different methods are available for calculating carbon monoxide uptake (expressed in terms of %COHb) or exposure dose (expressed as CO ppm min). The accuracy, range of application and complexity of different methods vary significantly, so that it is important to understand their limitations for specific applications. Since the physiological and pathological effects of carbon monoxide depend upon the blood carboxyhaemoglobin concentration, any variables affecting the relationship between carbon monoxide exposure and %COHb may need to be considered. The most important parameters affecting carbon monoxide uptake and %COHb formation are outlined:

- Carbon monoxide is both inhaled and excreted via the lungs. During the early stages of exposure to a maintained carbon monoxide concentration, uptake is linearly related to carbon monoxide exposure concentration, but the rate of increase falls off logarithmically with time as equilibrium is reached. For short exposure periods to high concentrations, the exposure dose required for incapacitation follows Haber's rule ($Ct = K$) where K is the exposure dose required for incapacitation) as illustrated by Fig. 4.7, but over longer time-scales or with small animals such as rodents, there is significant deviation from the Haber relationship as illustrated in Fig. 4.9. The equilibrium concentration depends upon the inhaled oxygen concentration and the Haldane constant (M) representing the ratio of affinity of haemoglobin for carbon monoxide and oxygen. M varies somewhat between individual humans, a value typically used for carbon monoxide uptake calculations being 218. It also varies significantly among species: 228 for dogs,[56] 195 for monkeys and 170 for rats. In humans the affinity of foetal haemoglobin for oxygen and carbon monoxide differs from that for adults, with implications for exposures during pregnancy.
- For any given carbon monoxide concentration, the rate of uptake depends upon the alveolar ventilation (litres/min) (V_A), which in turn depends upon the respiratory minute volume (V_E) and the lung dead space (V_D). Basically the greater the volume of air (and hence carbon monoxide) inhaled each minute, the more rapid the rate of uptake. The volume of air inhaled each



4.9 Rate of uptake of carbon monoxide as %COHb, time to and %COHb at incapacitation for rats, humans and macaque monkey at 1200 and 3000 ppm carbon monoxide exposure concentrations.

minute is increased during exercise and when inhaling atmospheres containing elevated carbon dioxide or hydrogen cyanide concentrations or reduced oxygen concentrations. However, the rate of carbon monoxide uptake is not directly proportional to V_A over the whole range of possible V_E, owing to diffusivity limitations for carbon monoxide (see DL_{CO} below)

- For any given carbon monoxide concentration the rate of uptake has a maximum limiting value DL_{CO}, the diffusivity of the lung for carbon monoxide, expressed in ml CO/min mmHg, where mmHg represents the partial pressure of carbon monoxide in the exposure atmosphere. DL_{CO} depends upon body size and lung function characteristics and has been measured directly in humans and a number of animal species. The main limitation on DL_{CO} is considered to be the rate of reaction of carbon monoxide with haemoglobin in red blood cells passing through the lung capillaries. Owing to DL_{CO} the rate of uptake of carbon monoxide is directly proportional to V_A at low V_A levels, but deviates increasingly at high values of V_E and V_A, with a maximum uptake rate in healthy adult humans at a V_E of approximately 30 l/min (V_A 26 l/min), which represents a moderate level of exercise (such as fast walking while escaping from a building) or inhalation of 6% carbon dioxide during a fire while at rest (or an equivalent combination of exercise and carbon dioxide inhalation). There is some uncertainty over this effect however, since DL_{CO} itself increases somewhat with increasing ventilation.
- For any given carbon monoxide concentration and inhaled carbon monoxide volume, the rate of increase in %COHb depends upon the mass of haemo-

globin in the body, which in turn depends upon the body mass, blood volume (ml/kg) and blood haemoglobin concentration (g/100 ml). In humans haemoglobin concentration varies somewhat between individuals. It is slightly lower in females than males, and in anaemic subjects. It is increased in smokers (a compensation for chronically increased carboxyhaemoglobin concentrations) and in subjects living at altitude (a compensation for reduced partial pressure of atmospheric oxygen). An important determinant of the rate of uptake of carbon monoxide and rate of increase in %COHb concentration is the relationship between respiratory V_E and body mass. As discussed in Chapter 8, V_E increases with body size squared, while body mass increases with the cube of body size, so that smaller animals or human children inhale more air per unit body mass than adult humans, with the result that the rate of uptake of carbon monoxide increases progressively as body mass decreases. This effect is illustrated in Fig. 4.9 which shows the rate of increase of %COHb with time for constant exposures to carbon monoxide at 1200 and 3000 ppm in different species. The uptake curves for rats have been calculated according to the equation derived by Hartzell *et al*. from experimentally determined data in rats.[57] The uptake curves for resting humans have been calculated using the CFK equation for a 70 kg man at rest with a V_E of 10 l/min.[41,55] The macaque data are experimental.[26] At 1200 ppm the time required to achieve 40% COHb (a concentration predicted to cause incapacitation in resting humans) is 76 min for a 70 kg man, 32 min for a 4 kg macaque monkey and 8.76 min for a 200 g rat. At 3000 ppm carbon monoxide the calculated time to 40% COHb for rats is 2.7 min, while that for an adult human is 27 min.

- Other factors that may have some influence on rate of uptake or equilibrium %COHb concentration are barometric pressure (at altitude or under compression) and inhaled oxygen concentration. At altitude, for a given carbon monoxide volume concentration, the carbon monoxide mass concentration is reduced, which reduces the rate of conversion of the body mass of haemoglobin to carboxyhaemoglobin for a given V_E. However, on acute exposure to altitude there is a degree of hyperventilation compensating for the reduced oxygen uptake, so that the overall difference in rate of %COHb formation at altitude is probably small, although the physiological effects of combined carbon monoxide intoxication and low oxygen hypoxia are considered additive. The inhalation of carbon monoxide in the presence of lowered oxygen concentration at sea level (for example during a fire) may lead to a somewhat increased rate of %COHb formation and increased %COHb equilibrium concentration, due partly to increased V_E and partly to the effect of the lowered blood oxygen/carbon monoxide (P_{O_2}/P_{CO}) partial pressure ratio.
- During inhalation of irritant fire effluents, changes in lung ventilation–perfusion ratio may reduce the efficiency of gas uptake in the lungs, reducing

effective DL_{CO}. Evidence for this effect has been observed during primate exposures to irritant smoke atmospheres containing carbon monoxide, when increases in V_E did not result in an increase in rate of %COHb formation.

Simple Ct exposure dose method

The simplest method for estimating time to incapacitation for an exposure to carbon monoxide is the *Ct* product exposure dose method. This method is derived from experimental animal exposure data and then applied to calculation models on the assumption that incapacitation or death occurs at fixed *Ct* product exposure doses, for any combination of concentration and exposure time. As illustrated in Fig. 4.7, this method works reasonably well for short exposures to high carbon monoxide concentrations under specific exposure conditions, but makes no allowance for the effects of any of the other variables listed. For active macaque monkeys (approximately 4 kg body weight) the exposure dose for incapacitation was approximately 27 000 CO ppm min.[1,35] For sedentary animals of the same body size (but with at rest with a lower V_E) the exposure dose to incapacitation was higher at approximately 48 000 ppm min.[1,26] For moderately active juvenile baboons (approximately 7–10 kg body weight), the exposure dose to incapacitation was 34 250 ppm min and for rats 33 900 ppm min (both for 5 min exposure periods).[16] The apparent similarity between rats and baboons is coincidental as discussed in Chapter 8, resulting from a combination of more rapid uptake approaching equilibrium in rats (as illustrated in Fig. 4.9) and a higher tolerance to hypoxia than in primates. In practice, even over relatively short exposure periods, $Ct \neq K$ for rats due to the non-linearity of the uptake curve, so that *Ct* for incapacitation was found to vary experimentally between 37 000 ppm min at 10 000 ppm CO and 126 750 ppm min at 1300 ppm CO. The *Ct* exposure doses for incapacitation and death in different species including humans at different levels of activity are shown in Table 4.7. Basically the *Ct* exposure dose for incapacitation in humans engaged in light to moderate activity

Table 4.7 ***Ct*** product exposure doses for incapacitation and death by carbon monoxide for different species at rest and during light activity

	Incapacitation		Fatal	
	CO at rest (ppm min)	CO light activity (ppm min)	CO at rest (ppm min)	CO light activity (ppm min)
Human 70 kg	80 000–100 000	30 000–35 000	~110 000–240 000	~60 000–190 000
Baboon ~ 20 kg		34 000		
Macaque 3–4 kg	38 000–40 000	27 000		
Rat ~ 300 g	30 000–40 000	22 000–36 000	162 000	

(fast waking) while escaping from a building is predicted to be approximately 30 000–35 000 ppm min, which is similar to that of lightly active baboons and macaques.

This *Ct* product exposure dose method is proposed for application to fire hazard calculations in ISO 13571,[58] with the proposed *Ct* exposure dose for incapacitation of 35 000 ppm min intended to represent humans engaged in moderate physical activity with a V_E of 20 l/min. The advantage of this method is that it is extremely simple to use in a fire hazard modelling context, and it is considered to be valid for moderately active adult humans under the high carbon monoxide concentrations and short exposure timescales usually occurring during fires (often a few minutes critical exposure period during flaming fires and seldom more than 60 min). A caveat is that for applications outside these limitations (such as application to children, long exposure periods at low carbon monoxide concentrations or other situations involving differences in the variables listed) more complex modelling methods may be indicated.

Calculation of %COHb using the liner uptake Stewart model

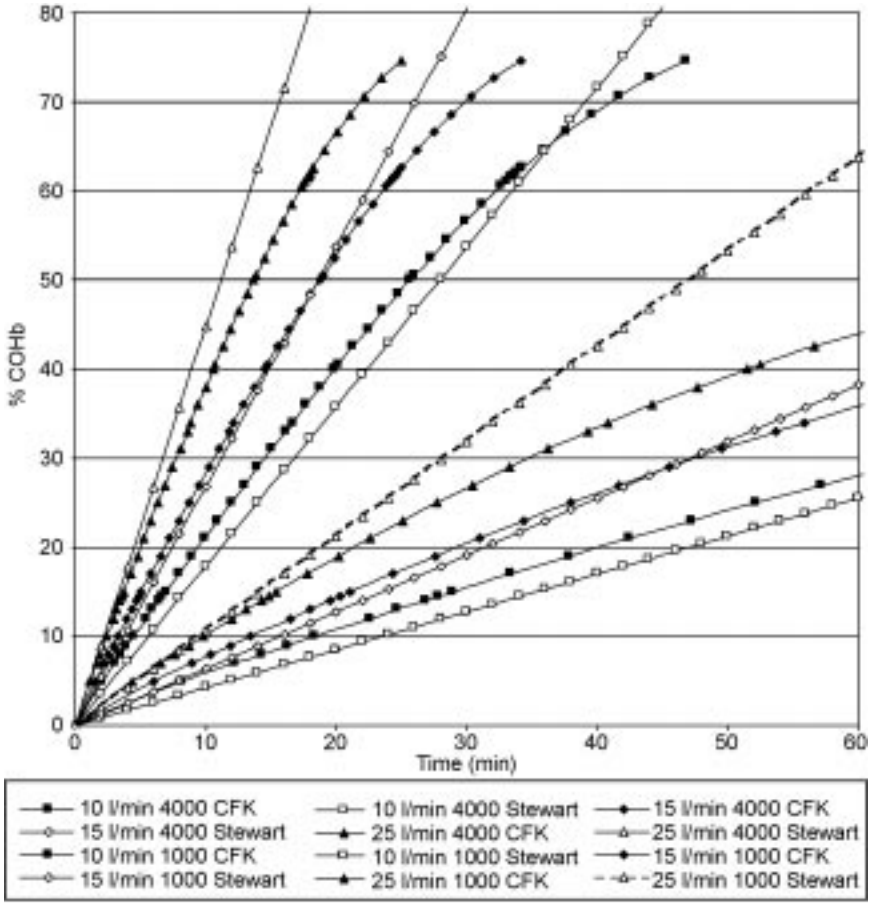
Other carbon monoxide uptake methods involve calculating %COHb rather than *Ct* product exposure dose. This is preferable because it is the main determinant of effects on exposed subjects. The most sophisticated and best-validated model is the CFK equation, which takes into account all the parameters listed and is described in the next section. The Stewart equation[37,45] is a much simpler method that was developed empirically using %COHb data obtained from adult male volunteers inhaling carbon monoxide at concentrations well in excess of the equilibrium concentration, when uptake is basically linear. The regression equation is simple to use and gives quite good agreement with the CFK equation method under these conditions. The basic equation is:

$$\%\mathrm{COHb} = (3.317 \times 10^{-5})(\mathrm{CO})^{1.036} V_E\, t \qquad 4.5$$

where CO = CO concentration (ppm), V_E = volume of air breathed each minute (l/min) (minute volume) and t = exposure time (min).

V_E depends primarily on the body size of the subject and the level of physical activity. Data can be obtained from reference sources (see Purser[1] and Table 4.4). V_E also depends upon the concentration of inhaled carbon dioxide according to Equation 4.2. This effect is negligible at ambient carbon dioxide concentrations but is an important factor in fires, where the concentration can be as high as 10% CO_2.

Figure 4.10 compares the predictions of the Stewart and CFK equations in young adult males (70 kg body weight) for carbon monoxide uptake expressed as %COHb calculated for carbon monoxide exposure concentrations of 1000 and 4000 ppm at different V_E levels. The Stewart predictions are linear, as are the CFK predictions for the first 20 min or so, but after this time the CFK



4.10 Comparison of calculated carbon monoxide uptake as %COHb using the Stewart and CFK equations for a 70 kg man (blood volume 5300 ml, Hb 15.94 g/100 ml, DL_{CO} 30 at V_E 10, 15 and 25 l/min, CO 1000 and 4000 ppm).

predictions become more curved as %COHb begins to approach equilibrium concentrations. The deviations for the CFK curves are more marked at higher V_E levels as equilibrium is approached more rapidly. At 10 and 15 l/min V_E the initial rate of uptake is somewhat faster for CFK than for Stewart, but at 25 l/min V_E the CFK curve becomes shallower than Stewart line. This is due to the influence of using a constant DL_{CO} limiting the rate of carbon monoxide uptake at high V_E levels in the CFK calculation, which is not taken into account by the Stewart equation (although the difference may be somewhat less if an expression for a variable DL_{CO} is used).

These deviations illustrate that the rate of carbon monoxide uptake is not a simple function of V_E. This limitation on the extent of increase in rate of carbon

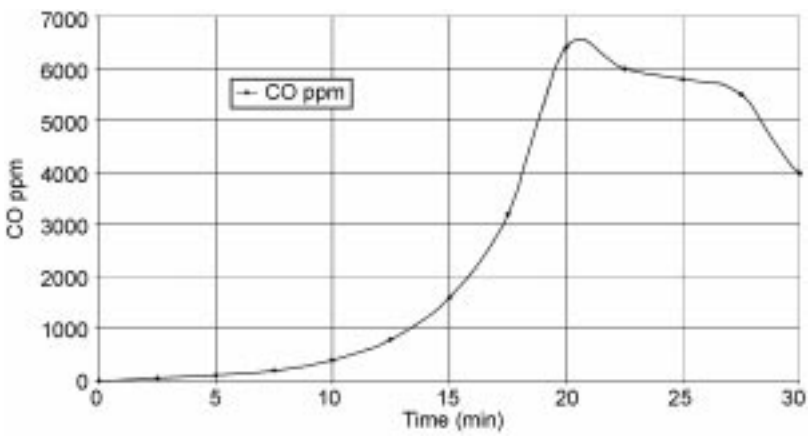
monoxide uptake with increasing V_E has been allowed for to some extent with the V_{CO_2} function, which is intended to be used as multiplier for the rate of carbon monoxide uptake during exposure to combined carbon monoxide and carbon dioxide mixtures in fire, allowing for the increase in V_E caused by the carbon dioxide. As described in Section 4.2.3 on carbon dioxide, Equation 4.2 is used instead of Equation 4.1 to allow for these inefficiencies in uptake with increasing V_E.

Perhaps a better approach would be to first estimate overall V_E as the V_E component due to activity level multiplied by V_{CO_2} using Equation 4.1 to provide an estimate of total V_E for different combinations of activity levels and inhaled carbon dioxide concentrations, and then apply a factor for the effect of DL_{CO} on carbon monoxide uptake rate. Such a factor has been derived using the CFK equation (described in the following section). The factor is:

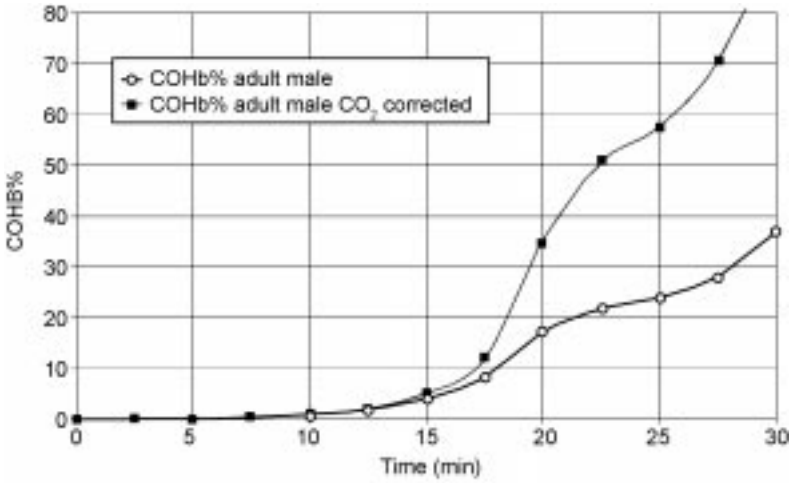
$$1.5 \times e^{-0.9173 \times V_E}$$

If the rate of uptake predicted by the Stewart equation at different V_E levels is corrected using this factor the initial rates of carbon monoxide uptake are closer to the CFK predictions, until the point is reached where the CFK predictions begin to depart from linearity.

Figures 4.11 and 4.12 show an example of the application of the Stewart equation with the V_{CO_2} uptake corrections from Equation 4.2 to a theoretical carbon monoxide concentration curve for a slowly growing fire in an enclosed room. The fire self-extinguishes when the carbon monoxide concentration reaches 6000 ppm. The CO_2 : CO ratio in the fire is assumed to be 10 : 1, a fairly typical value for an enclosed fire. On this basis Fig. 4.12 shows the rate of increase of %COHb with time predicted by the Stewart equation, applied using the FED method.[1] The results are shown for carbon monoxide uptake at a



4.11 Theoretical carbon monoxide concentration curve for a slowly growing enclosed fire that self-extinguishes after 20 minutes.



4.12 %COHb increase in an occupant of room during the fire shown in Fig. 4.3, predicted using the Stewart equation, and with correction for carbon dioxide-induced hyperventilation, carbon monoxide uptake is shown for a resting adult male and corrected for carbon dioxide-induced hyperventilation assuming a 10:1 CO_2:CO ratio for the fire.

normal resting value of V_E, and corrected for the hyperventilatory effect of the carbon dioxide. In practice, loss of consciousness would be predicted to occur after around 20 min, and death before 30 min.

Calculation of %COHb using the CFK equation

The basic CFK equation is a differential equation developed initially to calculate %COHb in blood for endogenous production of carbon monoxide using all the major physiological parameters.[41] The equation is written as follows:

$$\frac{d[HbCO]_t}{dt} = \frac{V_{CO}}{V_b} - \frac{1}{V_b\left(\frac{1}{DL_{CO}} + \frac{(P_b - P_{H_2O})}{V_A}\right)}\left(\frac{[HbCO]_t \bar{P}c_{O2}}{[HbO_2]M} - P_{Ico}\right) \qquad 4.6$$

Peterson and Stewart[54,55] used the model to calculate carbon monoxide uptake and %COHb for male students exposed to different inhaled carbon monoxide concentrations and found a good agreement. They used the following integrated form of the equation, which has been used to calculate the CFK uptake curves presented in this chapter:

$$\frac{A[HbCO]_t - BV_{CO} - P_{Ico}}{A[HbCO]_0 - BV_{CO} - P_{Ico}} = \exp(-tA/V_bB) \qquad 4.7$$

All volumes are STPD (standard temperature and pressure, dry, i.e. 1 atm and 0 °C) and the various terms in the two forms of the equation are as follows:

$$A = \bar{P}c_{O_2}/M[HbO_2] \quad 4.8$$

$$B = 1/DL_{CO} + P_L/V_A \quad 4.9$$

M = ratio of the affinity of blood for CO to that for O_2 (the Haldane constant)
$[HbO_2]$ = ml of O_2 per ml blood; this depends on the extent of saturation, but at 100% saturation 1 g of Hb will hold 1.38 ml of oxygen (or CO) (at STPD)

$$[HbO_2]_{max} = 1.38[Hb]/100 \quad 4.10$$

[Hb] = Hb concentration (g/100 ml whole blood) (normal ranges are: adult men 13.5–18.0, adult women 11.5–16.4).
$[HbCO]_t$ = ml of CO per ml of blood at time t
$[HbCO]_0$ = ml of CO per ml of blood at the beginning of the exposure, taken as 0.8% COHb = 0.001 76 ml CO/ml blood for non-smokers
$\bar{P}c_{O_2}$ = average partial pressure of oxygen in lung capillaries, mmHg
V_{CO} = rate of endogenous CO production ml/min, set at 0.007 ml/min
DL_{CO} = diffusivity of the lung for CO, ml/min/mmHg
P_B = barometric pressure (760 mmHg at sea level)
P_L = barometric pressure minus vapour pressure of water at body temperature (760 − 47 = 713 mmHg)
V_b = blood volume, ml, 74 ml/kg body weight (approximately 5500 ml for a 70 kg human)
P_{Ico} = partial pressure of CO in the inhaled air, mmHg
V_A = alveolar ventilation rate, ml/min
t = exposure duration (minutes)
exp = 2.7182

Expressions for different input terms required are as follows:

$$A_r\ (m^2) = 11.7(cm^2/g)W(g)^{0.667} \quad 4.11$$

where:

A_r = body surface area (m^2)
W = bodyweight in grams or kilograms as indicated

$$DL_{CO}(ml/min/mmHg) = \left(\frac{1}{\left(-0.0287\left(\frac{150}{W(kg)} \right)^{0.667} \right) + \frac{0.1188}{A_r(m^2)}} \right) \quad 4.12$$

Equation 4.12 is from Lambertsen.[59] Alternatively Bernard and Duker[60] treated DL_{CO} as a variable related to oxygen consumption (up to 4 l O_2/min) as in Equation 4.13.

$$DL_{CO} = 35 V_{O_2}{}^{0.33} \text{ (ml/min/mmHg)} \quad 4.13$$

$$V_{O_2} = 0.001 V_E \text{ (ml/min)}/22.274 - 0.0309 \text{ (l/min STPD)} \quad 4.14$$

(from Altman *et al.*[8])

$$V_A = 0.933 V_E \text{ (ml/min)} - 132f \text{ (m/min)} \quad 4.15$$

(from Peterson and Stewart[55])

$$f = \exp(0.0165 V_E) \text{ (ml/min)} + 2.3293 \quad 4.16$$

(from Peterson and Stewart[55])

where: V_{O_2} = rate of oxygen consumption (l/min STPD), V_E = respiratory minute volume (ml/min STPD) and f = respiratory frequency (breaths/min). Alternatively:

$$V_A = V_E \text{ (ml/min)} - (W(\text{kg})/V_T) V_D (\text{ml/min STPD}) \quad 4.17$$

$$V_D = 2.24 W(\text{kg}) (\text{ml STPD}) \quad 4.18$$

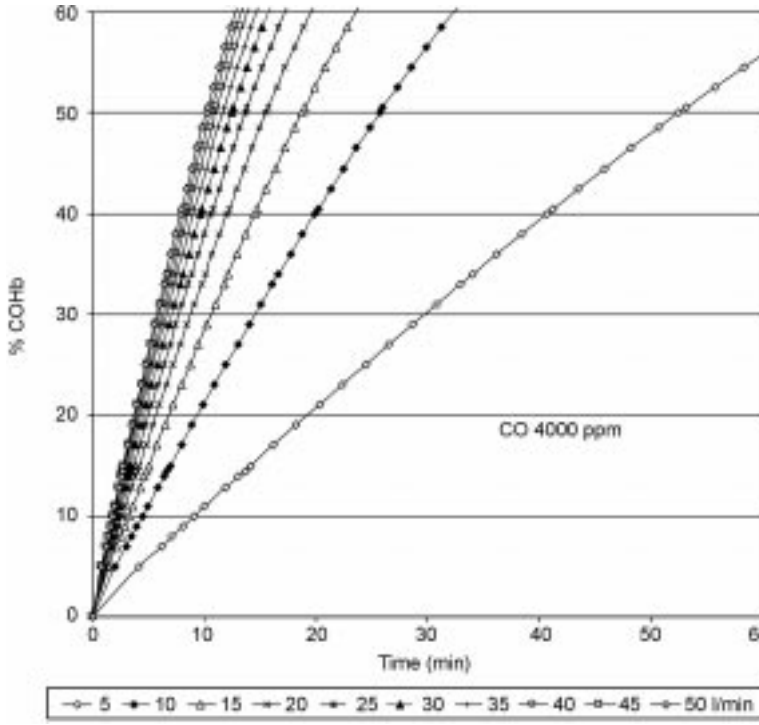
$$V_T = 7.4 W(\text{kg}) (\text{ml STPD}) \quad 4.19$$

where: V_D = anatomical dead space (ml STDP) and V_T = respiratory tidal volume (ml STDP).

As discussed in relation to the Stewart equation, the maximum rate of carbon monoxide uptake is limited by the maximum diffusivity of the lung for carbon monoxide (DL_{CO}). The effect of this is demonstrated by comparing carbon monoxide uptake rates at different V_E levels using the CFK equation as illustrated in Fig. 4.13, which shows calculated rates of carbon monoxide uptake at a constant 4000 ppm carbon monoxide. As V_E increases, the volume of carbon monoxide inhaled into the lungs per minute increases, approximately in proportion initially, but tending to a maximum at a V_E of around 50 l/min. However, this maximum does depend upon a constant value for DL_{CO}, so that if DL_{CO} increases significantly with V_E then the maximum value may also increase somewhat.

The reason for this effect is illustrated in Fig. 4.14, which shows the maximum possible rate of carbon monoxide uptake for an inhaled concentration of 1000 ppm carbon monoxide, assuming all the carbon monoxide in V_A is taken up by the blood for different V_E levels. At a V_E of around 30 l/min the maximum theoretical uptake reaches 22.8 ml CO/min, which is the maximum limiting rate for a DL_{CO} of 30 ml/min/mmHg. In practice the uptake is submaximal, so that the limiting value is reached at a V_E closer to 50 l/min.

The CFK equation is therefore a very versatile, fundamentally based, method for prediction of carbon monoxide uptake and %COHb formation for a wide range of different applications, which has been validated by experimental data. It is recommended for any applications other than short exposures of adults to high carbon monoxide concentrations.



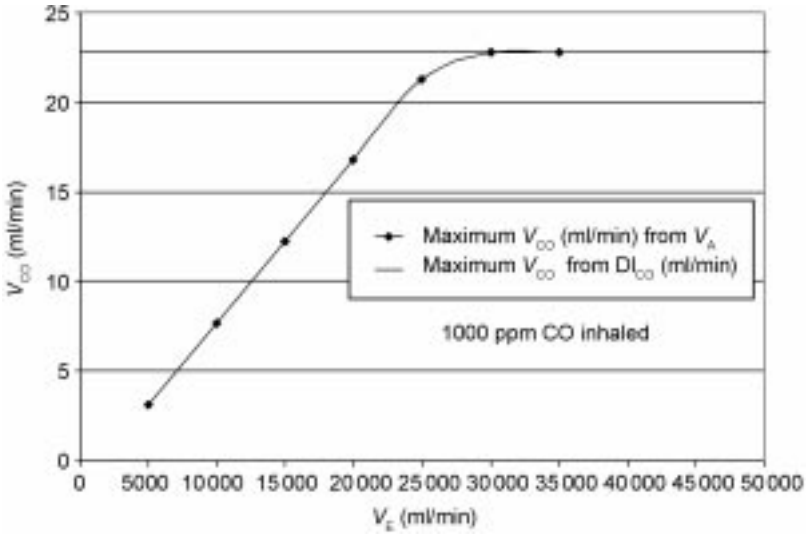
4.13 Rates of COHb formation at different V_E levels for a constant 4000 ppm exposure concentration calculated using the CFK equation assuming a constant DL_{CO} of 30 ml/min/mmHg.

Carbon monoxide excretion (washout) calculation models

In order to address the particular problem of excretion of carbon monoxide by adults and children after exposure, while breathing air or oxygen, a set of three models has been developed and validated against actual data involving serial %COHb measurements from several subjects at different times following exposure in fires. The three models include a simple calculation model based upon published data for the COHb half-life in adults breathing air or oxygen, a method based upon fundamental physiological parameters for calculating carbon monoxide washout and %COHb decay with time, and a direct application of the CFK equation to calculate %COHb decay with time.

Predicting excretion of carbon monoxide after exposure using an empirical model

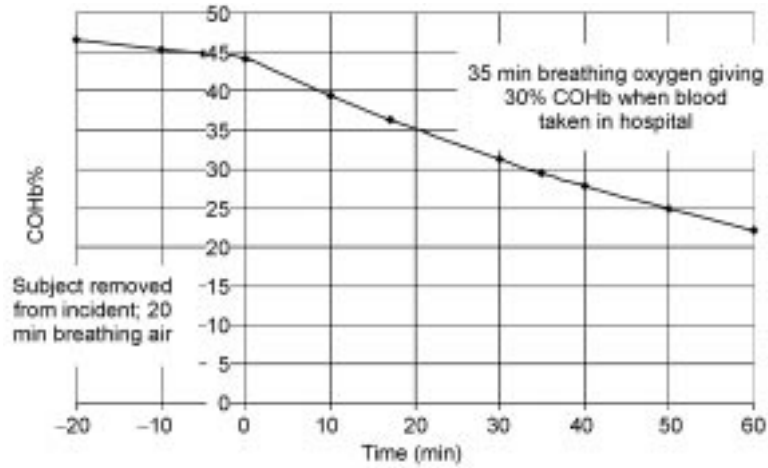
When a subject is removed from a carbon monoxide contaminated atmosphere and is breathing air or oxygen, carbon monoxide is gradually displaced from combination with haemoglobin in the blood and excreted via the lungs. If blood



4.14 Maximum theoretical rate of carbon monoxide uptake for different V_E levels assuming 100% absorption of inhaled carbon monoxide into the blood up to the maximum rate of 22.8 ml CO/min for a DL_{CO} of 30 ml/min/mmHg.

samples are taken from the subject at intervals it is possible to plot the exponential decay curve for the %COHb remaining in the body against time and calculate the half-life (the time required for the %COHb to decay to half the original level). When this has been done for adults at rest, the half-life has been found to be 4–5 hours.[39,41,54,61,62] When subjects are given oxygen to breathe the rate of excretion of carbon monoxide increases in proportion to the ratio of the elevated partial pressure (or concentration) of oxygen inhaled (P_{O_2}) compared with that in normal air.[53,61,62] Thus for a subject who is intubated and breathing pure oxygen, the inhaled oxygen concentration is 100%, compared with the 20.9% of air, so that the rate of excretion of carbon monoxide is increased by approximately a factor of 5. When hyperbaric oxygen is administered the rate of excretion is increased further depending on the increased oxygen partial pressure. Other variables are the body size of the subject and the subject's ventilation (V_E) l/min.

When patients are admitted to the emergency room following an exposure incident it is normal practice to take a blood sample for analysis of blood gases including %COHb, which may be repeated at intervals as the patient recovers. Some time will have elapsed between the time the patient was removed from the exposure incident and transported to hospital. Commonly, normobaric oxygen will have been administered in the ambulance either by face mask or by endotracheal tube. The %COHb in the patient on admission is therefore likely to be considerably lower than that attained at the time of the exposure, so that the clinician may have a false indication of the severity of the exposure. Taking the



4.15 Predicted curve for excretion of carbon monoxide for a subject breathing air for 20 min following a carbon monoxide exposure incident and then intubated on 100% oxygen for a further 35 min before a blood sample gave 30% COHb. The excretion curve is derived using 4.5 hours half-life on air and 1 hour half-life on 100% oxygen. The back-prediction gives a %COHb of 47% at the time the subject was removed from the carbon monoxide exposure and 44% when oxygen treatment was started.

%COHb concentration in the patient at the time of admission as a starting point, it is possible to plot a carbon monoxide excretion curve for the patient based upon the known half-life values (depending upon the time that the patient was breathing air and/or oxygen between rescue and the removal of blood in the emergency room). Using this curve it is then possible to back-calculate the %COHb at the time of the incident. Figure 4.15 shows an example of such a calculation for an adult at a normal resting breathing rate. In the theoretical example (which is very similar to anonymised data in an actual incident) it is assumed that the subject is removed from a fire incident and breathes air for 20 min before receiving medical attention. The subject at this point is comatose, intubated and given 100% oxygen. Thirty-five minutes later a blood sample is taken and found to be at 30% COHb. Assuming a half-life of 4.5 hours during the period when air was breathed and a half-life of 1 hour when oxygen was breathed it is possible to calculate the %COHb history using the expression in Equation 4.20. This is achieved by using an initial approximate estimate of the likely starting %COHb at the time of rescue, calculating the decay curve, and comparing the predicted and actual %COHb at the time of measurement in the emergency room. The starting %COHb concentration is then adjusted until the correct value is obtained for the time when the blood sample was taken. This starting value then represents the value predicted when the subject was removed from the exposure:

Table 4.8 Values of half-life constant (k) for different treatments and body sizes

Body size and air mixture inhaled	k	Resting metabolic rate (kcal/h/kg)
70 kg adult on air	0.0026	1.12
70 kg adult on normobaric oxygen	0.0115	1.12
70 kg adult on 3 bar oxygen	0.0301	1.12
28 kg child on normobaric oxygen	0.0167	1.63
14 kg child on normobaric oxygen	0.0219	2.1

$$\%\mathrm{COHb}_t = \%\mathrm{COHb}_0 \mathrm{e}^{-kt} \qquad 4.20$$

where: $\%\mathrm{COHb}_t$ = %COHb after t minutes, $\%\mathrm{COHb}_0$ = %COHb at start time and k = half-life constant depending upon treatment and body size.

The value of k depends upon the treatment (air, normobaric oxygen or hyperbaric oxygen) and the body size. Although the rate of excretion should be similar for adults, it is much more rapid in small children. The model can be applied to individuals by using a factor related to the ratio of basal metabolic rates in subjects with different body sizes obtained from published data. The predictions for children from the model have been validated against half-life data obtained from incidents involving children. For different body sizes and treatments k was therefore estimated in terms of the ratio of basal metabolic rates (Table 4.8). The results for an adult male, breathing air and then normorbaric oxygen, are illustrated in Fig. 4.15.

Predicting excretion of carbon monoxide after exposure using a physiological model

The empirical model has the advantage of simplicity, but has a limited ability to reflect the effects of physiological variables such as body size and respiration. A model has therefore been developed based upon fundamental physiological variables including those used in the CFK equation. The model requires as input the blood volume and haemoglobin concentration of the subject and a starting (notional) carboxyhaemogblobin concentration. From this is calculated the body burden of carbon monoxide (ml) and the partial pressure of carbon monoxide in the lung capillary bed (based upon the Haldane factor). From this is calculated the alveolar carbon monoxide concentration (with a correction for the lung diffusivity and arterial oxygen partial pressure (P_{O_2})). A value for the subject's V_{E} is then determined based upon body size and level of activity, from which V_{A} (ml/min) is calculated. From this the volume (ml) of carbon monoxide excreted in a minute is calculated. This is then subtracted from the starting blood carbon monoxide content (ml) and the process is repeated. From this a spreadsheet can be produced plotting the decay of %COHb with time. For an actual incident the time between removal of the subject from the incident and blood sampling is

noted. The %COHb predicted by the model at this time is compared with the actual %COHb measured. The starting %COHb concentration is then adjusted until the correct value for the time when the blood sample was taken is obtained. This starting value then represents the value predicted when the subject was removed from the exposure. The calculation is performed as follows:

$$\mathrm{COHb}_0 = V_\mathrm{B}\, 0.0022\%\mathrm{COHb}_0 \tag{4.21}$$

$$P_{\mathrm{A_{CO}}}(\mathrm{mmHg}) = \%\mathrm{COHb}_0\left(\frac{0.915}{100 - \%\mathrm{COHb}_0}\right)\left(\frac{P_{\mathrm{O_2}}}{M}\right) \tag{4.22}$$

$$F_\mathrm{Ico} = P_{\mathrm{A_{CO}}}/760 \tag{4.23}$$

$$\mathrm{CO_w}(\mathrm{ml/min}) = F_\mathrm{Ico} V_\mathrm{A} \tag{4.24}$$

$$\mathrm{COHb}_t = \mathrm{COHb}_0 - \mathrm{CO_w} \tag{4.25}$$

$$\%\mathrm{COHb}_t = \mathrm{COHb}_t/0.0022 V_\mathrm{B} \tag{4.26}$$

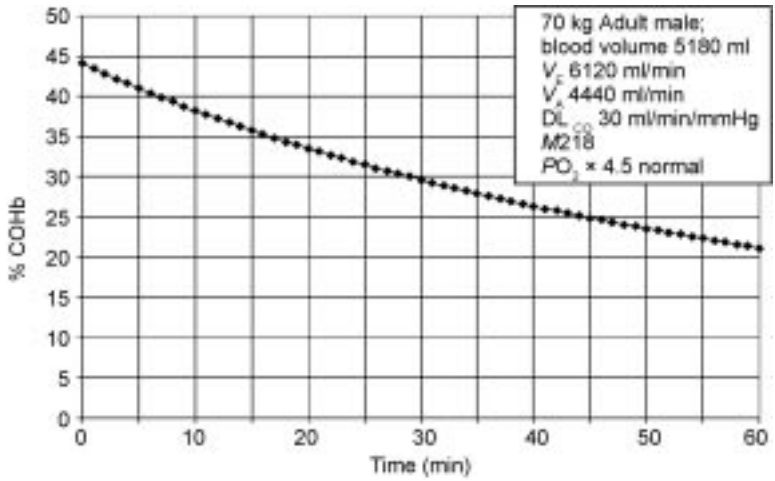
where: COHb_0 = total carbon monoxide in blood compartment of body (ml), $\%\mathrm{COHb}_0$ = %COHb at start time (e.g. time of rescue), $\mathrm{P_{A_{CO}}}$ = alveolar carbon monoxide partial pressure (mmHg), 0.915 = a constant to allow for minor differences between in carbon monoxide partial pressure between the blood and alveolar gas, $\mathrm{F_{Ico}}$ = alveolar carbon monoxide volume fraction, $\mathrm{CO_w}$ = volume of carbon monoxide washed out in 1 min, and COHb_t = total carbon monoxide remaining in blood compartment after 1 min. The calculation is repeated at 1 min intervals using a spreadsheet.

The decay curve derived using this method has been validated against actual data from incidents involving adults and children. In cases where several blood samples have been taken from the subject over a period of time it has been possible to validate the predicted curve by comparing predicted values against actual values for the excretion curve over a period of several hours.

Figure 4.16 shows an example calculated using this method for the carbon monoxide excretion curve for an adult breathing oxygen under the same conditions as those in Fig. 4.15. The calculation starts from the point where oxygen was administered when the %COHb is 44.1% as in Fig. 4.15. The model predicts a value of 28% COHb after 35 min when a blood sample is taken, which is close to the actual value at this time, and which is very close to the value of 30% predicted by the empirical method.

Predicting excretion of carbon monoxide after exposure using the CFK equation

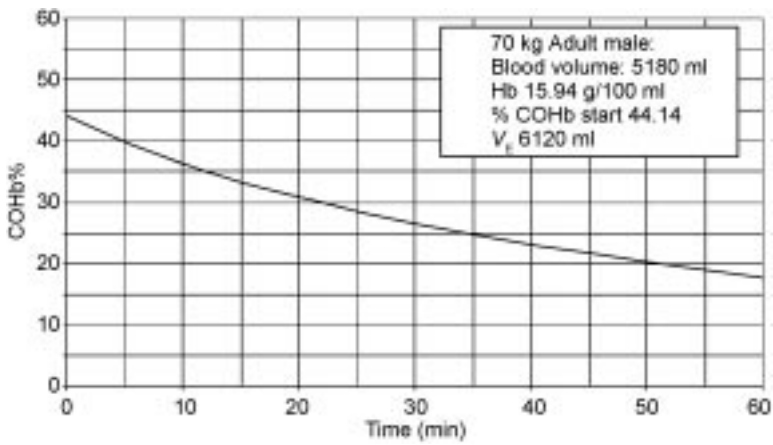
The CFK equation predicts the %COHB from a range of fundamental physiological values. It should therefore be possible to use it to predict %COHb continuously with time not only under conditions when inhaled carbon monoxide exceeds blood carbon monoxide so that %COHb is increasing (as it would during a fire) but also under conditions when inhaled carbon monoxide is less than blood carbon monoxide so that %COHb is decreasing. In particular, it



4.16 Carbon monoxide excretion curve for an adult breathing oxygen predicted using the Purser physiological model for the same case as in Fig. 4.15. The model predicts a %COHb of 28% after 35 min.

should be possible to model conditions when air or oxygen is breathed and carbon monoxide is being excreted. Figure 4.17 shows an example of the application of the CFK calculation model to the same case as in Figs 4.15 and 4.16.

With a starting value of 44.14% COHb, the CFK model predicts a value of 27% COHb after 30 min breathing oxygen, which is close to but slightly lower than the measured value of 30% COHb. In various cases the CFK model has



4.17 Carbon monoxide excretion curve for an adult breathing oxygen predicted using the CFK physiological model for the same case as in Figs 3.15 and 3.16. The model predicts a %COHb of 25% after 30 min, which is slightly lower than the true value.

been found to predict a slightly more rapid rate of excretion than the other models and actual data. However, the similarity of the predictions from all three models and closeness to the actual data confirm that they are all providing close and valid predictions of actual data.

4.5 Hydrogen cyanide

4.5.1 Importance of hydrogen cyanide as a potential cause of incapacitation and death in fires

Hydrogen cyanide is produced at significant yields and high concentrations when nitrogen-containing materials commonly used in building contents are combusted under conditions typical of fires in domestic dwellings.[24,26,63,64] The concentrations occurring during the early stages of fires involving items such as upholstered furniture and bedding often exceed concentrations causing incapacitation within a few minutes of exposure. Cyanide has also been measured in the blood of both fatal and non-fatal fire victims, but high hydrogen cyanide concentrations in fires are accompanied by high carbon monoxide concentrations, and in post-mortem studies of fire victims, high blood cyanide concentrations are not routinely determined (see Chapter 5), and usually associated with high blood carboxyhaemoglobin concentrations, so that the contribution of cyanide to incapacitation and death is difficult to determine.[25,65] This is to be expected since all fires producing cyanide also produce carbon monoxide, and combustion conditions producing high yields of hydrogen cyanide also produce high yields of carbon monoxide (see Chapter 14).[24,63,66]

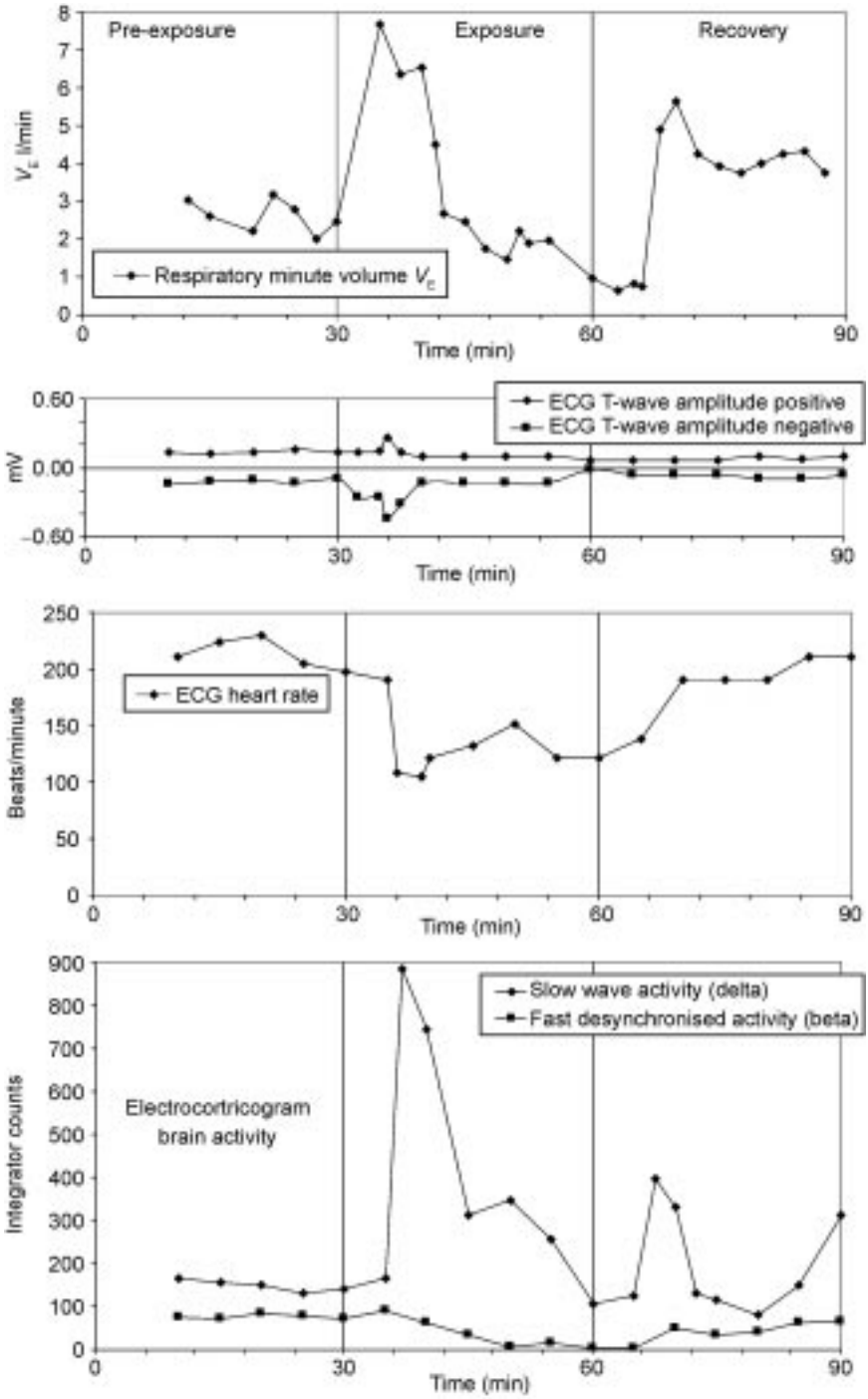
Another difficulty with the interpretation of blood data is that while carboxyhaemoglobin is stable in cadavers and in stored post-mortem blood samples, cyanide is unstable, the concentration in a body reducing by approximately 50% over 24 hours, and more slowly in stored blood samples.[67–69] Evidence for the importance of hydrogen cyanide toxicity in fire victims is provided by one study in which blood samples were taken from survivors at the fire scene.[70] High blood cyanide concentrations were found in many of these freshly obtained blood samples. Another difficulty with the interpretation of blood cyanide data is that the dynamics of uptake, distribution and removal from the blood are not well understood, so that it is difficult to relate signs and effects to blood levels, especially some time after an exposure has occurred.[23,71] A further complication with assessing the effects of different blood cyanide levels is that whereas with carbon monoxide the main toxic effects are related to the formation of caboxyhaemoglobin and its effects on the carriage and delivery of oxygen in the blood, with cyanide the target is the mitochondrial cytochrome in the tissues of the affected organs (particularly the brain and heart), so that the severity of toxic effects may not be directly related to whole blood cyanide concentrations.[1,18,23]

Based upon experimental studies of hydrogen cyanide intoxication it is considered that hydrogen cyanide is likely to be a major cause of incapacitation in many fire incidents, while the difficulties with interpretation of post-mortem blood data have led to the importance of its role in incapacitation and escape prevention being somewhat underestimated. However, as described in the following sections, the uptake of hydrogen cyanide by subjects tends to be self-limiting, and the dynamics of distribution within the body may result in severe but relatively short-lived incapacitating effects over timescales of a few minutes during exposure being followed by less severe effects over longer timescales.[1,23,26,36,71,72] For these reasons it is likely that while hydrogen cyanide is a major cause of incapacitation during exposure it may be less important as a direct cause of death. As described in Section 4.4 on carbon monoxide, post-mortem data appear to be consistent with carbon monoxide as the main cause of death from asphyxia during and immediately after exposure in fires, with some additive contribution from cyanide and other toxic species.

4.5.2 Physiological effects of acute hydrogen cyanide exposure

Hydrogen cyanide is an asphyxiant gas, and the ultimate effects of HCN exposure to it are similar to those of carbon monoxide, consisting of unconsciousness with cerebral depression, accompanied by a reduction of circulation and respiration.[23,26] However, the pattern of intoxication is very different. While the onset of carbon monoxide intoxication is slow and insidious, hydrogen cyanide intoxication tends to be rapid and dramatic. The physiological signs are illustrated in Fig. 4.18, which shows data from exposures of seated primates. These studies of the mechanisms of incapacitation involved exposure to hydrogen cyanide in air and to fire effluent mixtures containing hydrogen cyanide from the decomposition of polyacrylonitrile, and polyurethane foams (flexible and rigid). The effects of the exposure to polyacrylonitrile pyrolysis products, consisting mainly of hydrogen cyanide plus small amounts of other nitriles, were very similar to but slightly less toxic than equivalent concentrations of hydrogen cyanide in air.

The initial effects of exposure were minor, sometimes consisting of slightly increased ventilation, but at some time during the 30 min exposure period there was a marked increase in respiration (hyperventilation). The time during the exposure period at which this hyperventilatory episode started depended upon the exposure concentration, so that at concentrations of around 100 ppm hydrogen cyanide or less, ventilation was little changed for up to around 20 min, at which point the hyperventilation started, while at around 150 ppm or more, hyperventilation started more or less immediately upon exposure. Once hyperventilation started, V_E increased by up to a factor of 4 within a minute or so. Then, after 1–5 min of hyperventilation, the animals lost consciousness. As



4.18 Physiological effects of hydrogen cyanide gas (147 ppm) on a macaque monkey.

shown in Fig. 4.18, this was accompanied by brain-electrocorticogram (similar to EEG) signs of severe cerebral depression (including a large increase in delta-wave activity and a large decrease in beta activity); loss of muscle tone and marked effects on the heart and circulation, including a significant decrease in heart rate, arrhythmias and changes in the ECG waveform indicative of myocardial hypoxia. The hyperventilation was caused by the initial stimulatory effects of cyanide on respiration. Since the cyanide was taken in by inhalation, positive feedback resulted, whereby the increased breathing further increased the rate of hydrogen cyanide uptake, which in turn generated a stronger hyperventilatory stimulus.

This continued until the animals became unconscious, at which point the hyperventilation subsided, possibly owing to depression of the respiratory centre. At this point the condition of the animals tended to improve somewhat for a few minutes, with less cerebral depression, some signs of recovered consciousness, a reduction in ECG T-wave amplitude and a recovery in heart rate. After this, as the exposure continued they went into a slow decline, leading eventually to apnoea if the exposure continued for a sufficient time at higher exposure concentrations, which would have proved fatal if the exposure had not been discontinued. It was therefore possible for an animal to survive a continuous hydrogen cyanide exposure for some time after the point of incapacitation, and since the hydrogen cyanide was inhaled, and exposure led eventually to a reducing V_E, the toxic effects were to some extent self-limiting. This therefore differs from the effects of cyanide poisoning resulting from oral or intramuscular administration.

4.5.3 Dose–response relationships for hydrogen cyanide

In order to develop a calculation model for uptake and time to incapacitation for hydrogen cyanide, one possible approach is to use the *Ct* product exposure dose method, by determining the exposure doses required for incapacitation or death. However, unlike carbon monoxide, the *Ct* product exposure dose for incapacitation is not a constant, deviating considerably from Haber's rule. This is illustrated in Fig. 4.7 which compares the *Ct* relationships of carbon monoxide and hydrogen cyanide. While the *Ct* product dose for incapacitation by carbon monoxide in these primates was constant at approximately 27 000 ppm min irrespective of the exposure concentration, that for hydrogen cyanide varies considerably, in that short exposures to higher hydrogen cyanide concentrations above approximately 150 ppm hydrogen cyanide cause incapacitation within a minute or two, at low exposure doses, while at exposure concentrations of around 90 ppm or less, incapacitation occurs only after around 30 min. Exposure concentrations below approximately 80 ppm resulted in only minor effects, with mild background increases in ventilation, over exposures of up to an hour. The result is that the *Ct* product for

incapacitation by hydrogen cyanide varied from around 2610 ppm min at 87 ppm hydrogen cyanide to 270 ppm min at 300 ppm. It appears that time to incapacitation by hydrogen cyanide is partly related to the rate of hydrogen cyanide uptake and partly to the total uptake dose. Data on human exposures to hydrogen cyanide are limited, but Kimmerle[73] quotes some approximate data showing similar effects in humans, with incapacitation occurring after 20–30 min at 100 ppm, and after 2 min at 200 ppm, death occurring rapidly at concentrations exceeding approximately 300 ppm. Owing to scaling effects relating to energy consumption and body size, it is to be expected that incapacitation may require somewhat longer for resting 70 kg adult humans than resting 4 kg primates, although as with carbon monoxide the exposure dose to incapacitation for active humans may be similar to that for resting monkeys. This is supported by McNamara, who suggests 539 ppm as the 10 minute LC_{50} for humans,[74] and there is a report of a survival from an accidental human exposure to 444 ppm.[75] An experimental human exposure to 530 ppm hydrogen cyanide was survived without immediate symptoms for 1.5 min, although a dog exposed at the same time suffered respiratory arrest.[76] Dogs are considered to be particularly susceptible to cyanide poisoning, but it seems likely that body size influences time to incapacitation to some extent. Effects on young children should be similar to those on monkeys.

Data on the effects of hydrogen cyanide exposure in humans and larger animals are limited, but those summarised in Table 4.9 demonstrate that the primate data are in line with findings for humans. For given exposure concentrations up to around 500 ppm hydrogen cyanide it is likely that time to incapacitation will be somewhat longer for 70 kg resting humans than for 4.5 kg primates, but that active humans and resting children will show tenability times closer to the primate data.

Table 4.9 Incapacitation by inhaled hydrogen cyanide

HCN (ppm)	Species and effects	Author
100	Loss of consciousness after 23–30 min in primates and humans	Purser *et al.*,[23] Kimmerle[73]
200	Loss of consciousness after approximately 2 min	Purser *et al.*,[23] Kimmerle[73]
300+	Death occurs 'rapidly'	Kimmerle[73]
444	A man survived an accidental exposure	Bonsall[75]
530	A man, Barcroft, survived a 1.5 min exposure – his dog exposed at the same time died	Barcroft[76]
539	Suggested 10 min LC_{50} in humans	McNamara[74]
1000	One breath may cause loss of consciousness	Purser[1]

4.5.4 A model for the prediction of time to incapacitation by hydrogen cyanide

From the primate results it is possible to predict that hydrogen cyanide concentrations below a threshold of approximately 80 ppm will have only minor effects over period of up to 1 hour. From 80 to 300 ppm the time to incapacitation (loss of consciousness) lies approximately between 0.9 and 30 min according to the relationship

$$t_{I_{CN}}\,(\text{min}) = \exp(5.396 - 0.023[\text{HCN}]) \qquad 4.27$$

where [HCN] = HCN concentration (ppm). From this the fractional incapacitating doses expression for HCN (F_{ICN}) has been developed as follows:

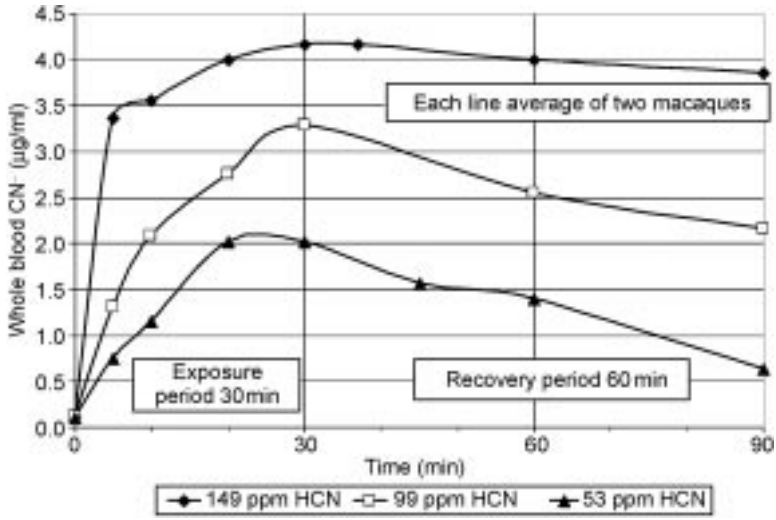
$$F_{I_{CN}} = \left[\left(\frac{\exp([\text{CN}]43)}{220}\right) - 0.0045\right]t \qquad 4.28$$

where [CN] = HCN concentration (ppm v/v at 20 ºC) and t = exposure time in minutes.

4.5.5 Relationship between hydrogen cyanide toxicity and blood cyanide concentration during and after exposure

In order to examine the relationships between hydrogen cyanide exposure concentration, exposure time, blood cyanide concentration and physiological effects, macaque monkeys were exposed to hydrogen cyanide while blood samples were taken from a catheter inserted into the femoral artery.[71] Two animals were exposed at each of three different exposure concentrations for 30 min, followed by a 60 min post-exposure observation period, while respiratory V_E was measured and clinical signs were monitored. Measurements of hydrogen cyanide concentration in exhaled air immediately following exposure showed low concentrations (<1 ppm hydrogen cyanide), the actual concentration being proportional to the whole blood cyanide concentration. Measurements of differences between inhaled and exhaled hydrogen cyanide during exposure showed that approximately 60% of inhaled hydrogen cyanide was taken up into the blood.

Figure 4.19 shows the results for cyanide uptake during exposure, and loss after exposure, expressed as arterial whole blood cyanide concentration. At each of the inhaled hydrogen cyanide concentrations the arterial whole blood cyanide concentration increased rapidly for the first 10–20 min, but then levelled off somewhat, despite the continued constant hydrogen cyanide exposure concentrations. After the end of the exposure period there was a slow decline in arterial blood cyanide over the next 60 min, the rate of decrease being inversely related to the total blood concentration achieved, with the most rapid rate of loss at the lower blood concentrations. The effects on the animals differed in severity at



4.19 Uptake and loss of arterial blood cyanide during and after 30 min exposures to hydrogen cyanide at three different exposure concentrations (average of two macaques exposed at each concentration).

different exposure concentrations. At 149 ppm hydrogen cyanide a marked hyperventilation occurred immediately on exposure until loss of consciousness after approximately 7 min followed by a depressed respiration until a few minutes after the end of the exposure, at which point the animals regained consciousness followed by a period of hyperventilation. At 99 ppm, hyperventilation developed more gradually and was less marked, with loss of consciousness occurring after approximately 23 min. Consciousness was regained after a few minutes recovery with some rebound hyperventilation. At 53 ppm there was no significant hyperventilatory episode and no loss of consciousness or rebound hyperventilation.

The physiological issues in relation to this data set are:

- The relationship between clinical condition and whole blood cyanide concentration during exposure and recovery.
- Effects of hypocapnia.
- The dynamics of cyanide uptake and dispersal into the blood and other body fluid compartments during exposure.
- The rate of loss of cyanide from the blood during the post-exposure period.
- Partitioning of blood cyanide between erythrocytes and plasma.

Relationship between whole blood cyanide and clinical condition

During inhalation of hydrogen cyanide, incapacitation (loss of consciousness) occurred following a period of hyperventilation when blood cyanide reached

levels of around 3.0 μg/ml. However, as described in the previous section, once the hyperventilation and hence the rate of uptake of cyanide had subsided there were some signs of recovery, despite the continued exposure. In these experiments the blood cyanide concentrations continued to increase until the end of the exposure and remained high for some time after exposure. Thus for the high dose pair of animals the whole blood cyanide concentration remained close to 4 μg/ml for up to an hour after the exposure, although the animals made a good recovery within a few minutes. For the intermediate dose pair the blood level remained just above 3.0 μg/ml for around 10 min after exposure but the animals also recovered within a few minutes. For the low dose group there were no significant adverse signs and the maximum blood level was 2.2 μg/ml.

On the basis of these results it is necessary to explain why, following a hyperventilatory episode and loss of consciousness at around 3.0 μg/ml, animals can make some degree of recovery during exposure, and a rapid recovery after exposure, when the whole blood cyanide concentration is increasing further and maintained at levels as high as 4.0 μg/ml for up to an hour. It is considered that there are several possible explanations for this finding, one relating to the dynamics of uptake and dispersal of cyanide in the body, another relating to the partitioning of blood cyanide between erythrocytes (red blood cells) and plasma and a third relating to the effect of hyperventilation on P_{CO_2} and blood pH.

When cyanide is taken up by the inhalation route it is absorbed from the lungs directly into the systemic circulation, passing with seconds through the heart and brain. In the blood, cyanide exists partly as free cyanide in solution in the plasma, partly bound to plasma proteins, but the largest proportion penetrates into the erythrocytes where most or all of it reacts with methaemoglobin to form cyanomethaemoglobin.[18,77–79] Of these three components the fraction in the erythrocyte is effectively detoxified, while a proportion of that in the plasma is free to disperse into the extracellular and intracellular fluid compartments, initially in the heart and brain, to exert toxic effects. These issues are discussed in more detail in the following sections, but one possibility in relation to the primate experiments is that during the hyperventilatory episode the uptake dynamics are such that a significant proportion of blood cyanide is in the form of free cyanide and is carried rapidly to the heart and brain, while at later stages of exposure, when ventilation has reduced, a greater proportion of blood cyanide is in a bound form in the erythrocytes. This may result in relatively high whole blood cyanide, of which only a relatively small proportion is toxicologically active. During the long recovery period it may be mainly this bound cyanide that is gradually removed from the blood. The detoxifying effect of methaemoglobin is well known, and induction of additional methaemoglobin is used as a treatment for cyanide poisoning.[18] The extent of this detoxification mechanism during exposure therefore depends upon the maximum amount of cyanide that can be sequestered by the erythrocytes and the rate of sequestration during rapid uptake from the lungs.

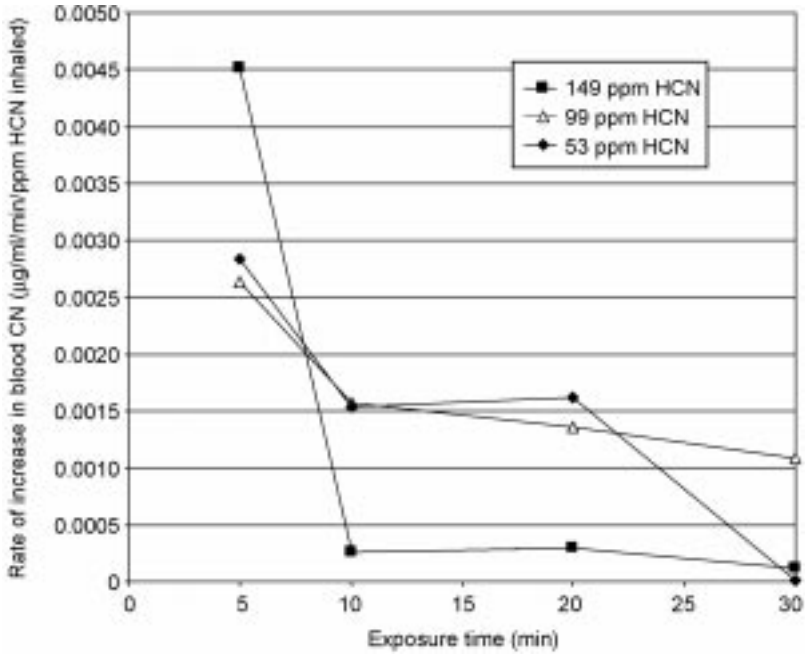
It may also be that during the initial uptake period most of the cyanide is limited to a small blood compartment consisting of the systemic and cerebral circulation, with a proportion as free cyanide, while over a longer period the cyanide becomes more mixed into other blood and body fluid compartments, with a higher proportion as bound cyanide.[71] Another factor is that during cyanide poisoning more erythrocytes are released from the spleen into the circulation, so that more are available to take up cyanide from the plasma.

Effects of hypocapnia

Another likely contributory cause of loss of consciousness during the hyperventilatory episode is a transient hypocapnia (lower then normal level of carbon dioxide in the blood) and respiratory alkalosis. During this episode ventilation increases by approximately a factor of 3, which will result in a temporary respiratory alkalosis with a reduction in blood P_{CO_2}. The pH change results in a left shift in the oxygen dissociation curve and the P_{CO_2} reduction in a reduced cerebral blood flow, effects known to result in syncope (loss of consciousness) in humans.[2] The effect is likely to be enhanced by the direct effects of cyanide on heart rate and cardiac output, as well as direct effects on cerebral metabolism. The combined result is the reported transient loss of consciousness. The loss of consciousness then results in a decrease in respiration and circulation, enabling P_{CO_2} and pH to recover towards normal levels, while the direct effect of cyanide on metabolism results in a metabolic acidosis and increased cerebral blood flow. This may be the reason that animals are seen to make some recovery during this stage of an exposure, followed by a slow decline until exposure is terminated. Effects on P_{CO_2}, pH and cerebral blood flow were measured in anaesthetised dogs by Klimmek *et al.*,[78] who found that intravenous infusion of potassium cyanide induced hyperventilation accompanied by hypocapnia, alkalosis and reduced cerebral blood flow. Similar combinations of initial hypercapnia and alkalosis and metabolic acidosis have been reported by Levine.[80] Djerad *et al.*[81] examined the effects of controlled respiratory alkalosis, normal pH state and acidosis on cerebral blood flow and distribution of cyanide to cerebral tissue. They found that brain uptake of cyanide was reduced under alkalosis but increased under acidosis, presumably due to the effects of P_{CO_2} on cerebral circulation. For these three studies the animals were anaesthetised, unlike in the primate studies, so that it was not possible to consider the relationship between hyperventilation, cyanide uptake and alkalosis followed by acidosis.

Dynamics of cyanide uptake and dispersal into the blood and other body fluid compartments during exposure

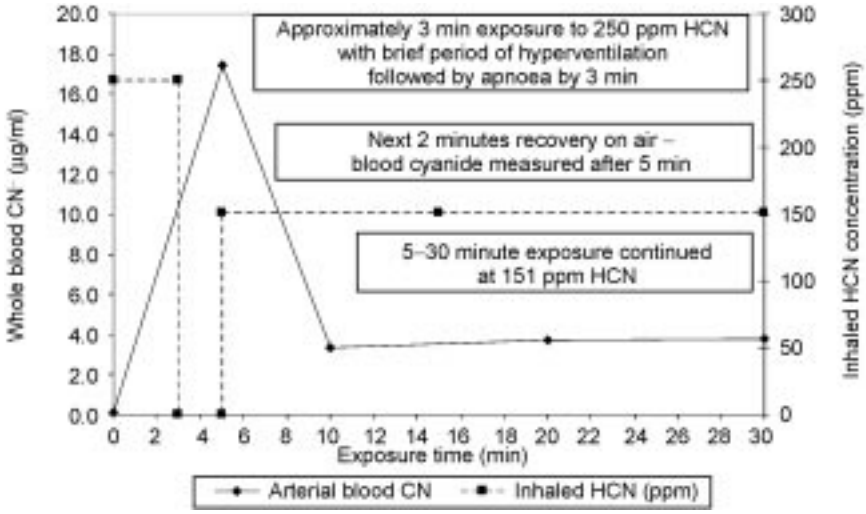
From the description in the previous section it is evident that uptake of cyanide into the blood is not a simple linear function of exposure concentration and



4.20 Rate of increase of blood cyanide during exposure (μg/min/ppm hydrogen cyanide).

exposure time. Figure 4.20 shows the normalised blood uptake expressed as micrograms increase in blood cyanide per minute per ppm hydrogen cyanide. At 149 ppm hydrogen cyanide the initial rate of cyanide uptake into the blood is very rapid due to the high inhaled concentration and the immediate marked hyperventilation, but by 10 min into the exposure the rate of further increase in blood cyanide concentration is very low, partly because of the reduced ventilation, but possibly because a higher proportion is passing out of the blood into the tissues. At 53 and 99 ppm the rate of uptake is somewhat higher initially, but is generally maintained at a relatively high rate throughout the exposure period.

A more extreme example of this dynamic situation is presented by a single exposure in which an animal was exposed for approximately 3 min to a higher hydrogen cyanide concentration than intended at around 250 ppm hydrogen cyanide (Fig. 4.21). This resulted in a brief period of strong hyperventilation followed by apnoea (cessation of breathing). The exposure was then paused, and followed by exposure to air for 2 min, after which a blood sample taken at 5 min showed a very high blood concentration of 17.45 μg/ml. The exposure was then resumed at 151 ppm, but at 10 min the blood concentration had decreased to 3.35 μg/ml. From this it is concluded that rapid uptake of hydrogen cyanide resulted in a transient, very high concentration in the systemic blood compart-



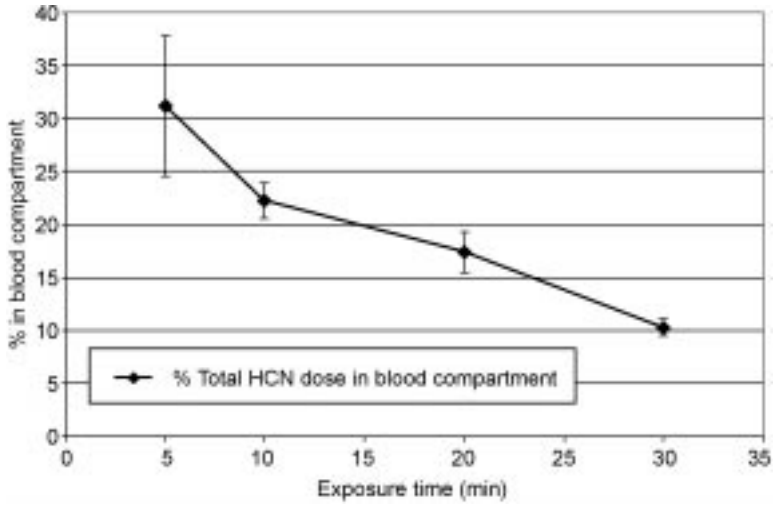
4.21 Arterial whole blood cyanide during and after exposure to ~250 ppm for 3 min, then 151 ppm hydrogen cyanide from 5 to 30 min.

ment, which then rapidly decreased, despite continued exposure, as the high concentration blood mixed with that in other compartments and a proportion of the cyanide was dispersed into the tissues.

By calculating the mass of hydrogen cyanide inhaled from during exposure as $0.6 \times V_E$ and relating this to the total blood volume it is possible to calculate the proportion of the inhaled cyanide dose in the whole blood compartment of the body, the remainder therefore being in the extracellular and intracellular tissue fluid spaces. The results (Fig. 4.22) show that during the early stages of the exposures the proportion of the total inhaled dose in the whole blood compartment was 25–38%, but that the proportion in the blood then decreased throughout the remainder of the exposure period until only about 10% remained in the blood at the end of the exposure. Almost all the remaining 90% was therefore in the extracellular and intracellular tissue fluid compartments, with a small amount possibly having been metabolised.

The rate of loss of cyanide from the blood during the post-exposure period

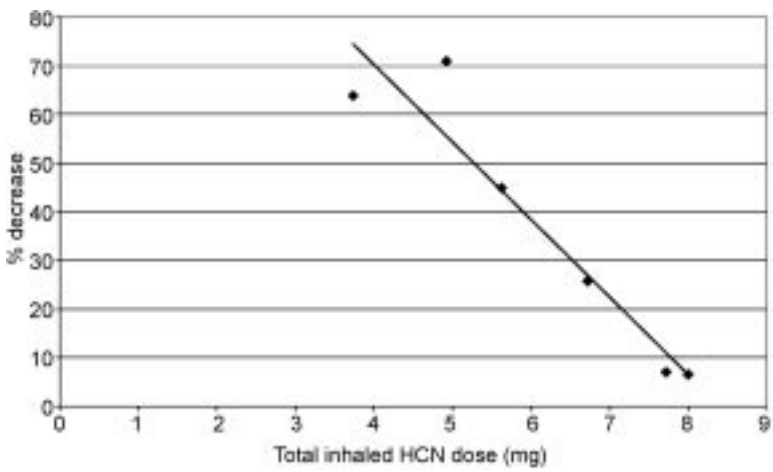
At the end of the exposure period approximately 10% of the inhaled hydrogen cyanide dose remained in the blood while 90% was in the tissues. This total body burden of cyanide then gradually decreased as it was metabolised (presumably to thiocyanate and other metabolites) and excreted. In these experiments it was found that the decrease in blood cyanide concentration after 60 min recovery was much slower when larger doses had been inhaled and blood concentrations were high. This is illustrated in Fig. 4.23 which shows the



4.22 Percentage of total inhaled hydrogen cyanide dose in the blood compartment throughout exposure.

percentage decrease in blood concentration after 60 min as a function of total inhaled dose. For the two high concentration exposures at 149 ppm hydrogen cyanide, the total inhaled dose was 8 mg cyanide and the blood concentration decreased by only 5% over 60 min; a greater decrease occurred for the intermediate doses; and around 70% for the 53 ppm exposures with doses of around 4–5 mg. The body weight of the animals was approximately 4–5 kg.

Table 4.10 summarises the blood decrease data. As shown in Fig. 4.19, the rate of decrease in blood cyanide during the recovery period was approximately



4.23 Relationship between percentage decrease in blood CN^- concentration and total inhaled hydrogen cyanide body dose after 60 min recovery.

Table 4.10 Decreases in blood cyanide during 60 min recovery period and half-lives

HCN (ppm)	Blood CN^- after 30 min exposure (μ/ml)	Blood CN^- after 60 min recovery (μg/ml)	Decrease after 60 min (μg/ml)	Rate of decrease (μg/ml/h)	Half-life (min)	Cyanide removed in 1 hour (mg)	Removal rate (mg CN^-/kg/min)
149	4.56	4.23	0.34	0.30	417	0.53	0.002
99	3.22	2.42	0.81	0.67	115	2.12	0.009
53	2.35	0.60	1.75	0.82	74	2.94	0.012

linear. On this basis, the half-life for the high dose animals was approximately 417 min, decreasing to 74 min for the low dose animals.

Assuming the total body burden of cyanide was in proportion to the whole blood concentration, the mass of cyanide metabolised in 60 min was approximately 5.5 times greater for the low dose animals than for the high dose animals. It is considered likely that the greater degree of hypoxic stress in the high dose animals inhibited the metabolism of hydrogen cyanide in the liver or other sites. These figures compare with reported two-phase half lives in dogs, for which the first phase was 18.4–24 min and 330 min for the second phase.[79] Djerad *et al*.[81] reported a three-phase half-life for low intravenous instantaneous doses of radiolabelled cyanide in rats, involving an initial rapid distribution phase with a half-life of 21.6 seconds, a second phase with a half-life of 2.4 min and a long phase with a half-life of 87.4 min. These reports appear to be consistent with the findings from the primate work in that there is obviously a very rapid distribution phase occurring during continuous inhalation dosing over timescales of a few seconds to a minute or so, and a longer detoxification phase following the end of dosing with a half-life of around 74 min at relatively low dose levels, which is similar to that reported for rats of 87.4 min. The rate of detoxification (removal) at the low dose level (~0.012 mg/kg body weight/min) is also comparable with that of 0.017 mg/kg/min estimated for humans by McNamara.[74] However, the long detoxification timescales associated with high dose levels do not appear to have been reported previously.

Partitioning of blood cyanide between erythrocytes and plasma

Cyanide can exist in several different forms in blood, with differing degrees of binding. In studies of cyanide added to blood samples *in vitro*, and of blood samples taken from animals dosed with cyanide intravenously or by intramuscular injection, a proportion of blood cyanide was found in free solution in plasma or serum, while a proportion of plasma cyanide was protein bound, but the greatest proportion of cyanide was recovered from the erythrocytes.[77] A proportion of erythrocyte haemoglobin is in the form of methaemoglobin (range 0.01–0.5 g/100 ml – average 0.16–0.32 g/100 ml in humans),[21] and this reacts with cyanide to form cyanomethaemoglobin. The ferric haem group competes with cytochrome *a*3 for cyanide by complexing in the ionic form.[18] The affinity of methaemoglobin for cyanide exceeds that of cytochrome *a*3. Cyanomethaemoglobin is a dissociable complex so some free cyanide is present.[18] Erythrocytes have a high affinity for cyanide and there is rapid uptake of plasma cyanide by erythrocytes.[82–86] McMillan and Svoboda[87] confirmed rapid assimilation by erythrocytes and demonstrated that it passes through the erythrocyte membrane as HCN, where it is sequestered, but that erythrocytes play no role in cyanide degradation. It is therefore likely that most if not all erythrocyte cyanide is in the form of cyanomethaemoglobin, as

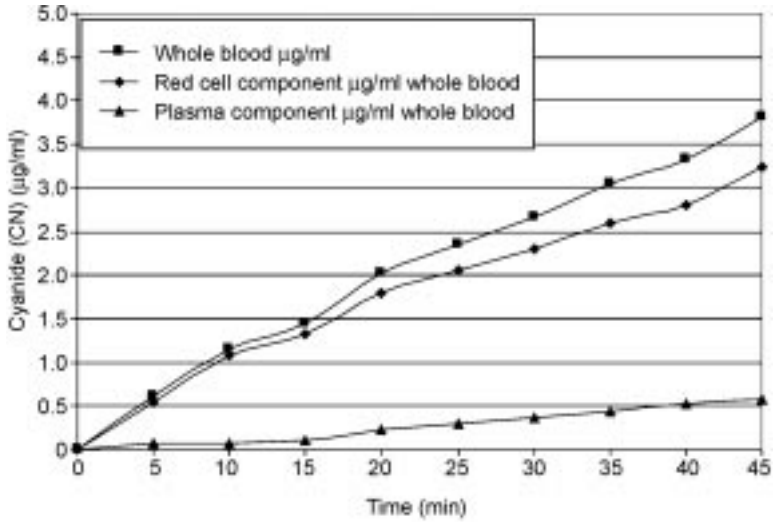
demonstrated *in vitro* by Lundquist *et al.*[88] over a range of whole blood concentrations.

During and immediately after exposure to hydrogen cyanide, uptake is via the lungs and cyanide in blood is rapidly circulated to key target organs, including the heart, the aortic and carotid bodies and the brain. The acute physiological effects therefore depend upon the changing cyanide concentrations in the tissue of these key organs. Since creation of additional methaemoglobin is an effective treatment for cyanide poisoning, and cyanide is tightly bound to methaemoglobin, it is likely that normal methaemoglobin acts to some extent as a protective buffer to cyanide poisoning, and that any cyanide sequestered into the erythrocyte is rendered relatively non-toxic. It therefore seems that the severity of acute cyanide poisoning is likely to be more closely related to plasma cyanide concentrations than whole blood cyanide,[82,84] and that the penetration of cyanide into tissue extracellular and intracellular fluid compartments is likely to relate to plasma cyanide or at least to the concentration of free cyanide in plasma, since protein-bound cyanide may also be at least temporarily unavailable for penetration to the mitochondria in affected tissues. There is some evidence that brain exposure to cyanide is related to plasma cyanide levels, in that Ballantyne found similar average cyanide concentrations in blood plasma or serum and cerebrospinal fluid (CSF) in sheep dying following intramuscular cyanide injection.[89]

If plasma cyanide is the key parameter, then it is important to determine the dynamics of uptake and partitioning of cyanide between erythrocyte and plasma with time during an acute exposure, and possibly also the dynamics of partitioning between protein-bound and free cyanide in plasma. If effectively all cyanide in blood is rapidly sequestered by methaemoglobin up to a high saturation level, so that only above this does it appear in the plasma (as proposed by Lundquist *et al.*[88]), then cyanide should be relatively non-toxic up to a critical dose level. If there is a more dynamic partitioning between erythrocyte and plasma cyanide, then red cell sequestration may offer some degree of protection, but the plasma concentration may increase in parallel with the red cell concentration until the plasma concentration (and tissue concentration) becomes high enough to exert toxic effects. Another issue arises once intake ceases. At this point does the red blood cell cyanide remain relatively stable for a period while the plasma cyanide disperses throughout the body and is detoxified, so that the plasma concentration decreases more rapidly than the whole blood or erythrocyte cyanide, and is the cyanide then gradually released from the red cells, maintaining a low plasma level until detoxification is complete?

The key problem is to determine the time–concentration relationships between exposure conditions and plasma cyanide. A number of experiments have been performed that provide some data relating to these problems, but the situation has not yet been fully resolved.

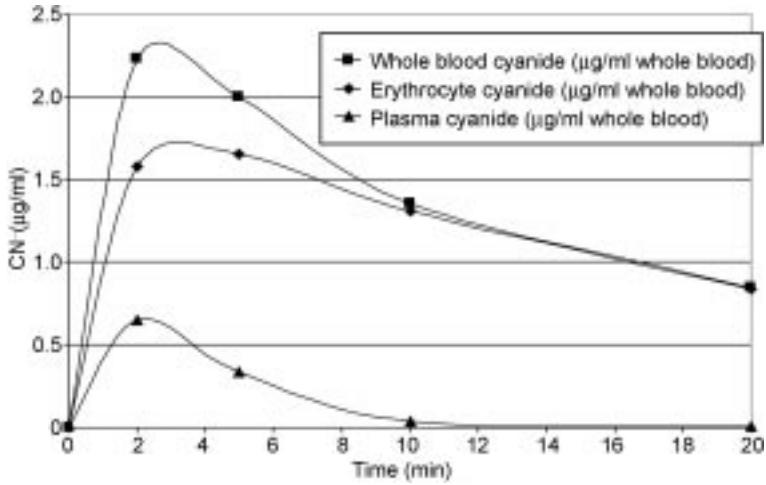
In addition to the primate studies described, there have been two studies in which whole blood, erythrocyte and plasma cyanide have been measured in dogs



4.24 Cyanide concentrations in erythrocytes, plasma and whole blood during continous intravenous infusion of potassium cyanide 0.07 mg/kg/min in a dog. Concentrations are expressed as fractions of whole blood volumes.

at intervals during or following intravenous dosing with potassium cyanide at toxic but sub-lethal dose levels. For one of these experiments Christel *et al.*[77] exposed an anaesthetised dog to a continuous intravenous injection of potassium cyanide at a rate of 0.07 mg/kg/min. After 45 min the whole blood concentration reached 3.9 μg/ml and there was a marked decrease in respiration and heart rate, at which point sodium thiosulphate was administered as an antidote. The relationship between whole blood, erythrocyte and plasma cyanide is shown in Fig. 4.24. The results show that under these conditions of continuous potassium cyanide infusion, there was a steady increase in both plasma and red blood cell cyanide. For the first 15 min approximately 90% of whole blood cyanide was in the erythrocytes, with very low plasma concentrations, but above whole blood cyanide concentrations of approximately 2 μg/ml the plasma component increased significantly, representing approximately 16% of whole blood cyanide. When the physiological changes became marked after 45 min the plasma concentration was approximately 0.6 μg/ml and the whole blood concentration 3.9 μg/ml. Since 60% of plasma cyanide was found to be protein-bound, the free cyanide concentration at this point would have been approximately 0.24 μg/ml.

This experiment therefore confirms that during steady continuous uptake of cyanide, similar to that occurring during hydrogen cyanide exposure by inhalation, some plasma cyanide is always present in addition to erythrocyte cyanide. Also, no saturation point was reached for erythrocyte cyanide in this experiment, so either the methaemoglobin was not exhausted or red cells sequester cyanide in addition to that reacting with methaemoglobin, although there was an increase



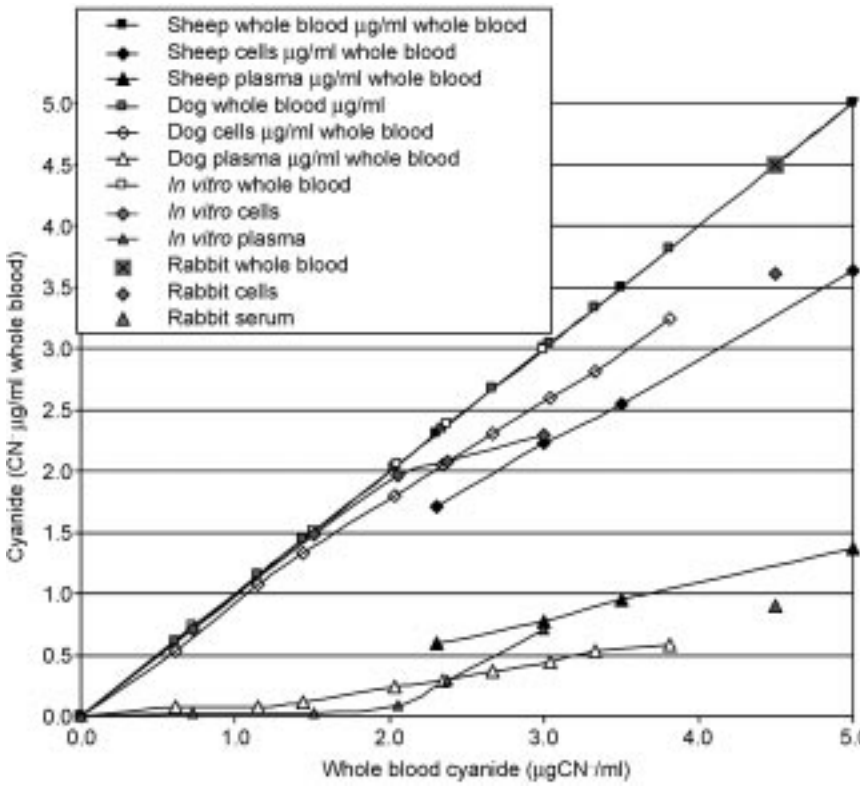
4.25 Cyanide concentrations in erythrocytes, plasma and whole blood during single intravenous injection of potassium cyanide (16.77 μmol/kg) in a dog. Concentrations are expressed as fractions of whole blood volumes.

in the proportion of cyanide in plasma. A question arising from this experiment is what would have happened if the potassium cyanide injection had been stopped. Would the amounts and proportions of cyanide in the cell and plasma have remained approximately constant before gradually decreasing, or would the plasma cyanide have preferentially decreased?

For a second dog experiment, which was performed by Vesey and Wilson,[85] the potassium cyanide (16.77 μmol/kg) was injected instantaneously, and the results are illustrated in Fig. 4.25. During this experiment the initial effects are similar to those following continuous infusion, in that there is a rapid increase in both erythrocyte and plasma cyanide, with the greater proportion in the erythrocytes. However, the rate of increase to toxic levels is very rapid, and at 2 min the proportion in the plasma is greater than in the previous experiment, at approximately 30% of whole blood cyanide. After the peak at around 2 min there is gradual decline in erythrocyte cyanide to 47% of the peak level over 15 min. Presumably this is mainly due to dispersal and mixing throughout the different body blood compartments, and may partly result from losses into the tissues and metabolism to thiocyanate. The plasma level decreases rapidly to near zero after 10 min, and this is presumably also due to a combination of dispersal into the extracellular and intracellular body water and detoxification. This experiment also shows erythrocyte and plasma cyanide increasing in tandem during the first 2 min, without any obvious lag before erythrocyte uptake.

From the results of this experiment it would appear that uptake into both plasma and erythrocytes is rapid, but that plasma cyanide disperses rapidly out of the blood compartment when uptake ceases, leaving erythrocyte cyanide as the main component of whole blood cyanide.

Other experiments were carried out by Ballantyne on sheep and rabbits.[89,90] For these experiments anaesthetised animals were given lethal intramuscular injections of potassium cyanide, and the plasma, serum and whole blood cyanide was measured in samples taken from the heart and other tissues after death. The distribution of cyanide therefore represents that at death, which occurred 11–26 min after administration. Although the results obtained showed quite a wide scatter, they are useful in indicating the partitioning between erythrocytes and plasma at high (lethal) blood concentrations, and provide further data on the upper limits (if any) of erythrocyte cyanide capacity. Figure 4.26 shows the results from Ballantyne's experiments and the dog experiments plotted against whole blood cyanide concentrations. Also plotted are the results of Lunquist *et al.*'s *in vitro* experiments, in which potassium cyanide was added to 3 ml blood samples. The amounts of cyanide in the different fractions are expressed per ml whole blood, so that for any particular sample the whole blood concentration

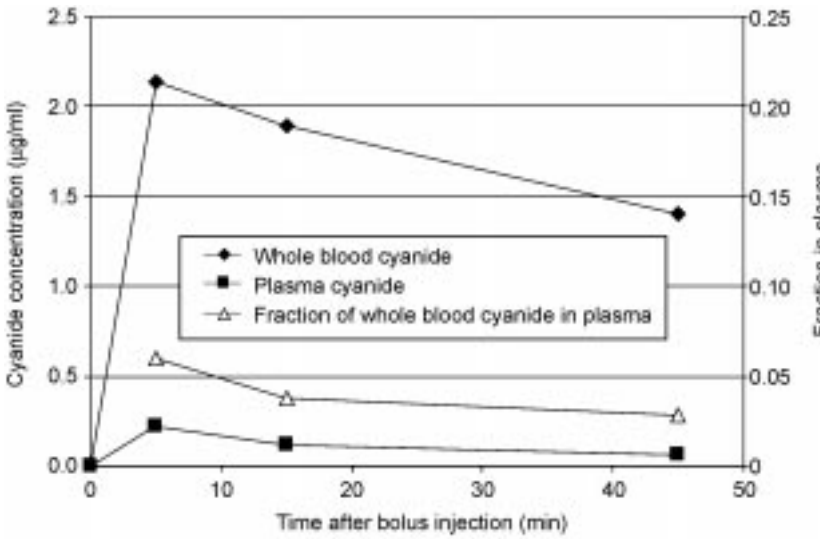


4.26 Cyanide concentrations in different blood fractions including whole blood, erythrocytes (cells), plasma or serum from different *in vivo* and *in vitro* experiments plotted against whole blood concentrations. The concentration for each component is expressed as μg CN^- per ml whole blood.

represents the sum of the erythrocyte and plasma concentrations. The total whole blood cyanide is plotted on the *x*-axis, while the *y*-axis shows the concentration in the specific blood compartments, but expressed as concentrations per ml whole blood. For example, the right hand side of the figure illustrates that when sheep had whole blood cyanide concentrations of 5 μg/ml, the amount in the plasma represented a concentration of 1.4 μg/ml whole blood, while that in the cells (erythrocytes) represented 3.6 μg/ml whole blood. Summing these to fractions gives the total whole blood concentration of 5 μg/ml.

A comparison of the results from the different experiments shows that for the dog, sheep and rabbit experiments there appears to be no upper limit for erythrocyte cyanide for whole blood concentrations of up to 5.0 μg/ml containing an erythrocyte concentration of 3.6 μg/ml and a plasma concentration of 1.4 μg/ml. In none of these experiments was the background methaemoglobin concentration stated, but based upon human data with average values of 0.16–0.32 g/100 ml, this would be sufficient to sequester approximately as much as 2.7–5.3 μg CN^-/ml blood. This contrasts with the *in vitro* study, in which the measured methaemoglobin of 0.11 g/100 ml became saturated with cyanide at 2.31 μg/ml. Plasma levels were minimal below whole blood concentrations of 2 μg/ml in the *in vitro* experiment although this measured only free cyanide. The levels in the dog experiment, which included total plasma cyanide, were somewhat higher. At 3 μg/ml whole blood, the plasma and cell concentrations in the *in vitro* and sheep lethality studies were the same, with a higher proportion in the plasma than in the dog study. This may be indicative of the dynamics of plasma levels. In the sheep experiment the whole blood levels had increased to lethal levels, so that the rate of uptake of cyanide was sufficiently rapid to produce lethal plasma levels, while in the dog experiment the slower rate of infusion may have enabled some of the plasma cyanide to flow away into the tissues. For the *in vitro* experiment the plasma cyanide was trapped in the dish, so once the cells had reached saturation point the rest of the cyanide remained in the plasma.

Experiments by Marrs and Bright[79] using dogs, provide further data on the dynamics of whole blood and plasma cyanide. For these experiments beagle bitches were injected with an intravenous single doses of 0.67 mg/kg hydrogen cyanide (similar to the low dose primate inhalation exposures of approximately 0.96 mg/kg hydrogen cyanide). Whole blood and plasma cyanide were measured 5, 15 and 45 min after injection. The results, summarised in Fig. 4.27 show that whole blood cyanide peaked at 2.14 μg/ml cyanide after 5 min (compared with 2.02 μg/ml after 30 min exposure in the primates). At this time in the dogs the plasma cyanide concentration was approximately one-tenth of the whole blood concentration at 0.22 μg/ml. Plasma volume is 0.59 of whole blood volume, so concentrations measured in extracted plasma need to be multiplied by 0.59 for direct comparison with concentrations measured in whole blood. The right hand axis shows plasma plotted as a fraction of whole blood concentration rather than the directly measured plasma concentrations on the left hand axis. From these peak values the whole



4.27 Cyanide concentrations in whole blood and plasma and during intravenous bolus injection of hydrogen cyanide (0.67 mg/kg) in a dog.

blood cyanide decreased gradually over the next 40 min to 1.4 μg/ml, with a half life of 71 min (compared with 74 min in the primates). However, the plasma concentration decreased much more rapidly to 0.07 μg/ml after 40 min, with a half-life of only 22 min. At 5 min the plasma cyanide represented 6% of the whole blood cyanide, while 10 min later it was 4% and after 40 min, 3%.

These dog experiments therefore confirm that uptake, dispersal and removal of plasma cyanide follow different dynamics from whole blood or erythrocyte cyanide, decreasing relatively rapidly following exposure. The findings support the concept that during short periods of rapid uptake of inhaled hydrogen cyanide during periods of hyperventilation, there is likely to be a short-lived peak in plasma cyanide over a period of a few minutes, which in combination with the effects of hypocapnia, result in syncope in exposed subjects. This supports the observation that primates make a rapid recovery over a period of a few minutes after the end of a 30 min exposure period, despite showing no significant decrease in whole blood cyanide. Based upon the dog experiments it is likely that plasma cyanide concentrations (and by inference tissue cyanide concentrations) are likely to decrease significantly during this period, enabling the animals to recover consciousness.

Forensic considerations with respect to hydrogen cyanide exposure and post-mortem blood cyanide

Following fire incidents, measurements of blood carboxyhaemoglobin and blood cyanide may be important in order to establish the nature and extent of exposure

to fire effluents during the incidents and possible causes of incapacitation and death. Fire survivors with significant blood concentrations of hydrogen cyanide have been found to have high concentrations of carboxyhaemoglobin, and treatment with oxygen is known to be beneficial for both toxicants. As stated, the uptake and effects of hydrogen cyanide inhalation tend to be somewhat self-limiting during fire incidents, so that cyanide is considered more important as a cause of rapid incapacitation during a fire rather than as a primary cause of death. Based upon experience with primate exposures it is considered that exposed subjects surviving long enough to reach hospital are likely to recover from the effects of hydrogen cyanide inhalation at the fire scene with supportive therapy. A number of treatments are available for cyanide poisoning, but most have certain limitations. Treatment may be indicated if cyanide can be smelled on the breath, and as stated it has been found that the hydrogen cyanide concentration in exhaled breath correlates well with blood cyanide concentration.

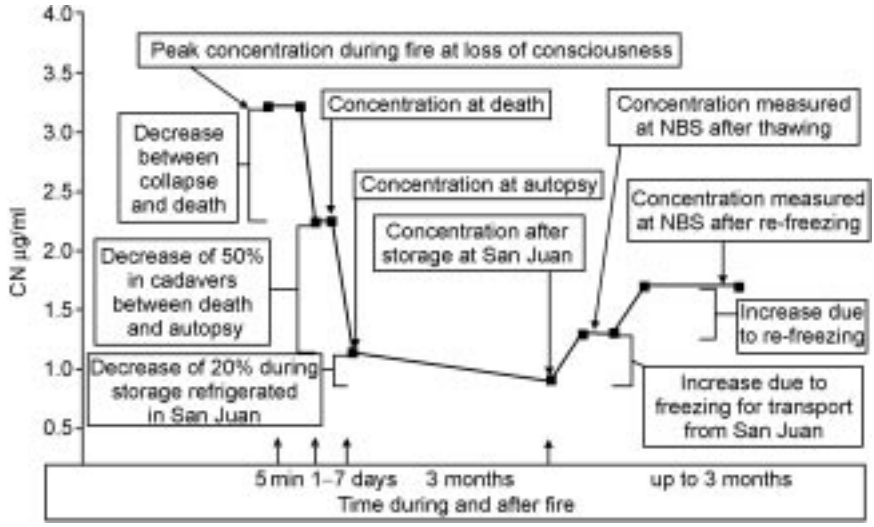
From the perspective of establishing the extent of exposure to hydrogen cyanide at the fire scene and the likely contribution of hydrogen cyanide exposure to incapacitation and death during an incident it is necessary to establish the relationship between blood cyanide and tissue cyanide measurements made from samples taken at autopsy and the likely blood cyanide concentrations at the time of exposure. Unlike the relationship between post-mortem blood carboxyhaemoglobin concentration and carbon monoxide exposure at a fire scene, which can be assessed quantitatively (as described in a previous section), interpretation of blood cyanide data is much more challenging. A particular set of issues relates to changes in cyanide levels in cadavers and in stored blood samples. These have been reviewed in some detail by McAllister *et al*.[69] Essentially the main issues with respect to interpretation of blood cyanide data are as follows:

- There is a low natural background concentration of cyanide in blood, which is slightly elevated in smokers and following ingestion of certain foodstuffs (non-smokers 0.075 μg/ml, smokers 0.184 μg/ml).[65]
- As described in the previous section, short exposure to high cyanide concentrations can cause incapacitation at a fire scene within a few minutes in association with transient high blood cyanide concentrations, which can then decrease to much lower levels once incapacitation has occurred, so that blood concentrations at a fire scene at the time of death may be considerably lower than during the critical exposure period when incapacitation occurred.
- Cyanide is unstable in the blood of cadavers and there can be a considerable decrease between death at a fire scene and the time when a blood sample is taken at autopsy. Curry[67] found in a case of death by inhalation of cyanide vapour that the blood level taken at the moment of death was 3.5 μg/ml while samples taken at autopsy the next day were 1.0 μg/ml (femoral) and 0.5 μg/ml (carotid), a decrease of approximately 79%. Ballantyne *et al*.[68] took samples at intervals from 15 rabbits killed by intravenous potassium cyanide (8 mg

CN^-/kg body weight) stored at a temperature of 10–15 ºC. The blood concentrations decreased from 5.41 μg/ml immediately after death, by 30% after 1 day and 62% after 3 days, and then to near zero after 14 days.

- Another problem is that cyanide levels continue to decrease in blood stored after removal. Ballantyne[91] studied the effect of storage under three conditions (room temperature 20 ºC), refrigerated (4 ºC) and frozen (−22 ºC). The results were that at room temperature and 4 ºC there were considerable decreases of blood level, which fluctuated with time. After 3 months at 4 ºC there was an approximate 20% decrease in concentration.
- Change in cyanide concentration in frozen blood samples. In the above study, small changes occurred in blood samples following freezing and re-thawing. And frozen samples containing significant cyanide concentrations were generally the same after 3 months as when they were first taken. The exception was the control blood, which showed a small increase of approximately 0.1 μg/ml within a few days of freezing, the levels then remaining constant for the remainder of the 3 months. Although this was a small increase it represented a large percentage change in the control value of 0.03 μg/ml. The increase is considered to be due to re-conversion of small amounts of thiocyanate to cyanide. This effect is considered likely to be significant only when examining low concentrations of cyanide such as is found in the blood of smokers, but minor in the context of blood cyanide concentrations relevant to cyanide poisoning during fires.
- In some situations large increases in blood cyanide have been found to occur in stored blood samples. Although not fully understood this phenomenon is considered to be due to contamination of samples by cyanogenic bacteria. However in several large studies of post-mortem blood samples taken from fire victims[65,69,70] such increases have not been reported.

An example of how changes in blood cyanide can affect the interpretation of conditions during a major fire incident is presented in Fig. 4.28, which summarises opinion on likely blood cyanide concentration during exposure of decedents in the San Juan Dupont plaza hotel fire.[92] In this incident the bodies of decedents contained different concentrations of carboxyhaemoglobin depending upon their location during the fire. Some victims exposed to intense flaming conditions had relatively low concentrations, while those exposed to fire effluent in more protected locations had much higher carboxyhaemoglobin concentrations consistent with incapacitation and death from asphyxia. The blood samples also contained cyanide, but there was some question as to whether the measured concentrations were sufficient for hydrogen cyanide to have made a significant contribution to incapacitation and death at the scene. When frozen samples shipped to the National Bureau of Standards (NBS) were thawed and tested, the average cyanide concentration was 1.3 μg/ml but when sample were refrozen and subsequently re-thawed an increase of 0.4 μg/ml occurred, most



4.28 Predicted changes in blood cyanide concentrations in sample between exposure and analysis – San Juan Dupont Plaza hotel fire.

likely due to re-conversion of thiocyanate to cyanide.[93] If this is subtracted from the original measured value it gives a 'true' average value of 0.9 μg/ml in the frozen samples sent from San Juan. However at San Juan, the blood sample taken from the decedents had been stored under refrigeration for 3 months, during which time it is estimated that cyanide concentrations would have decreased by approximately 20%, giving a value of 1.125 μg/ml at the time the samples were taken at autopsy. Also, owing to the large number of bodies involved, the autopsies and blood samples were taken over a period of 6 days, so that over this period it is estimated that blood cyanide concentration would have decreased by at least 50% on average in cadavers, giving a value of 2.25 μg/ml at time of death during the fire. Based upon the primate work it is likely that the concentration at death would have been significantly lower than that at the time of incapacitation. Assuming even a small decrease of 30% means that the blood concentration at the time of incapacitation could have been at least as high as 3.2 μg/ml, which is a typical concentration associated with loss of consciousness. Based upon these data and the fuels involved in the fire, it was concluded that although the actual blood concentrations measured at the NBS were relatively low, they were sufficient to indicate the presence of hydrogen cyanide inhaled by the victims (since they were well in excess of control levels), and that owing to the effects described, they were consistent with concentrations at the fire scene sufficient to have caused incapacitation.

Table 4.11 summarises reports and opinion on blood cyanide concentrations associated with signs of different severity, although these should be taken as only a very approximate guide for the reasons stated.

Table 4.11 Blood cyanide concentrations and signs

Blood cyanide (μg/ml)	Signs
0.2–0.5	No signs (Hall *et al.*[94])
0.5–1.0	Flushing, tachycardia (Hall *et al.*[94])
1.0–2.5	Intoxicated, narcotised (Hall *et al.*[94])
1.0–2.0	Lowest level suggested as compatible with death from acute cyanide poisoning (Ballantyne and Marrs[95])
1.7	Human fatality (Ballantyne and Marrs[95])
2.0	Concentration immediately after death in rabbits (Ballantyne[90])
2.15	Rapid loss of consciousness in dogs (Ballantyne and Marrs[95])
2.4	Human fatality (Ballantyne and Marrs[95])
2.5	Rapid loss of consciousness in primates (Purser *et al.*[23])
2.5–3.0	Coma (Hall *et al.*[94])
3.4	Rapid loss of consciousness in primates (Purser *et al.*[23])
3.5	Human case at death -0.75 μg/ml at autopsy next day (Curry[67])
3.6	Rapid death in dogs (Ballantyne and Marrs[95])
5.0	Human fatality (Ballantyne and Marrs[95])
In summary:	
~2.0–2.5	Concentration in fresh post-mortem blood consistent with incapacitation due to HCN
~3.0	Concentration in fresh post-mortem blood consistent with death due to HCN
~1.0–1.25	Concentration consistent with incapacitation due to HCN in post-mortem blood not taken and analysed immediately after exposure
~1.5	Concentration consistent with death due to HCN in post-mortem blood not taken and analysed immediately after exposure

4.6 Low oxygen hypoxia

The effects of exposure to lowered inspired oxygen concentrations depend upon a number of factors including the inhaled carbon dioxide concentration, the physical activity of the subject and their health status. Lowered oxygen in the inspired air, or lowered oxygen in the lungs or blood resulting from exercise or lung pathology, can be tolerated to some extent, owing to compensatory mechanisms. These include increased cerebral blood flow and more efficient unloading of oxygen into the tissues from oxyhaemoglobin at low oxygen partial pressures.[39,96] However, a point is reached where these compensatory mechanisms fail and a marked cerebral depression occurs. In primates, cerebral depression occurred as a result of inhaling 10% oxygen at normal pressure,[36] and similar effects have been reported in human volunteers breathing 12% oxygen for periods of 15 min or more[39,96] (consisting of lethargy and impaired

consciousness). The effects of hypoxia induced by reduced atmospheric pressure at altitude are well known and are basically similar to those of exposure to equivalent reduced oxygen concentrations at sea level pressure. When a subject becomes equilibrated to different equivalent sea level oxygen concentrations the effects are as shown in Table 4.12.[96]

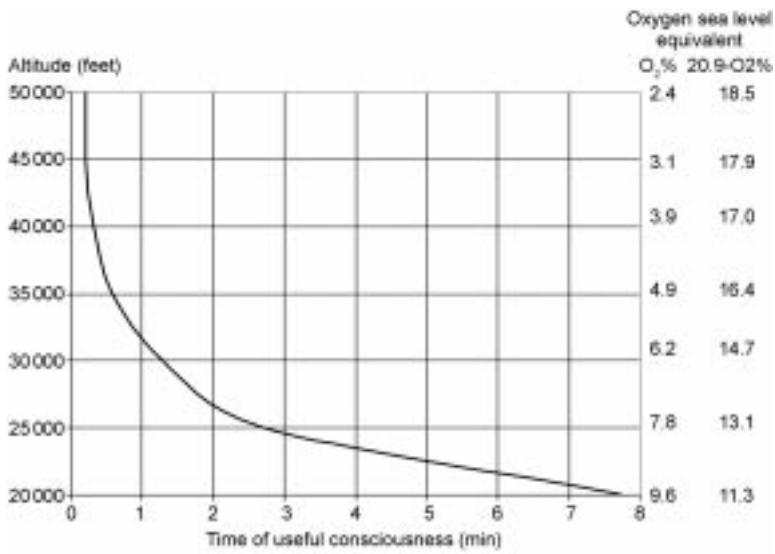
Two important considerations in relation to the effects of sudden hypoxia are first that the severity of the effects does not increase linearly with the degree of oxygen deprivation and secondly that the effects do not occur immediately, but require a certain time to develop depending upon the inhaled concentration and the time for equilibrium to be established between the air, the lungs, the blood circulation and the tissues. With regard to the severity of the effects, the body is designed to cope with a certain degree of hypoxia as a result of situations that may occur naturally and has mechanisms to compensate for a decreased blood oxygen, such as increases in respiration and in cerebral blood flow. However, once a point is reached where these mechanisms are no longer able to compensate, decline in function can be dramatic. The critical point for hypoxia at rest appears to be around 10–12% O_2. Above 12% effects are relatively minor

Table 4.12 Effects of low oxygen hypoxia at altitude and equivalent sea level reductions in percent oxygen

Sea level–3000 m equivalent to 20.95–14.4% O_2 at sea level	**Indifferent phase** Minor effects on visual dark adaptation and beginnings of effects on exercise tolerance towards 15% O_2
3000–4500 m equivalent to 11.8–14.4% O_2 at sea level	**Compensated phase** Relatively mild effects, slightly increased ventilation and hear rate, slight loss of efficiency in performance of complex tasks and short-term memory, some effects on judgement Maximal exercise work capacity reduced
4500–6000 m equivalent to 9.6–11.8% O_2 at sea level	**Manifest hypoxia** Degradation of higher mental processes and neuromuscular control, loss of critical judgement and volition, with dulling of the senses and a marked increase in cardiovascular and respiratory activity. Emotional behaviour may vary from lethargy and indifference to excitation with euphoria and hallucinations. Particularly dangerous during fire exposures, representing the catastrophe point as a victim passes from this stage into the fourth stage at approximately 10% O_2
6000–7600 m equivalent to $<$ 7.8–9.6% O_2 at sea level	Rapid deterioration in judgement and comprehension leading to unconsciousness followed by cessation of respiration and finally of circulation at death

but below 10% loss of consciousness is likely to occur. When primates were exposed to 10% O_2 at rest for 30 min,[14,36] they remained conscious but became very lethargic, with clear signs of cerebral depression (increased slow wave brain activity, impaired reflexes, ventricular extrasystoles, reduced peripheral nerve conduction velocity and effects on auditory evoked potentials). Another problem in low oxygen environments is reduced exercise capability. At 11–12.6% O_2 maximal oxygen consumption is reported to have decreased by 24–35%, with a greatly reduced endurance time (78% reduction).[97]

When a subject is suddenly introduced to a low pressure or low oxygen atmosphere, loss of consciousness occurs when the partial pressure of oxygen in the cerebral venous blood falls below 20 mmHg. Owing to the effects of the compensatory mechanisms, to residual oxygen in the lungs, and to oxygen stores available from the blood, a certain period of time elapses before the oxygen partial pressure of the venous blood declines to this critical level. The time taken for this depletion depends upon the level to which the oxygen concentration falls, but also on the activity level of the subject (which affects oxygen demand) and the minute volume (which determines the time for the air in the lungs to reach equilibrium with the inspired oxygen concentration). Measurements of these effects are made frequently on human subjects being exposed to sudden decompression to different simulated altitudes for the measurement of time of useful consciousness (Fig. 4.29). Based upon the results of such studies an expression has been developed for time to loss of consciousness (t_{Io}) for a



4.29 Time of useful consciousness on sudden exposure to high altitudes (less than 1 second transition time).[96] Scales also show equivalent sea level percentage oxygen concentration and percent oxygen vitiation (decrease below 20.9% O_2). (50 000 feet = 15 240 metres.)

subject exposed to a hypoxic environment, as follows:

$$(t_{Io})\ \text{min} = \exp\ (8.13 - 0.54(20.9 - \%O_2) \qquad 4.29$$

so that F_{Io} (the fractional of an incapacitating dose of low oxygen hypoxia) is given by:

$$F_{Io} = t/(\exp[8.13 - 0.54(20.9 - [\%O_2])]) \qquad 4.30$$

where $[\%O_2]$ = oxygen concentration (% v/v at 20 °C), t = exposure time in minutes and I = exposure dose for incapacitation.

Although it is possible to maintain consciousness for a minute or so by holding one's breath with a lung full of normal air, continuing to breathe at low oxygen concentrations causes loss of consciousness within approximately 15 seconds, owing to the removal of air from the capillaries of the pulmonary artery into the lungs. In this situation the lung works in reverse, actually removing oxygen from the body instead of delivering it. A lethal short-term exposure concentration in humans is around 8% oxygen. For rats the 30 min LC_{50} concentration was measured at 5.4% by Levin.[20] Rats appear to be somewhat more resistant to hypoxia from all forms than humans and other primates.

4.7 Interactions between the effects of different asphyxiant gases

Since all the asphyxiant gases basically cause hypoxia, interactions between them are likely to be additive. For direct additivity, exposure to half an incapacitating fractional dose of one gas (for example carbon monoxide) plus half a fractional incapacitating dose of another gas (for example hydrogen cyanide) should result in incapacitation when the summed FED reaches unity. In practice the degree of additivity may be less than this or the effects may be greater (synergistic).

4.7.1 Interactions between carbon monoxide and hydrogen cyanide

The effects of carbon monoxide and hydrogen cyanide have been found to be basically additive. Although both carbon monoxide and hydrogen cyanide cause tissue hypoxia, an additive or synergistic interaction may not be expected. This is because the primary mechanism of action of carbon monoxide is usually considered to be an impairment of the transport and delivery of oxygen to the tissues, while the primary mechanism of action of cyanide is impairment of the use of oxygen at the cellular level. Under some circumstances it might be expected that either one or the other gas would determine the rate-limiting step in oxygen supply and utilisation.[36] Thus when animals were exposed to hydrogen cyanide, there was usually excess oxygen in the venous blood, which

had the bright red colour of arterial blood. However, the results of experimental exposures in rats to carbon monoxide and hydrogen cyanide mixtures show some degree of additivity[20,72,98,99] and experiments with primates have shown that time to incapacitation by hydrogen cyanide is reduced by the presence of near toxic concentrations of carbon monoxide.[72] There are several reasons why this might be the case. One reason is the hyperventilation resulting from hydrogen cyanide exposure (see Fig. 4.18), which further increases the rate of uptake of cyanide and of any carbon monoxide present. Another possibility may relate to competition for sites on cytochrome *a*3 between oxygen and cyanide. Since carbon monoxide exposure reduces oxygen delivery and arterial P_{O_2} this may alter the balance in favour of cyanide binding to the *a*3 sites at the mitochondrial level. Certainly it was found that administration of oxygen was beneficial to cyanide intoxicated primates, improving their clinical condition, and the beneficial effects of oxygen have been reported in a number of other studies. Since oxygen is known to be present in excess during cyanide intoxication it is difficult to understand why administration of further oxygen would be beneficial, unless it improved the competitive balance with cyanide at the active sites.

Another possible reason derives from a proposed mechanism of carbon monoxide toxicity. Carbon monoxide has been found to exert a direct tissue toxicity at the mitochondrial level in addition to its effects on the blood.[22] Particularly when the uptake of carbon monoxide is rapid, it has been suggested that sufficient dissolved carbon monoxide may reach the tissues to exert direct toxic effects. *In vitro*, carbon monoxide has been shown to exert an inhibitory effect on oxygen metabolism. Although the affinity of cytochrome oxidase for carbon monoxide is considerably less than that of cyanide, it is possible that some degree of additive inhibition of oxygen metabolism may occur at the tissue level. Piantadosi *et al.*[22] studied cytochrome oxidation–reduction responses to carbon monoxide and hydrogen cyanide in the intact brains of fluorocarbon-circulated rats (i.e. with all haemoglobin removed) and found that carbon monoxide and hydrogen cyanide caused inhibition at two different sites in the electron transport chain, whereby *b*-type cytochromes were sensitive to carbon monoxide but not cyanide, while cytochrome aa_3 and $c + c_1$ were sensitive to cyanide but not carbon monoxide. Although the effects of such interaction in intact animals are not fully resolved, it raises the possibility of some form or additive interaction between carbon monoxide and hydrogen cyanide at the mitochondrial level.

Whatever the reason for the observed effects, it is therefore safest to assume that these gases are directly additive in terms of exposure doses for incapacitation and death, so that an end point will be reached when the fractions of the toxic doses for each individual gas add up to unity.

The effects in an accidental exposure will therefore depend to some extent on the relative concentrations of the two gases present. In flaming domestic fires,

typical hydrogen cyanide concentrations range from 0 to 3000 ppm while carbon monoxide concentrations may range from 1000 to as high as 20 000 ppm.[1,34] When the nitrogen content of the fuel is low (less than approximately 1% by fuel mass), so that the hydrogen cyanide concentration remains below approximately 100 ppm and the fire becomes sufficiently vitiated to produce carbon monoxide in excess of 5000 ppm, then the main toxic effects are likely to be due to carbon monoxide, with some minor additive contribution from hydrogen cyanide. When the nitrogen content of the fuel is greater than 1%, such as with vitiated fires involving upholstered furniture, then hydrogen cyanide often exceeds 200 ppm when carbon monoxide is less than 5000 ppm. In this case incapacitation is predicted from hydrogen cyanide before a large dose of carbon monoxide can be inhaled. Once a subject has become unconscious due to the effects of cyanide, breathing continues, during which time there is a continued uptake of carbon monoxide until death from asphyxia occurs. In this situation a subject could reach high or even fatal carboxyhaemoglobin concentrations, even though the initial collapse was caused by hydrogen cyanide exposure.

4.7.2 Interactions between carbon monoxide, cyanide and low oxygen hypoxia

The effects of carbon monoxide and low oxygen hypoxia are additive, since both reduce the percentage oxygen saturation of arterial blood, and carbon monoxide also impairs the delivery of oxygen to the tissues by causing a leftward shift of the oxygen dissociation curve.[100] It is possible that during the early stages of carbon monoxide exposure in hypoxic subjects the carbon monoxide occupies the upper, oxygen-free part of the oxygen dissociation curve, and therefore has little effect. At altitude, subjects at rest have been reported to remain symptom free at low levels of carbon monoxide saturation.[47] However, more severe carbon monoxide exposures have been reported to be additive with the effects of altitude.[101,102] The hyperventilation resulting from exposure to low oxygen concentrations will lead to some increase in the rate of carbon monoxide uptake, but for a given carbon monoxide volume concentration this is countered to some extent by the lower P_{CO} and hence carbon monoxide mass concentration. The %COHb at equilibrium with any specific carbon monoxide volume fraction is slightly higher at attitude or under lowered sea level oxygen concentrations.

Based upon these findings it is considered that fractional incapacitating doses of carbon monoxide should be considered additive with fractional doses of hypoxia, and also with fractional doses of hydrogen cyanide. For the effects of carbon monoxide and low oxygen hypoxia the main criterion is resultant venous P_{O_2}, which can be calculated as a function of the inhaled gas mixture. However, since cyanide inhalation results in an increased venous P_{O_2} in conjunction with inhibition of oxygen consumption at the mitochondrial level it is less clear how effects on overall tissue oxygen consumption might be calculated directly.

4.7.3 Interactions between carbon monoxide, cyanide, low oxygen hypoxia, nitrogen oxides and irritants

During exposure to fire effluent, inhalation of sensory irritants in humans and other primates results in temporary breath holding, over a period of a few tens of seconds, followed by compensatory deeper breaths and more continued hyperventilation resulting from stimulation of lung irritant receptors (see detailed description in Chapter 3).[103] The hyperventilatory phase is accompanied by bronchoconstriction and most likely also changes in ventilation–perfusion ratios in different parts of the lung. The overall effect found in primates is that during this phase the rate of uptake of carbon monoxide is not increased, despite an increase in respiratory V_E. Overall it is considered that the presence of irritant particulates and gases during exposure to fire effluents is likely to somewhat impair overall oxygen exchange in the lung, and is therefore proposed as a minor additive term in the assessment of overall asphyxiant hypoxia.

Nitric oxide and nitrogen dioxide affect the carriage of oxygen in the blood, forming nitrosylhaemoglobin with rapid oxidation to methaemoglobin, in which the haem iron changes from ferrous to ferric, which does not carry oxygen.[18] The effects of nitrite are similar to those of carbon monoxide in that the amount of oxygen carried in the blood is reduced in relation to the proportion of haemoglobin converted to methaemoglobin, and also that the oxygen dissociation curve is left shifted, although not by as much as that caused by carbon monoxide. The affinity of nitrite with haemoglobin is 1500 times greater than that of carbon monoxide. The overall effect is to cause tissue hypoxia by reducing venous P_{O_2} and oxygen delivery to the tissues. The effects are therefore additive with those of carbon monoxide.

The other effect of methaemoglobin is to reduce the toxic effects of hydrogen cyanide inhalation by conversion to cyanomethaemoglobin in the red blood cells.[18] As described in Section 4.5 on cyanide this has a role in limiting the effects of cyanide asphyxiation. Under normal conditions the methaemoglobin content of blood is small (0.01–0.5 g/100 ml), but during the early stages of fires involving materials containing nitrogen, a small proportion of fuel nitrogen is released as NO_x, mainly in the form of NO. This nitric oxide will somewhat increase the methaemoglobin content of the blood, contributing slightly to hypoxia as described. As compartment fires grow, they tend to become vitiated, so that a significant proportion of fuel nitrogen is then released in the form of hydrogen cyanide (see Chapter 14), but very little as NO_x.[24] Under these conditions, the methaemoglobin formed as a result of the initial NO_x exposure will remove a proportion of the inhaled cyanide from circulation, somewhat offsetting the inhaled cyanide toxicity. On the other hand such fire effluent atmospheres also contain other nitriles in addition to hydrogen cyanide, which exert effects found to be somewhat similar to those of hydrogen cyanide. This presupposes that the victim inhales both the early fire gases, of lower toxicity as

well as the more toxic effluents from developed fires. In practice, this is not very likely, as early flaming fires are small and produce less effluent (and exposure would normally lead to extinguishment or escape responses). However, in poorly designed fire toxicity tests using animal exposure, where well-ventilated and under-ventilated fire stages follow concurrently, this could lead to under-estimation of the fire toxicity of a nitrogen-containing material. In addition, the fire effluent will tend to flow upwards and collect at ceiling level, so inhalation of NO_x is less likely than hydrogen cyanide, which will be present as the smoke layer descends to breathing height.

Overall it is considered that irritants exert a minor asphyxiant effect during exposure to fire effluents, while oxides of nitrogen exert an additive asphyxiant effect proportional to the extent of methaemoglobin formation but also a protective effect (subtractive component) of the asphyxiant contribution from cyanide.

4.7.4 Interactions between carbon dioxide and other asphyxiant gases

Carbon dioxide interacts in several different ways with the effects of other asphyxiant gases. The principal effect of inhalation of increased carbon dioxide concentrations is hyperventilation, so that for example inhalation of 3% carbon dioxide approximately doubles V_E (see Fig. 4.3). As detailed in the section on carbon dioxide this therefore increases the rate of uptake of any other gases present. Another important effect of carbon dioxide is that it causes a rightward shift in the haemoglobin oxygen saturation curve, thereby enhancing the delivery of oxygen to the tissues and increases venous P_{O_2}. It also increases cerebral blood flow, which further improves oxygen delivery to brain tissue. These different effects have different implications for the asphyxiant effects of different gases.

4.7.5 Effects of carbon dioxide on low oxygen hypoxia

In fires carbon dioxide is always present in combination with reduced oxygen concentrations. Inhaled carbon dioxide has long been known to have beneficial effects during low oxygen hypoxia so that time to incapacitation is increased and the degree of incapacitation at different maintained oxygen concentrations is reduced.[4,104]

The deleterious effects of inhaling low oxygen mixtures result partly from effects on blood pH and P_{CO_2}. A reduction in arterial oxygen concentration stimulates respiration and increases cerebral blood flow, but these result in a reduction in blood carbon dioxide concentration (P_{CO_2}). Since carbon dioxide itself has a powerful effect on both respiration and cerebral blood flow, the reduced P_{CO_2} and resultant alkalosis mask the peripheral chemoreceptor

respiratory stimulation by hypoxia and also reduce the respiratory drive by respiratory centres in the brain. The lowered respiration and cerebral blood flow result in an increased hypoxic effect.

The hyperventilatory effect of carbon dioxide increases the rate of oxygen uptake, and there is also a benefit from the rightward shift in the oxygen dissociation curve caused by carbon dioxide. This improves the delivery of oxygen to the tissues, counteracting the respiratory alkalosis that otherwise occurs.[4,32,33,104] The beneficial effects of exposure to 5% carbon dioxide during exposures to 10–12% oxygen for periods of up to an hour have been demonstrated in experiments on human volunteers.[5,34] Six male human volunteers were exposed for 20 min to an atmosphere produced by mixing and inert gas mixture containing carbon dioxide with air to obtain an oxygen concentration of 12–13% and a carbon dioxide concentration of 3–4%. Respiratory minute volume was doubled but there were no adverse clinical signs, and tests of cognitive function indicated that the subjects remained alert during exposure. At even lower oxygen concentrations 5% carbon dioxide has been shown to prolong time of useful consciousness at oxygen concentrations of 10, 8, 6, 4 and even 2%.[4]

Under more extreme conditions the effects may be less beneficial, possibly due to the combined effects of metabolic and respiratory acidosis. In rats, when effects on lethality were studied, carbon dioxide was found to increase the toxic effects of hypoxia. Thus the 30 min LC_{50} for rats exposure to low oxygen alone was found to be 5.4% oxygen, while the addition of 5% carbon dioxide gave an LC_{50} concentration of 6.4% oxygen.[105]

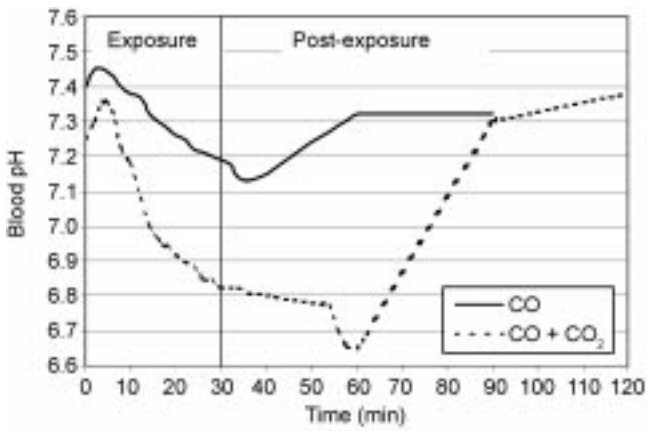
4.7.6 Effect of carbon dioxide on CO toxicity

When considering time to incapacitation (loss of consciousness) in humans, it is considered that the main effect of carbon dioxide will be to increase the rate of uptake of carbon monoxide and thus reduce time to loss of consciousness on a *pro rata* basis. Compared with this it is likely that other interactions will have relatively minor effects. It is possible that the presence of increased carbon dioxide may somewhat counteract the leftward shift of the oxygen dissociation curve caused by carbon monoxide so that deleterious effects on oxygen delivery to the tissues may be somewhat reduced.[47,100] On the other hand the combination of a respiratory acidosis induced by carbon dioxide with a metabolic acidosis induced by carbon monoxide may have some deleterious effect. This beneficial effect of carbon dioxide may partly explain why some fire fatalities are found with very high %COHb concentrations above 80%. It may be possible that they were exposed to a combination of carbon dioxide at concentrations above 3% at the same time as lethal concentrations of carbon monoxide. The protective effect of carbon dioxide on the oxygen delivery may have enabled them to achieve higher concentrations than the 50% COHb normally considered fatal. This could also precipitate a crisis in a subject rescued alive with a high

%COHb level above 50% in the presence of a high carbon dioxide concentration. As soon as such a subject is exposed to fresh air (or even oxygen) the protective effect of an elevated blood P_{CO_2} is lost.

The latter certainly seems to be the case when exposures are continued to lethal levels in rats. The effect on the uptake and toxicity of carbon monoxide has been confirmed in rats by Levin *et al.*[106,107] Exposure to carbon dioxide not only increased the rate of uptake of carbon monoxide but also caused a greater lethality for a given carboxyhaemoglobin concentration. In these experiments, the synergistic effects of carbon dioxide on carbon monoxide lethality increased up to 5% CO_2. Above 5% CO_2 the toxicity of carbon monoxide reverted back to the toxicity of carbon monoxide itself. During exposure to 5% CO_2 with carbon monoxide the rate of uptake of carbon monoxide was increased during the first 15 min of a 30 min exposure period, at which point the rats became comatose. Deaths occurred both during and some time after exposure when CO_2 + CO mixtures were used, but during exposure only when carbon monoxide alone was used. During these experiments the degree of acidosis induced by 5% carbon dioxide and 2500 ppm carbon monoxide was considerably greater than for 2500 ppm carbon monoxide alone (Fig. 4.30).[107] Recovery from this acidosis required more than 90 min in surviving rats. It is likely that the increased mortality resulted from a combination of prolonged tissue hypoxia with an increased metabolic and respiratory acidosis, although it is not clear why the synergism decreased at higher carbon dioxide concentrations.

In order to model the lethal effects in rats of carbon dioxide in combination with carbon monoxide and other gases Levin *et al.*[105,107] developed terms for input into their N-gas equation. These terms 'm' and 'b' represent the slope and intercept of the line for the relationship between carbon dioxide concentration and lethal carbon monoxide concentrations for a 30 min exposure period. These



4.30 Changes in blood pH in rats during and after exposure to 2500 ppm carbon monoxide alone and 2500 ppm CO + 5% CO_2 (Levin *et al.*[106]).

are −18 and 122 000 respectively for carbon dioxide concentrations of 5% or less, or 23 and −38 600 for carbon dioxide concentrations above 5%. It is assumed that carbon dioxide had no effect on the toxicity of other inhaled gases, and that the hyperventilatory effect of carbon dioxide behaved as step function at 5.0% carbon dioxide.

Based upon the same data, Purser developed a somewhat different approach (see Chapter 8). At 5% carbon dioxide it was assumed that the enhanced lethality was partly due to the increased rate of uptake of carbon monoxide and partly due to acidosis. A multiplicatory factor was developed for the hyperventilatory effect of carbon dioxide on the uptake of carbon monoxide (and any other toxic gases present) and an additive term for the acidosis effect as follows:

$$\text{Multiplicatory } CO_2 \text{ factor for rat lethality} = 1 + \{\exp(0.14 \times [CO_2]) - 1\}/2 \quad 4.31$$

$$\text{Additive acidosis factor for rat lethality} = [CO_2] \times 0.05 \quad 4.32$$

The full equations are discussed in more detail in Chapter 8. At 5% carbon dioxide the effect is to increase the inhaled carbon monoxide dose by 50% with an additive acidosis factor of 0.25. Thus for rats with an LC_{50} concentration for a 30 min of 5700 ppm carbon monoxide, 50% lethality is predicted following a 30 min exposure to half this concentration.

4.7.7 Effects of carbon dioxide on toxicity of inhaled irritants

When rats and mice are exposed to irritants the reflex depression of breathing tends to decrease the rate of uptake of other toxic gases.[1,108] If this respiratory depression is counteracted to some degree by exposure to carbon dioxide, then an enhanced toxicity is likely to occur. This has been found experimentally when rats inhaled irritant acid gases in the presence of carbon dioxide, with increased deaths possibly caused by post-exposure acidosis and increased lung damage.[105,107,109] Exercise also causes a carbon dioxide driven hyperventilation, and there is evidence that this may also cause death when rodents are exposed to irritants at normally sub-lethal concentrations. This is of particular concern with respect to occupants attempting to escape from fires, and fire victims often suffer from post-exposure lung inflammation and oedema, which is sometimes fatal.

4.8 Conclusions

The role of the major asphyxiant gases present in fire effluents has been discussed. All the asphyxiants cause incapacitation (loss of consciousness), preventing escape and, without the intervention of rescue services, resulting in death. In terms of toxicological significance carbon monoxide is important as a

cause of incapacitation and the major cause of death in most fires. Hydrogen cyanide is likely to be a major cause of incapacitation in fires involving more than 1% N_2 in the fuels (such as fires involving upholstered furniture and bedding). Oxygen depletion also contributes to incapacitation in some fires, particularly during later stages. Nitrogen oxides have only minor effects but may need to be considered in some cases. Carbon dioxide has a major influence on time to incapacitation by increasing the rate of uptake of other asphyxiant gases. All the asphyxiants affect exercising subjects more severely than static ones, although much of the existing data relate only to static subjects. In addition to effects occurring during exposure at a fire scene, exposure to asphyxiants can result in long-term post-exposure health problems, primarily owing to effects on the central nervous and cardiovascular systems.

It has been possible to develop physiologically based calculation expressions for each asphyxiant gas and for the interactions between them, enabling calculations of time to incapacitation and death for humans exposed to fire effluent mixtures. These are summarised in Chapter 19 along with the expressions for calculating time to incapacitation by smoke and irritants, and some worked examples of applications to fire hazard analysis are presented.

Post-exposure and post-mortem blood carboxyhaemoglobin concentrations provide a good indication of the extent of carbon monoxide exposure at the fire scene, but blood cyanide concentrations can be misleading as indicators of extent of hydrogen cyanide exposure. This is due to the complex dynamics of uptake and dispersal of cyanide in the blood during exposure, and its instability in cadavers and stored samples.

The major cause of death in fires appears to be carbon monoxide, with some contribution from other toxic gases including hydrogen cyanide. Although hydrogen cyanide inhalation causes rapid incapacitation associated with a brief period of hyperventilation, the effects are somewhat self-limiting, so that it does not appear to be a major cause of death during fires.

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5

Effects of fire effluents on fire victims

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Abstract: In the UK forensic pathologists examine all fire fatalities. This chapter explores the reasons why this is required and the information sought. It also describes other physical manifestations of fire, such as burns, and the difficulties faced when examining fire victims. The primary purpose of any such investigation is to establish whether the victim was breathing at the time of the fire. This is most often demonstrated by determination of carboxyhaemoglobin levels in the blood.

Key words: forensic, investigation, fire, burns, carbon monoxide, carboxyhaemoglobin, COHb.

5.1 Introduction

The toxicity of fire effluents, generally accepted to be the major cause of death in fires, has been studied from several perspectives. Materials' developers work alongside fire safety engineers to minimise the harmful effects of fire, particularly in sensitive environments such as mass transport (passenger aircraft, trains and ships) and high rise buildings. Fire investigators, forensic scientists and health and safety professionals investigate real fires, and for example in cases of unexpected death or injury, may even recreate the fire (see Chapter 18), or undertake detailed modelling of the gas generation and transport (see Chapter 20). In each case, there is missing information. Monitoring equipment is absent in real fires, and there are large gaps in our knowledge and understanding of the effluent composition between the fire starting and the investigators piecing together the evidence that remains. Fire victims themselves could provide vital clues to both the nature and development of the fire and the toxic insult they suffered. At present, the role of the forensic pathologist is limited to answering a few simple questions, such as whether the victim was breathing at the time of the fire and had the victims suffered any other injuries, preventing escape. They have not been concerned with the relative effects of various toxic and irritant components of fire effluents. The role of the forensic pathologist in fire investigation is discussed, together with the types of evidence available and currently used.

5.2 Legal aspects of the investigation of sudden or unnatural deaths

5.2.1 Medico-legal system in England and Wales

In all advanced societies, there are legal and medical mechanisms for the investigation of sudden, suspicious or unexplained deaths. The aim of these investigations is essentially three-fold:

- To establish the cause of death.
- To identify possible homicides.
- To identify any public health concerns.

In England and Wales the legal authority for the investigation of these deaths rests with the coroner who has to rely upon the local police force and any other statutory bodies (e.g. the Air Accident Investigation Branch, AAIB) to conduct the investigations and to present their findings at an inquest. Coronial inquests are held, with or without a jury, into most unnatural deaths. Inquests tend to be relatively brief proceedings where witnesses are heard under oath and where the identity of the deceased is established, details of the events surrounding the death are given by eyewitnesses and other evidence including the medical cause of death is given by professional and expert witnesses.

The coroner, or the jury if one has been empanelled, having heard all of the evidence will reach a verdict that establishes 'who, when, where and by what means' the deceased came by their death. The potential verdicts are now severely limited, in scope and application, by the rulings of higher courts and include:

- lawfully killed;
- unlawfully killed;
- accidental death;
- killed himself/herself;
- open verdict.

Recently, there has been a move towards a 'narrative' verdict which lists the relevant facts of a case without applying any single 'old style' verdict.

5.2.2 Other medico-legal systems

In Scotland the legal authority is the Office of the Procurator Fiscal which is historically linked to the continental European system where a legally qualified 'Juge' is in charge of every aspect of all investigations and who forms a final conclusion. In Scotland, the procurator fiscal has the power to control and to personally direct the investigations of the police. The procurator fiscal may hold a Fatal Accident Inquiry (FAI) into a single death, or into a group of deaths. These inquiries are less frequent than the coronial inquests and are held

only for the more serious deaths which attract the greatest public interest and concern.

In the USA, some states have maintained a coronial system (albeit with many variations from the original system) while others have developed a medical examiner system where the local forensic pathologist will determine both the cause of death and also the manner of death without the need for an individual legal hearing.

5.3 Death investigation

5.3.1 General

In all sudden, suspicious or unexplained deaths two fundamental possibilities exist: that the death was the result of natural disease or that it was unnatural. If the death was unnatural then, at the start of any investigation, three further distinct possibilities exist as to the mode of death: homicide, suicide or accident. The aim of all of the investigations into the death is to determine not only the cause of death and the mode of death, but also to determine how any injuries were caused. The answers to these questions will be required for any legal inquiry, by the coroner, or possibly in a higher court if a murder or manslaughter charge has been made.

5.3.2 Fire death investigation

The examination of a fatality associated with a fire will, in England and Wales, be on the authority of the Coroner and in Scotland under the direction of the procurator fiscal. In the UK the post-mortem examination will often be performed by a forensic pathologist, who will have special experience and expertise in trauma and in fire deaths. However, this is not always the case and on occasions a local hospital pathologist will perform the examination.

Limitations of the forensic pathological investigation

The extent and the detail of the post-mortem examination of fire victims will depend primarily on the skills and experience of the pathologist but also on the degree of police concerns surrounding the investigation of the death. In general terms if there are any concerns about the events leading up to the fire or the events during or after the fire, a skilled forensic pathologist should be engaged. The quality of the examination and the subsequent report is directly related to the experience and skills of the pathologist and the time available to perform the examination. Unfortunately some examinations in the past have been very cursory and while they may provide sufficient information to determine a medical cause of death they yielded little or no information that might be useful in the later reconstruction of the events of the fire.

Fire scene investigation

Fire scenes are notoriously difficult to investigate, because almost all of the available evidence will have been consumed by the fire. A typical example of a potential homicide scene is shown in Fig. 5.1. The specialist forensic fire investigator should be able to provide details of how the fire started and the way it spread since, in trying to understand why some individuals die in fires while others survive, it is also crucial to have a full understanding of the conditions in which any particular individual was placed during the fire in terms of heat, flame, noxious gases and physical trauma caused by falling or by being struck by debris. Thus there should be some documented evidence of the fire stage and type of fuels, which may suggest the toxicants present. However, the remit of the forensic pathologist does not extend to consideration of the toxicants present in a fire.

The primary investigation of any body will begin at the scene of the fire and should include a full description of the position of the body in relation to other significant features (walls, doors, windows, other bodies, other significant findings). If the body is on the floor there should be a description of the way the body is lying: face up, face down, on the side. Descriptions of the observed clothing and of the obvious absence of any parts of the body must be made at this time. It is also important to record if the area beneath the body shows evidence of burning or not. Full forensic and fire scene photographs of the body *in situ* and the site once the body has been removed are essential.

Collection of evidence

The evidence collected from a victim of a fire will depend upon whether the fire is considered to be accidental or suspicious and whether it is in a house or industrial premises, in a car or other vehicle, or if it is outside. Fire scene

5.1 Charred body – is this homicide or an accident?

investigators and fire scene forensic examiners will usually be responsible for sampling the scene.

All evidence taken for later analysis and use at a trial must be taken, labelled, exhibited, stored, transported and analysed so that there is a clear and unbroken 'chain of evidence'. Faults in this process may make evidence derived from that sample inadmissible in court. The careful examination for, and recovery of, trace evidence from a body recovered from a fire is essential, with careful photography before final recovery and exhibiting.

5.4 The pathology of heat trauma

The manner in which a body exposed to heat will be affected by that heat will depend on many factors, including the amount of heat produced by the fire, the closeness of the exposure, and the length of time of exposure. A fatality recovered from a fire may only show evidence of exposure to smoke and fumes. However, if the body is exposed at sufficient temperature and for sufficient time there will be a number of effects upon the tissues and organs of the body.

5.4.1 Scalds and burns

Medically, heat applied to the body by a fluid will result in scalds, which usually show one of two appearances, depending on the mechanism of injury. If fluid is thrown or poured onto an individual this will produce a geographic distribution which will commonly have 'trails' or 'runs' formed by movement of the hot liquid under gravity. If the individual falls or is placed into a hot fluid there will often be a 'tide mark' that equates with the interface at the top of the liquid.

Hot, solid objects, flames or radiant heat will cause burns which, while often irregular in shape, do not show the same 'flowing' or 'tide mark' features. The distinction between a scald and a burn is seldom of clinical relevance and it achieves significance only if it is important, forensically, to establish the type of medium that caused the injuries.

5.4.2 Factors influencing the appearance of burns

It is perhaps self-evident that the longer an individual is exposed to heat and the greater the heat they are exposed to, the greater the damage caused to the body. Pathologists are seldom required to make any assessment about the length of time of exposure although it is possible that this may be relevant in a few civil claims for damages.

The skin, the linings of the air passages and the lungs are all highly sensitive to heat. Human skin will be damaged by exposure to temperatures as low as 44 ºC but only if the exposure lasts for several hours. As the temperature increases so the time required to cause damage reduces rapidly and at 60 ºC

damage will occur after a few seconds. The linings of the air passages and the lungs are even less resilient than skin, and damage to these tissues will occur both faster and at lower temperatures.

The damage to different parts of the body at high temperatures, such as those found in a fire, is dependent on the heat capacity (volume, etc.) of that body part. For example, when considering a charred body the time to appearance of the following features have been observed at 680 ºC:

- 10 min – arms charred;
- 14 min – legs charred;
- 15 min – facial bones exposed;
- 15 min – arm bones exposed;
- 20 min – skull and ribs exposed;
- 25 min – tibia and fibula exposed;
- 35 min – legs fractured, femurs exposed.

In real life many factors (clothing, debris, obesity, etc.) will conspire to vary these experimental findings.

Since the degree of burning depends independently of the time and temperature of exposure, it is difficult to establish a clear set of indicators that could be reliable and of use to the pathologist. Any potential reliability is reduced further by the variation in human skin: male or female, young or old, well nourished or poor diet, etc., which would confound any simple analysis.

5.4.3 Extent of burns

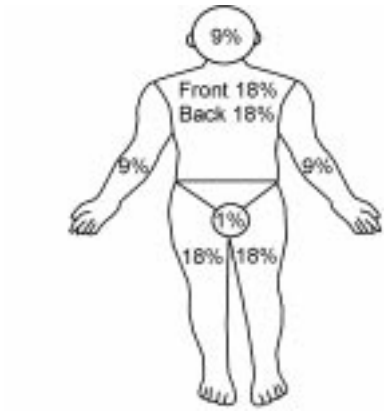
The size of the area of burns is extremely important for the assessment of the clinical prognosis of a burn victim. It can be difficult to measure with any accuracy the size of the burns and so a rapid assessment method has been developed. This method is called ‘The Rule of Nines’ (see Fig. 5.2). Burns of over 50% of the body surface of an adult are associated with a poor chance of survival.

5.4.4 Burn severity

Three grades of burns are described:

- Grade 1 – redness and blistering of the skin.
- Grade 2 – burning of the whole of the outer skin layer (epidermis) and exposure of the underlying tissues (dermis).
- Grade 3 – destruction of the epidermis and dermis with exposure of the underlying tissues. Figure 5.3 shows extensive Grade 3 injuries with exposure of the bowel in body exposed to a severe car fire.

Grade 1 burns will heal without scarring, but grade 2 and grade 3 burns will



5.2 The Rule of Nines.

result in scarring. All burns result in loss of fluid either directly from the damaged skin surface or into blisters. The hair may simply be singed or it may be completely burnt away in severe fires.

Bodies recovered from fires may have suffered burns both before and after death. It may, on occasions, be important to attempt to distinguish between these injuries. Unfortunately it is not always possible to make this distinction with any degree of certainty. In general terms a burn caused when the individual is alive will result in a circumferential rim of erythema (redness) around the damaged skin. This represents the normal, vital, response of the body to tissue injury. Burns that have occurred after death will not usually show this erythematous margin. However, it is now accepted that a rim of erythema may occasionally also develop in a burn that has been caused up to an hour after death. This variability renders this method of distinction, at best, unreliable.

There is no doubt that in many fatal cases, areas of ante-mortem burns are subsequently burnt again after death, adding further to the difficulties in determination of the time of receipt of the injury. Blistering is the result of a

5.3 Severely charred body in vehicle with exposure of loops of bowel.

5.4 Severe burns – skin splitting due to heat not injuries.

physical effect of heat and so can occur either before or after death. The protein content of blisters cannot be used to determine whether a burn was ante- or post-mortem.

Heating and charring of the skin will initially result in burns and blisters, but continued heating may cause charring and splits that have, in the past, been misinterpreted as severe injuries, a mistake that has triggered a number of murder inquiries. An example is shown in Fig. 5.4. The heating of the muscles causes them to shorten and, as the flexing (bending) muscles of the body are stronger than the extending (straightening) muscles, the body may adopt a posture that resembles that of a fighter with arms bent toward the face. This is the so-called 'pugilistic attitude'.

Heating of internal organs and skeleton may produce severe artefacts, including fractures of the long bones and of the skull that may confuse the inexperienced examiner. This confusion may be compounded when the fracture of the skull is associated with collections of blood within the skull (subdural haemorrhages) which are called 'heat haematomas'. Subdural haemorrhages most commonly associated with direct blows to the head and so their presence may raise concerns about the possibility of trauma. On occasions the effect of fire is so severe and prolonged that the body is cremated and all that remains are some charred fragments of the skeleton.

5.5 Examination of the victims

5.5.1 Survivors

The treatment of the living victims of fires is, in general terms, based on the symptoms they show. Difficulties with breathing are treated with artificial ventilation and possibly by bronchial lavage (washing out of the air passages), and skin burns may be simply dressed or may require surgical incision and skin

grafts depending upon their severity. The delayed medical complications of burns are treated as and when they occur; for example, kidney failure will be treated with dialysis. Other injuries are treated as necessary, lacerations are sutured and broken bones are immobilised with plaster of Paris splints or by surgical repair.

Only very scanty analysis is usually undertaken in hospital to confirm exposure to toxic substances; this is because there are few facilities within hospital laboratories to perform such tests, because these tests are of little clinical relevance as they would not affect the symptomatic treatment of the individual and, finally, because there will have been such huge changes in the concentrations of all chemicals in the body caused by a combination of the extensive loss of body fluids through the burns and the rapid infusion of large quantities of fluid required to replace that fluid loss, that no test would provide quantitatively reliable results. Despite these comments some extremely simple analysis is performed and this is limited to the tests that are routinely available in most hospitals: alcohol, paracetamol, aspirin and carboxyhaemoglobin. It is not at all unusual that the only analysis that will be performed is to determine the carboxyhaemoglobin level as this may possibly be of some clinical value. However, it must be borne in mind that the methods used to assess carboxyhaemoglobin in hospitals will also vary and, owing to the lack of experience in performing the test together with the fundamental unreliability of some testing methods used, great care must be taken in interpreting the results of these analyses. In my experience no attempt is made routinely to assess the concentration of cyanide or the concentrations of any other commonly occurring fire-related toxins in living victims.

5.5.2 Fatalities

The problems faced by the forensic pathologist when examining the victim of a fire are uniquely difficult. In no other situation does the environment in which the person has died, and which may or may not be the cause of their death, continue to affect them so rapidly and significantly after death.

The exact nature of the post-mortem examination will depend on whether the examination is performed by a forensic pathologist with a full team of crime scene investigators and photographers in support or by a hospital pathologist acting on their own. The authority of the coroner must be obtained before any examination can be performed. The following is a brief description of a forensic examination.

The body will be received into the mortuary in a sealed body bag. If this is an incident that has resulted in a single death there should be no difficulty in establishing the chain of evidence from the police or the fire officers that this is the body recovered from the fire in question. If there have been multiple fatalities the situation becomes more complicated, and each body, or body part,

should have been given a unique number at the scene and that number should be clearly displayed on the body bag and on the body (or body part). Management of mass disasters is a specialist area and should be attempted only by those with training and experience.

A full photographic survey of the body before and after removal of clothing is essential. The burns and other injuries to the body are all documented, described and photographed. This can be a time-consuming process but it is essential if no injuries are to be missed. The pathologist will determine whether each burn or injury is ante- or post-mortem in origin, and whether the injuries could have been caused in the fire or whether some other event (e.g. fall, assault) could be the cause.

It is common practice to take X-rays of fire victims so that any extraneous metal objects can be identified. This is particularly important when the damage to the body is severe so that it is not possible to exclude gunshot injuries that may be obscured by burns, charring or partial destruction. The pathologist will also note any evidence of disease externally and will determine if any of these could have limited the mobility of the individual and made them more susceptible to dying in the fire.

Samples

It is usual for the first set of samples to be taken before commencing the internal examination. The samples are handed to a police officer who documents them as official exhibits. These routine samples are:

- clothing – all bagged separately and described;
- footware – all bagged separately and described;
- trace contacts – head hair;
  – pubic hair;
  – fingernail clippings or scrapings;
- sexual swabs – external anal swab;
  – internal anal swab;
  – external vaginal swab (female);
  – internal vaginal swab (female);
  – penile swab (male);
  – mouth swab;
- toxicology – nose swab for cocaine.

A full post-mortem examination will then be performed with the opening of the body cavities and the removal and dissection of all of the body organs that remain within the body. This part of the examination will necessarily involve making incisions into the body. The removal of the internal organs enables proper and full examination and also the sampling of the blood and urine.

The following samples are taken internally if the damage to the body has not removed the relevant fluids, tissues or organs:

- toxicology – blood (preserved and unpreserved);
  – urine (preserved and unpreserved);
  – stomach contents;
  – liver sample (especially if no blood available);
  – deep muscle for carboxymyoglobin;
- biochemistry – vitreous humor (fluid from eyeballs);
- identification – deep skeletal muscle for DNA;
  – spleen for DNA.

All of the internal organs that remain within the body are examined for the presence (or absence) of natural disease and injury. Any abnormalities are photographed. Small samples are usually retained from each of the organs for later microscopic examination.

Analyses

Toxicological analysis is always essential in deaths in fires. Samples of blood and urine (both preserved with sodium fluoride (NaF) and unpreserved) are extremely valuable but are not always available owing to destruction of the body. If no blood is available then a sample of liver should be retained to enable analysis for drugs, and a sample of muscle should be retained for analysis for carboxymyoglobin.

The small samples of all of the identifiable internal organs are examined microscopically to identify or exclude the presence of underlying natural disease. Examination of the trachea, bronchi and lungs microscopically may also identify the presence of soot or carbon particles, possibly associated with an inflammatory reaction to heat damage, irritant gases or respirable particulates, which can be useful evidence to support active inhalation of smoke and hot fumes. Unfortunately, the body's response to heat or chemical insult is indistinguishable; both result in inflammation which may be masked by the presence of soot particles.

Fingerprints, odontological and/or anthropological examinations may be made to assist in the establishing of identity. These examinations are still extremely useful despite the ubiquity of DNA testing and maintain their value mainly because they are cheap and easy to perform. In England and Wales it is the coroner (or the jury) who forms the final opinion as to the identity of the deceased.

Report

It is essential to remember that not all individuals who are found dead at the scene of a fire have died as a result of that fire. Some of them may have died as a result of natural disease, some may have died as a result of an accident that preceded the fire and some may have been murdered. It is not unusual for a fire to be used in an attempt to conceal a murder and, on occasions, to conceal a

suicide. The pathological examination of a victim found at the site of a fire must consider all of these possibilities.

5.5.3 Assessment of pre-fire behaviour

Any assessment of the behaviour of, and the possible activity by, the victims will depend on an understanding of the findings of the full post-mortem examination (presence of natural disease, immobility, etc.), the toxicological analysis (drugs, alcohol, etc.), a thorough investigation of the scene (accelerants, smoking materials, bottles of alcohol, etc.) and the background of the victim (alcohol abuse, smoking habits, etc.). Even with these basic assessments it is very difficult for a pathologist to predict, with any degree of certainty, how any single individual would have reacted when faced with a fire. On occasions severely inebriated individuals may make an escape while other sober, apparently sensible, individuals may panic and become trapped and killed. The pathologist may, however, comment on the possibility that natural disease and/or alcohol and drugs may have contributed to an inability to make an escape.

It is also almost impossible for the pathologist to form any useful opinion about the effects the fire effluents since the only analysis of the fire effluents that is likely to have been performed is that of carboxyhaemoglobin, and their examination of the airways and lung. The evidence obtained by the pathologist is just one strand of the complete set of evidence in any case and ultimately it is for the coroner, or the jury, to determine if the death is natural, homicidal, suicidal or accidental.

5.6 Fire effluents

An individual exposed to a fire will also be exposed to the fire effluents and many, if not most, of the immediate fire deaths are related to the inhalation of these hot, toxic gases. In routine forensic practice the most important of these gases is carbon monoxide since it is the most stable and most readily analysed by the toxicologist. It is accepted that fire effluents are highly complex mixtures of high temperature gases which almost always also contains soot and other carbon debris. It is the deposition of soot and evidence of heat injury to the lips, mouth and nose that will first indicate to the pathologist that it is possible that fire effluents may have been inhaled.

During a full post-mortem examination the whole of the respiratory tree – from mouth and nose, the larynx to the bronchi and lungs – will always be examined. The crucial features to be considered are the presence of heat damage to the delicate linings of these air passages and the presence or absence of soot and other particulate fire debris. The presence of these features beyond the mouth is considered to be conclusive evidence that the individual was exposed to the hot fire effluents.

In routine coronial practice the role of toxicology is restricted in deaths associated with fires and it would be usual for the toxicologist to perform analyses for only alcohol and drugs, both medicinal and illicit that may have contributed to the pre-fire behaviour. Analysis for effluents is limited to carbon monoxide. This is not because the complexity of the chemical composition of the fire effluent is not known to either the pathologist or the toxicologist but simply because there is little call at present, in the post-mortem setting, for a full analysis of the possible constituents of these gases. This is a direct consequence of the narrowness of the function of the inquest – to establish the cause of death, and not the reasons why. However, this information, such as the attribution of the cause of death to carbon monoxide poisoning, is then used for accident and disaster prevention; it is important to recognise that it was not collected for that purpose. This lack of interest in the toxicological aspects of fire deaths is based upon and continues to be compounded by a lack of funds available to the coroner to pay toxicologists for performing any additional tests.

Asphyxiation occurs when insufficient oxygen reaches the tissues. There are many reasons why this may occur but in a fire two main factors apply: lack of environmental oxygen and poisoning that prevents transportation of oxygen in the body or its utilisation at cellular level. It is most likely that both factors will exert some effect although the exact proportions will vary during the period of living exposure and also depend on the individual variations in the physiology and biochemistry of the victim.

Carbon monoxide exerts its effects by binding with the haemoglobin molecules in the red blood cells and, by doing so, prevents the transport of oxygen. When carbon monoxide binds to the haemoglobin molecule it results in a spectrographic shift and, as a result, the blood develops a classical 'cherry red' colour. It is not uncommon for the uninjured areas of skin of a fire victim to exhibit this 'cherry pink' colouration which can also be identified in the muscles and some of the internal organs. This colour change is not limited to carbon monoxide derived from exposure to fire fumes, it is specific to carbon monoxide and can be seen in any form of carbon monoxide poisoning.

Hydrogen cyanide blocks the metabolic pathways at a cellular level preventing the basic cellular chemical respiration reactions. There are no specific features of inhalation of hydrogen cyanide fumes that can be used by the pathologist as a marker for the presence of this chemical in the effluent. Toxicological tests are seldom performed but, as the chemical is volatile, and detection limits are dependent on sampling procedure and treatment, they would perhaps be of little use anyway.

Exposure to fire effluents is most likely to result in all three of these effects and the exact effect of each of the components will depend upon the exact nature of the fire. Elsewhere in the book (Chapters 3–4), it is shown that lethality for carbon monoxide or hydrogen cyanide normally occurs before oxygen depletion from fire atmospheres. In general terms, there is no need for a pathologist to

determine which of these three components was more likely to have contributed to the death with or without the concomitant effect of any burns.

There is very little pathological evidence relating to the irritating effects of fire effluents (organoirritants, acid gases, particulates, etc.). However, a recent review[1] of the treatment of fire victims considered the flooding response of lung tissue (oedema), advising that

> airway oedema may not be maximal until up to 24 h after injury and is often precipitous following fluid resuscitation
>
> Lung injury usually takes several hours or even days to progress and the clinical course may reflect this. Radiographic changes often do not appear until 24 h or more after the insult and thus a normal chest radiograph at presentation does not exclude a significant inhalation injury. Arterial blood gas analysis is invaluable for:
>
> - assessing the state of respiratory adequacy
> - excluding carbon monoxide toxicity
> - raising suspicion of cyanide poisoning.

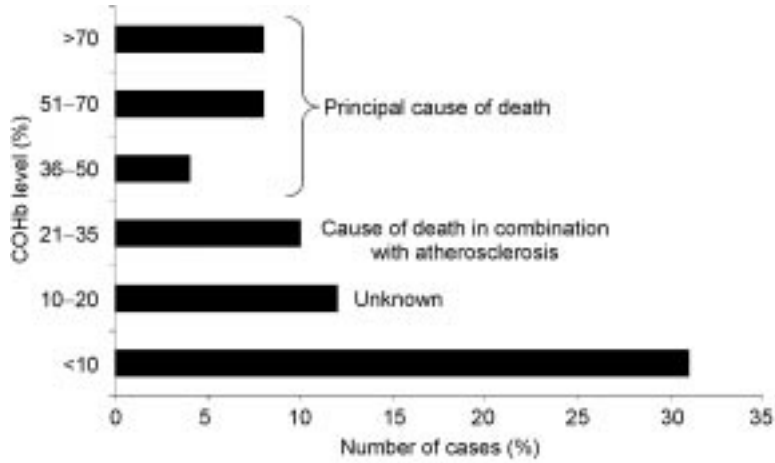
Thus, the severe effects of non-asphyxiant components of fire effluents do manifest themselves, but only while fire victims remain alive.

In a potentially more controversial recent review of existing forensic evidence, surprisingly low levels of carboxyhaemoglobin had been recorded in many of the 73 carbonised bodies investigated over a 10-year period in Belgrade, Serbia.[2] However, the group may be unrepresentative of typical fire victims; although 81% were described as accidental deaths, these were mostly traffic accidents, differing significantly from the majority of fire victims who perish in domestic fires. The investigation found that many victims had carboxyhaemoglobin (COHb) levels consistent with being heavy smokers, and less than 25% had carboxyhaemoglobin levels normally considered to correspond to a lethal dose (Fig. 5.5).

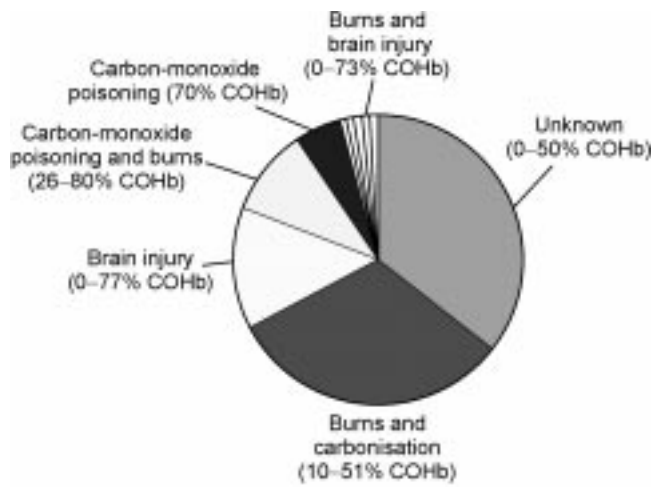
The carboxyhaemoglobin concentration was related to the reported cause of death (Fig. 5.6), indicating a higher portion of burns than carbon monoxide, but leaving a large portion of unexplained deaths, which could include other toxicants (such as hydrogen cyanide from burning polyurethane in automobile seats, or irritancy hindering escape from hydrogen chloride or particulates). Other authors have attributed up to 80% of smoke inhalation fatalities to carbon monoxide.[3,4]

5.7 Conclusions

The pathologist has a crucial role to play in the investigation of any death associated with fire. Indeed these are some of the more complex and difficult deaths that are encountered in forensic practice due to the destruction of the tissues that may obscure other relevant findings. The pathologist's role is limited by the current coronial system which is only concerned with the cause of death of that single individual rather than the larger public health issues of why people die in fires.



5.5 Saturation level of carboxyhaemoglobin in victims' blood, and assertion.[2]



5.6 Reported cause of death.

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6

Experimental methods in combustion toxicology

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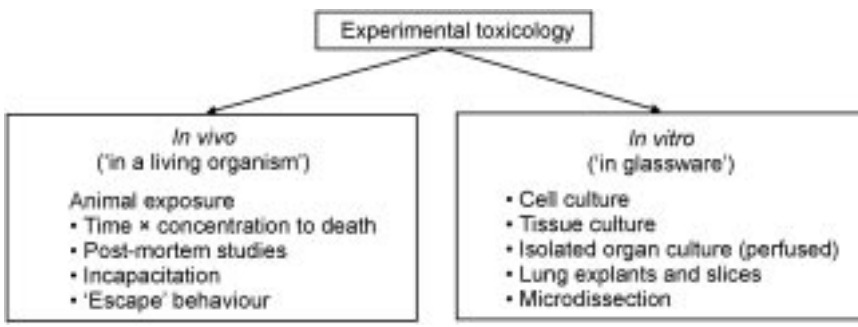
Abstract: Determining robust toxicological data which can be applied to humans is not straightforward. Information from animal toxicology tests is useful in determining the potential toxicity of a compound to humans. Together with *in vitro* tests, animal tests should be applied as biological markers of chemically induced risks. The range of methodologies and effects are discussed to introduce the reader to specific methods developed for research in fire toxicity.

Key words: fire, toxicity, *in vivo*, *in vitro*, animal, biological.

6.1 Introduction

Models of toxicity in humans range from exposed mammals (primates, rats, mice, etc.) through to numerical models relating the chemical composition, species present and their concentrations, to a particular end point (Fig. 6.1). Such models rely on assumptions as to how combinations of toxicants act together. Ultimately these assumptions are based on animal exposure experiments.

This chapter outlines the range of biological techniques available to the experimental toxicologist, ranging from live animal exposure (discussed in detail in Chapter 7), creation of models from such experiments (Chapter 8), cell culture experiments (Chapter 9) and the isolated lung model (Chapter 10). The most important factor comes from interaction of different toxicants on individual species. This increases the need to rely on some animal exposure data.



6.1 Experimental toxicology.

6.2 Principles of toxicology and toxicity

Toxicology is defined as the study of the adverse effects of any substance (referred to as toxins or toxicants) *on living organisms*.[1] It includes the identification of the substances' chemical properties and biological effects, as well as the treatment of conditions that they cause. As a result it is possible to determine symptoms and mechanisms, and to detect the effects they cause.

Toxicity is the amount of a poison that, under a specific set of conditions, causes toxic effects or results in detrimental, biological changes. Toxicity can refer to the effect on a whole organism, such as an animal, and as well as the effect on a substructure of the organism, such as a cell or tissue (cytotoxicity) or an isolated target organ, such as the lungs.[1] (This book is correctly called *Fire Toxicity* and not *Fire Toxicology*, to address the wider effects of toxicants on people caught in fires.)

Dose is the quantity of toxicant that comes into contact with the target organ or tissue, where it exerts a toxic effect, within the organism.[1] The size of the dose causing a particular effect is dependent on the absorption, distribution, metabolism and elimination of the organism exposed to the toxicant.[1] The route and site of exposure exert significant influence in determining the toxicity of a substance.[2] The major routes by which toxic agents gain access to the body are the gastrointestinal tract (ingestion), lungs (inhalation), skin (dermal), etc. In combustion toxicology, only the lungs need to be considered. Toxic agents generally produce the greatest effect and the most rapid response when they are introduced directly into the bloodstream (the intravenous route).[1,2] The order of effectiveness for other routes from fastest to slowest is:

intravenous → inhalation → oral → dermal

6.2.1 Factors influencing toxicity

The toxicity of a substance is affected by many different factors. Several terms used to describe these factors are explained below.[1–3]

Routes of administration (inhalation, injection, ingestion, skin, etc.) and site of exposure[1] *(specific target organ or multi-organ exposure)*

Substances may be lethal to the entire body, or be lethal to or damage specific organs. Blood can carry the toxicant to the site of toxic action, from its site of action, to organs of transformation (metabolism), and to organs of elimination (pulmonary and others). In addition the agent may remain largely within the blood system through being strongly bound to plasma protein or through being distributed to various organs (some low molecular weight water-soluble compounds), cells or tissue. However, the most common trend is a combination of all the above. Therefore toxicity can be measured by the effects on the organism target, organ, tissue or cell.

Duration of exposure

- *Acute exposure* – a single exposure to a toxic substance which may result in severe biological harm or death; describes the effects of a single dose or multiple doses during a 24 hour period.[4]
- *Chronic exposure* – continuous or repeated exposure to a toxin over an extended period of time, often measured in months or years; can cause irreversible side effects.[1,4]

Interaction of toxicants

It is more difficult to assess the toxicity of chemical mixtures than of single, pure chemicals because each component displays its own toxicity and components may produce enhanced or diminished effects. The most common are:

- *synergism* – describes the situation when the combined effects of two or more chemicals produce greater effect than the sum of individual effects (contribute to the toxicity);
- *antagonism* – describes the situation when two chemicals administered together interfere with one another's action (result in a less than additive toxic effect).

6.2.2 Lethal concentration and units

Concentrations in the gas phase may be expressed as a ratio of gaseous volumes, equal to the molar ratio (since equal numbers of molecules of any gas occupy the same volume at the same temperature and pressure), or as a mass/volume ratio, or a mass/mass ratio. For example:

- volume/volume (% or ppm), 1.0% = 10 000 ppm;
- mass/volume (mg/litre);
- mass/mass (mg/kg).

Toxicity is usually expressed as milligrams of toxicant per kilogram of body weight that will produce a defined biological effect (e.g. mg/kg) or as chemical concentrations that are often expressed in parts per million (e.g. LC_{50} in ppm).

6.3 Descriptive animal toxicology tests

Extrapolating the results of toxicity testing using animals to human exposure requires careful consideration of the parameters of the animal tests,[2] as toxic substances may have different physiological responses in the human system. Toxicants can be classified according to the physiological effects they have on the human body; however, this is somewhat arbitrary, since the classification implies the route of administration, dosage, duration, individual differences,

effect of a particular material, etc. Some of classes and effects of toxic agents on human exposure are presented in Table 6.1.

Determination of the toxicity of a substance is not simple. For most of the millions of new substances synthesised and characterised no determination of toxicity has been made. For those materials for which toxicity determinations have been made, the majority have been based on animal studies in which LD_{50} or LC_{50} has been determined.

No single mammalian species accurately mimics human physiology and metabolic activity. The goal of using animal models in toxicological assessment is based on their ability to reproduce the effects seen with chemical exposure to humans. Although no perfect surrogate for humans exists, each species contributes distinct features that underscore biological and physiological differences among the various groups. The inhalation toxicity of combustion gases has been studied over the years by many investigators. These studies have frequently been reported in terms of the lethal concentration to 50% of the

Table 6.1 Physiological classification of toxic substances[5]

Class	Effect	Examples
Asphyxiants	Deprive the cells of the body of their oxygen supply, and cause suffocation by displacing oxygen or interfering chemically with oxygen absorption, transport or utilisation.	Simple asphyxiants are inert elements that, in sufficient quantity, exclude oxygen from the body, O_2 depletion, CO, HCN and indirectly CO_2.
Irritants	Can cause inflammation of the mucous membrane (skin, eyes, nose, or respiratory system).	HCl, HF, HBr, NO_2, H_2S, organoirritants.
Blood-damaging agents	Blood-damaging agents break down the red blood cells or chemically affect the haemoglobin in the blood.	Benzene (C_6H_6), pyridine (C_6H_7N).
Anaesthetics	Depress the central nervous system.	Acetylenic hydrocarbons, paraffin hydrocarbons and aliphatic ketones.
Neurotoxic agents	Damage the nervous system, ultimately leading to loss of senses and paralysis.	Organophosphates.
Hepatotoxic agents	Damage the normal functioning of the liver.	Tetrachloromethane (CCl_4), tetrachloroethane ($C_2H_2Cl_4$).
Nephrotoxic agents	Damage the functioning of the kidney.	Halogenated hydrocarbons.

Table 6.2 Biological and physiological differences among mammalian species commonly used in toxicological investigations and humans[5]

Characteristics	Mouse	Rat	Rabbit	Dog	Human
Adult weight	18–40 g	250–800 g	2.5–5 kg	Varies	75 kg
Number of chromosomes	40	42	44	78	46
Body temperature (°C)	37.1–37.4	37.1–37.4	38–40	38–40	37
Age at puberty	2.5–7 weeks	3–7 weeks	8–22 weeks	32–56 weeks	624–780 weeks
Heart rate (bpm)	310–840	320–480	150–300	70–130	60–90
Systolic/diastolic blood pressure (mmHg)	145/105	100/75	110/80	145/82	120/80
Whole blood volume (ml/100 g)	5.8	5.6–7.1	6.0	6.0–7.0	6.5–7.5
Respiratory rate (rpm)	163	85–110	32–65	10–30	12–18
Plasma pH	7.2–7.4	7.4	7.4	7.4	7.4

exposed population (LC_{50}) for a fixed exposure time. In such studies, various animal species were used to evaluate single and mixed gases on different toxic gases at different physical activity levels. It is generally accepted that differences in absorption, distribution, biotransformation and elimination of chemicals exist among animal species, and between an animal species and humans, thus necessitating careful interpretation of toxicological data.[5] Table 6.2 lists some of the major characteristics of mammalian species commonly used in toxicological investigations and considerations affecting the selection and incorporation of animals in toxicology testing studies.[5]

As with the selection of an appropriate route of administration, in designing toxicological studies, it is important to consider several criteria before selecting a suitable animal species. The criteria include the following:[2]

- Classification of the toxic agent according to human exposure.
- Anatomic, physiological and metabolic similarity of the animal species to humans.
- Sizes, ages, life expectancies and sexes of the animals.
- Cost efficiency of toxicology study (housing requirements, and daily care for the species).
- Objectives of experiment (establishment of routes, exposure, duration and frequency of dosing).

Animal models are selected based on their ability to replicate the effects seen with chemical exposure to humans. The classification of the chemical determines the route of administration, duration, and dosage and subsequently influences species selection. Dosage in any animal species must be adjusted, for

Table 6.3 Factors affecting the concentration of toxicant[2]

Parameter	Factors for consideration
Concentration of delivered test agent	Air flow into chamber Air temperature and humidity
Particle size	Particle size determines distribution to target organ (lower or upper respiratory tract), size influences solubility of toxicant in air
Respiration rate	Cycles affect respiration rate, contact with irritant induces behavioural and inflammatory responses, altering the exposure rate
Control groups	Influence of solvents, additive and pressure

example based on metabolic rate and knowledge of historical dosages required for rodent species. Intraspecies variability is also minimised by selection of animals with uniform characteristics; this helps to decrease experimental variability (strains of animals, uniform mean body weights, responses to standard diet, etc.).[2]

The actual concentration of an inhaled toxicant is calculated as the total amount of test substance delivered through the inhalation system. However, there are factors which have to be included and taken into consideration (Table 6.3).

Lethal toxic potencies of potential fire effluents (CO, HCN, HCl, NO_2, NO) (30 min exposure) for different animals, presented in Table 6.4, have been experimentally determined. Hartzell and co-workers[6,7] suggests that when considering lethal effects, primates may resist about 1.3 times greater concentrations of hydrogen chloride and hydrogen cyanide than rats, while rats resist about a 1.6 times greater amount of carbon monoxide. It is recognised that rats are reasonably suitable animal models for human exposure to smoke, when the principal effects are due to inhalation of asphyxiant toxicants.[6] It has been argued that for acute toxicity studies, the rodent model (rat or mouse) is often the most appropriate, based on versatility of administration and the short duration corresponding to the physiological parameters of rodents[2] (see Chapter 7 and 8).

Table 6.4 A comparison of lethal toxic potencies of potential fire effluents (30 minutes exposure) for different animals[6,7]

Chemical agent	Mice	Rats	Guinea pigs	Primates/humans
CO (ppm)	3500	5000–6600	17 500	2500–4000
HCN (ppm)	–	110–200	201	170–230
HCl (ppm)	2644	3800	1 350	5000
Low oxygen (%)	6.7	5.4	–	6–7

One source shows the differences between different species, but the actual lethal concentrations depend on the details of measurement (see Chapters 3 and 4).

A significant body of information has been generated in experimental animals during the past decades for the estimation of the acute inhalation toxicity of irritant gases and asphyxiants. However, individual fire gas toxicants may exert quite different physiological effects through different mechanisms. When present in a mixture, an individual toxicant may have physiological effects other than those of its principal specific toxicity. The effect of interactions between combinations of various gases on the time to incapacitation in fires is an area that requires further investigation; the best that can be done currently is to suggest likely degrees of interaction based on existing experimental data for different gas combinations.

Measurements using these gases indicate whether the combinations are additive, synergistic or antagonistic. This provides a useful tool in combustion toxicology for the calculation of toxic potencies from combustion product analysis data, as well as for the assessment of potential toxic hazards to humans. In addition, different combinations can occur and they may not occur simultaneously, but serially. For a fire victim these combinations are both time and space dependent.[8]

Studies have been conducted on animals establishing the combination effects of various toxicants (e.g. O_2 depletion with CO and HCN and even with other gases in fire smoke such as CO_2, HCl, NO_2),[9,10] so an accuracy assessment of a physical fire model can be present performed without the use of laboratory animals (see Chapters 7 and 8).

The value of the LC_{50} for a particular substance yields little information about the mechanism of its toxicity or mode of action. Therefore laboratories usually use currently available *in vitro* toxicology screening protocols and assays in addition to *in vivo* studies.[2] *In vitro* studies are particularly beneficial as preliminary screening tests prior to animal toxicity studies. They are also used to supplement, reduce or refine animal testing as well as yield mechanistic data in support of LC_{50} determinations.[2]

6.4 Standardisation and validation of alternative methods

At present, *in vitro* methods cover a broad range of techniques and models (Table 6.5), and validated *in vitro* tests can be used for assessing acute toxicity.[11] *In vitro* toxicology describes the study of toxic effects of substances using isolated organs, tissues and cell culture (also referred to as cytotoxicology). Socioeconomic factors have also influenced the development of *in vitro* toxicity by encouraging a reduction in the number of test animals in research, refinement of test protocols to minimise suffering, and replacement of current animal tests with appropriate *in vitro* tests with the need for valid

Table 6.5 Advantages and limitations of *in vitro* toxicity studies[12]

Advantages of *in vitro* studies

- Either concentrated or diluted product can be tested
- Either single or complex mixtures can be evaluated
- Provide evaluation of actions/effects on intact animal and organ/tissue interactions
- Test can be either single end point (lethality, corrosion) or multiple end point
- Quantitative and qualitative tests with scoring system are generally capable of ranking materials as to relative hazards
- Amenable to modification to meet the requirement of special situations
- Time-dependent studies
- Controlled testing conditions
- Reduction of variability between experiments
- Same dose range can be tested in a variety of test systems (cell and tissues)
- Very small amount of material is required
- Ease of performance and relatively low capital costs
- Reduction of testing in animals

Limitations of *in vitro* studies

- Complications and potential confounding or masking findings of *in vitro* systems
- Does not perfectly predict results in humans if the objective is to exclude or identify severe-acting agents
- May only assess short-term site of application or immediate structural alterations produced by agents
- Lack of standardisation
- Structural and biochemical differences between test animals and humans make extrapolation from one to the other difficult
- Large biological variability between experimental units
- Variable correlations with human results
- General side effects cannot be assessed
- Systemic effects cannot be evaluated
- Interactions between tissues and organs cannot be tested
- Specific organs sensitivity cannot be assessed

toxicological data.[11] *In vitro* screening may identify fundamentals for understanding and developing critical procedures in cellular and molecular biology, as well as in pharmacology, genetics, oncology, etc.

Several approaches to *in vitro* toxicity or target organ models are available and are listed below.

- *Cultured cell* models can use either primary or transformed (immortalised) cells. Primary cells have significant advantages as predictive target organ models, since they can be used to identify and evaluate interactions at the cellular, subcellular, molecular level on an organ- and species-specific basis. The disadvantage is that over time the response becomes decreasingly

representative of what happens *in vivo*.[12] *In vitro* exposure techniques include direct exposure of cells to the test substance itself, cell exposure to collected air samples containing the substances of interest, or submerged cells undergoing intermittent or continuous direct exposure under conditions that support their growth, differentiation and stability.[11]

- *Tissue or organ culture* maintains the ability for multiple cell types to interact in a near-physiological manner. They are not generally as complex as the perfused organs, but they are stable and useful over a longer period of time. They occupy the middle ground between perfused organs and cultured cells. Good models performing in a manner representative of the *in vitro* organ are available only for relatively simple organs (e.g. skin and bone marrow).[12]
- *Isolated organ exposure* (pefused organ) is a technique where the organ to be studied is physically removed from the animal and kept functioning with a 'synthetic blood' known as the perfusate. The principal advantage of physically isolating an organ is the elimination of interactions between the organ being perfused and other tissues and organs present in the body.[2]
- *Lung explants and slices* – slices and explants from conducting airways or the lung parenchyma (spongy tissue) allow the biochemical and morphological changes to be examined, without intervening complications from cells migrating into the tissue (e.g. leucocytes – white blood cells). If the lung is first inflated with agar, the alveolar space remains open in the explant. Slices prepared in this way can be kept available for several weeks. Also the mechanisms of the development of chronic lesions (abnormal structural changes) can be studied.[1]
- *Microdissection* – many inhalants act in particular regions of the respiratory tract, such as the terminal bronchioles, a region especially rich in Clara cells (cells found in the small airways of the lungs that protect the bronchiolar epithelium).[1] Microdissection of the airways consists of the stripping of small bronchi and terminal bronchioli from the surrounding parenchyma and maintenance of the isolated airways in the culture. Specific biochemical reactions predominantly located in the cells of the small airways then can be studied with biochemical or morphologic techniques.[1]

6.4.1 Cell culture methods for assessment of toxicity

No single method can cover the complexity of toxic effects in humans or animals. Since 1990, the development of various types of non-genetic, systemic and local *in vitro* methods as alternatives to animal testing has increased rapidly. *In vitro* toxicology is generally referred to as the handling of tissue outside intact organ systems under conditions that support their growth, differentiation and stability.[5] Data obtained from animal exposure experiments yield information relating the dose for lethal or sub-lethal toxicity to the many different toxic mechanisms and effects. Similarly, *in vitro* cell systems also detect a wide

spectrum of unspecified mechanisms and effects. However, in contrast to animal experiments, currently acute toxicity cell tests measure the concentration of a substance that interferes with or alters components, structures or biochemical pathways within cells. Thus cell culture does not attempt to represent the whole human organism, but can significantly contribute to our understanding of the workings of its components, through investigation of isolated cells without the influence of other organ systems.[5]

The response of a mammal to a potential toxin involves various physiological targets, and a variety of complex toxicokinetic factors. A number of questions have emerged as a result of validation studies of the prediction of systemic and local toxicity by *in vitro* tests:[5]

- Are they capable of modelling different types of quantitative toxicity, such as acute and systemic toxicity or local irritancy? In acute toxicity, the response is immediate and typically reversible; in systemic toxicity, the effects occur remotely from the exposure site; in local irritancy, the effects occur at the site of first contact between the biological system and the toxicant.
- Are the results generated from these methods predictive of basal cytotoxicity? Basal toxicity affects basic cellular functions and structures, common to the specialised cells of all human and animal species regardless of the organ of origin.[5]
- Are quick, simple and economic *in vitro* cell systems capable of maintaining standards of safety and public health regulation?

The first goal may require several relevant systems such as human hepatocytes, lung, nerve cells, and other cell lines of applicable and relevant importance. Although difficult to reliably transpose, the dose–effect relationships are established by *in vitro* systems to human exposure. Highly controlled, refined *in vitro* systems may further increase understanding as to how the targeted biological system interacts with combustion effluents in isolation and in complex smoke mixtures. Many cell culture procedures were adapted and established as empirical measures of many types of toxicity (dermal and ocular local toxicity). Other proposed *in vitro* tests are being standardised within single laboratories and among institutions, such as testing for acute systemic, and target organ toxicity (including liver, kidney, lung, etc.). Alternative *in vitro* procedures have been used to examine the acute toxic effects of fire effluents. The principles of *in vitro* bioassays are developed in Chapter 9.

6.4.2 Isolated perfused lung

The information derived from animal toxicity tests is useful in determining the potential toxicity of a compound in humans. Together with *in vitro* tests, animal tests are applied as biological markers of chemically induced risks, whether synthetic or naturally occurring.

The non-respiratory capabilities of the pulmonary tissues have received increasing interest in recent years as they have become apparent. The isolated perfused lung method is widely used in pharmacy applications[1] and it is apparent from an increasing number of studies that the lungs have the capacity to accumulate, bind and metabolise a variety of substances, both endogenous (inside the system) and exogenous[13,14] (outside the system). The technique of organ perfusion lies between the isolated organelle preparation, the tissue homogenate and slice, and the intact animal. The lung, *in situ* or removed, is perfused with blood or a blood substitute through the pulmonary artery,[15] while also being ventilated. Toxic agents can be either introduced into the perfusate or the inspired air. Repeated sampling of the perfusate allows determination of the rate of transfer of metabolism of toxins and the metabolic activity of the lung.

In contrast to other *in vitro* methods, cells in the isolated perfused lung are maintained in their 'normal' anatomical and physiological associations and are not fragmented or dispersed; therefore, transcellular transport (substances travel through the cell) and diffusion of agents are probably not altered.[13] There are very few transected cells leaking their contents into the medium of the isolated perfused lung, compared with tissue slicing methods, and there is no dilution of intracellular (within the cell) cofactors, especially when using whole blood, as occurs in homogenate or isolated organelle experiments.[13] The isolated perfused lung preparation, in addition to metabolic studies, also offers the opportunity to investigate administration of multiple agents in different physical forms, the effectiveness of particle size and the distribution and binding of substances throughout the pulmonary system as mediated by the lungs composite metabolic machinery, i.e. pulmonary alveolar macrophage, tracheobronchial tissue, endothelial cells and alveolar tissue.[13] Detailed descriptions of the experimental preparation as elements in evaluating data from combustion studies are given in Chapter 9.

6.5 Conclusions

The information from descriptive animal toxicology tests is useful in determining the potential toxicity of a compound to humans. Together with *in vitro* tests, animal tests are suitable as biological markers of chemically induced risks. In the short term, the isolated perfused lung offers the greatest potential to improve our understanding of the toxicological effects of mixtures of fire effluents, because of the complex structure of the lung, its position at the front line of the body's defence against fire effluents, and the relatively good understanding of the effects of carbon monoxide and hydrogen cyanide leading to hypoxia, compared with the large gaps in our knowledge in the effects of irritants and particulates on lung function.

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7

Animal exposure studies

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Abstract: This chapter addresses the principles of hazard identification of smoke. The experimental conditions of these tests are designed to meet the criteria for hazard identification rather than attempting any quantification of risks. The focus is on material-specific attributes which can only be identified when the variables involved in the 'dynamics of fire effluent generation' are rigorously standardised. The key objective of animal bioassays is to compare toxic potency estimates from analytical-mathematical approaches based on the toxicity of the toxic species analysed in exposure atmospheres. This assay integrates the toxicity of fire effluents as a whole. Its role is to cross-validate the bottom-up single-component summation procedures which cannot address the yet unknown factors related to toxic interactions, analytical interferences, and whether analytes are present in the gas or aerosol phase.

Key words: acute lethal toxic potency, LC_{50}, incapacitation, inhalation toxicity, hazard identification, animal bioassay.

7.1 Introduction

This chapter addresses principles of hazard identification of smoke released from materials combusted under specified laboratory- or bench-scale conditions. The experimental conditions for these tests are designed to meet the principles defined for *hazard identification* rather than attempting any quantification of risk – which would involve additional variables, such as likelihood and intensity of exposure of a specified human population over a defined time period. Suffice to say, especially in combustion inhalation toxicology, physical factors (e.g. ignitability, fire growth, prevailing fire stage and associated yield of toxicants from thermolytically degraded polymeric structures, heat dissipation, smoke intensity, and an oxygen vitiated environment) need to be judiciously outweighed against toxicological factors. Conceptually, in combustion toxicology, animal studies have successfully been used to determine the relative acute toxic lethal potency of materials under standardised worst-case conditions, i.e. conditions resembling a fire stage that produces the highest yield of toxic effluents. By testing the toxic potency of known benchmark materials (e.g. wood or material-specific reference standards) under otherwise identical conditions, such an approach allows a comparison of the relative acute toxic potencies of materials under highly

standardised and reproducible laboratory conditions. Often misunderstood by fire engineers, this objective can be achieved only when the variables involved in the 'dynamics of fire effluent generation' are rigorously reduced and standardised. Hence, the more stringent the degree of standardisation, the less this benchmark test resembles a 'real fire'. To accommodate the latter, the outcome of 'hazard identification' needs to be accompanied by a subsequent *risk assessment* process. The ultimate goal of risk assessment is to develop a reliable characterisation of exposure–dose–response relationships for people exposed to airborne toxic fire effluents from specific materials in their end use configuration.

A prerequisite for animal bioassays is to expose experimental animals to temporally stable, conditioned (aged and oxygenated) and analytically well-characterised atmospheres. Then reproducible inhalation toxicity testing is experimentally feasible, supplemented by more refined analytical methodologies. These may range from real-time monitoring using Fourier transform infrared (FTIR), non-disperse IR spectroscopy, aerosol photometers to chemical-specific sampling activities with subsequent in-depth chemical analysis. Particle-size analyses require additional sampling activities. They focus on measurements of the particle behaviour (diffusion, aerodynamics) and not necessarily the particle property (projected area, geometric diameter). Hence, animal inhalation studies focus on the generation of data concerning the consequences of human inhalation exposure to complex mixtures comprising multiple toxicants present as gas, aerosol or as combined phases. The information gained from animal studies generally consists of key symptoms and their progression or regression over time, along with internal (e.g. carboxyhaemoglobin, cyanide in blood or any other biological exposure index) and external exposure data. Animal bioassays integrate the toxicity of fire effluents as a whole. They are of great importance to cross-validate bottom-up single-component summation procedures which cannot address compounding factors related to interactions, interferences and toxic potentiation or antagonism. Ideally, the yield-related toxic potency per se as well as the associated clinical picture and lung pathology should be used to verify the conclusions on toxic hazards drawn from 'animal-free' tests with unknown materials. Laboratory tests do not aim to produce an exact duplication of any fire scenario likely to occur under any real-life condition. This source of difficulty lies in doubts concerning the atmospheres of fire effluents derived from the various test systems used and their relevance to the yield and quality of atmospheres found during the complex processes occurring in real fires. Part of this concern has centred on unrealistic expectations of what the objectives of hazard identification are, and what such a test system can achieve and deliver.

The objective of this chapter is to address the rationale of bioassays and what they can contribute in addition to mathematical modelling with the common focus of estimating the fractional effective dose of toxic fire effluents and the associated time to incapacitation or irreversible health effects. Immediate incapacitation can be caused by asphyxiants (e.g. hydrogen cyanide, carbon

monoxide) or high concentrations of irritant gases leading to eye and respiratory tract irritation and damage of the lung. Because of the controversy over combustion test methods and their use and predictability, the focus of this chapter is on bioassay procedures rather than fire models or stages.

7.2 Principles of combustion inhalation toxicology

7.2.1 Interaction of fire effluents with structures of the respiratory tract

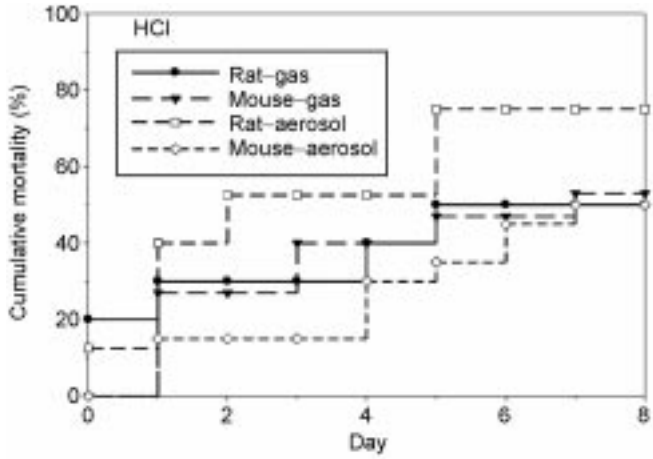
When an organ system is as complex as the respiratory tract, it is convenient to simplify it by forming conceptual anatomic units or 'compartments'. Conventionally, one may think in terms of three major compartments which divide the respiratory tract into regions based upon anatomical features and upon particle deposition and clearance phenomena that occur within the tract and are specific to each compartment. The regions are called the nasopharyngeal (NP), the tracheobronchial (TB) and the pulmonary (P) compartments. The NP compartment begins at the anterior nares and includes the respiratory airway down to the level of the larynx. People possess the ability to detect volatile chemicals via sensory perception. In the nose, this ability is provided by two separate but interrelated sensory pathways, the *olfactory* nerve and the *trigeminal* nerve. Stimulation of the olfactory nerve results in sensations of smell, whereas stimulation of the trigeminal nerve gives rise to chemical irritation or pungency or intranasal chemesthesis (response to chemicals). Commonly the olfactory system is stimulated at concentrations well below those which will elicit trigeminal activation. Odour perception does not reliably signify the presence of a toxicant. However, such cognitive characteristics are often perceived as potential for adverse health effects to occur.[1] This means that for a meaningful risk assessment, debilitating effects must be clearly distinguished from perceived sensations.

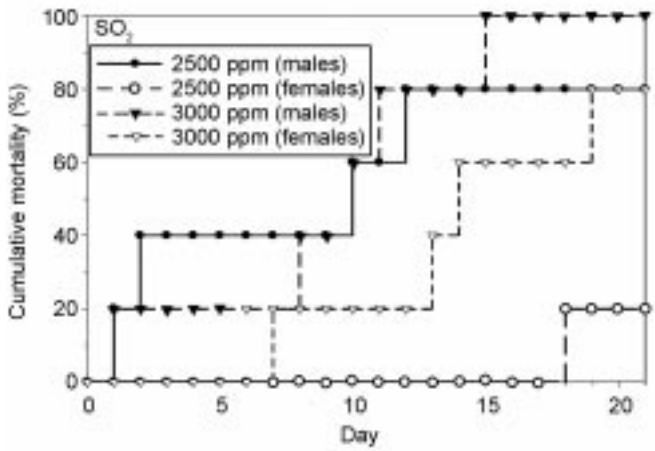
In laboratory animals the intensity of trigeminal stimulation has been used to compare the relative potency of upper respiratory tract sensory irritants. Typical combustion gases deposited in the upper airways are ammonia and volatile aldehydes. Depending on the particle size or water solubility and chemical reactivity inhaled substances penetrate the NP region and are then deposited in the fluids lining the airways leading to the alveolar region (trachea, bronchi). Chemicals causing airway injury (e.g., hydrogen chloride, sulphur dioxide, volatile aldehydes and isocyanates) often cause epithelial desquamation ('delamination' of cells lining the airways) with ensuing obliterating bronchitis (obstruction of airways due to mucus secretion and inflammation). The result may be protracted and sustained damage within the airways caused by inflammation and overproduction of mucus leading to loss of airway patency (free from obstruction). In the absence of damage to the alveoli, alveolar perfusion

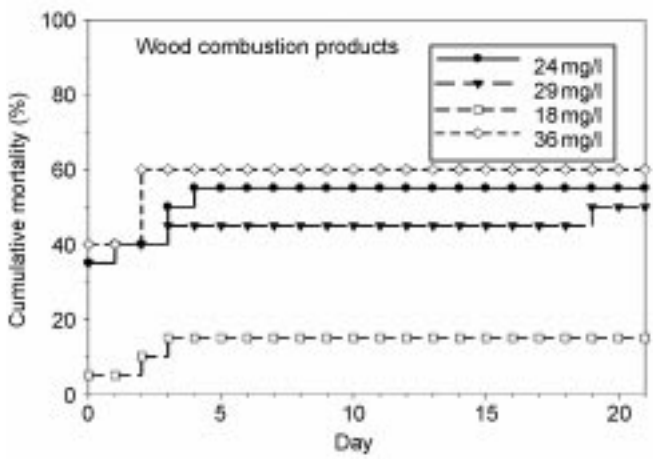
continues but gas exchange does not occur owing to airway blocking, and blood returning to the heart is not adequately oxygenated. Thus, blood entering the lung does not participate in gas exchange, i.e. discharge of metabolic carbon dioxide and uptake of oxygen. This type of ventilation-related disturbance in gas-exchange and associated *venous admixture* or *shunted blood* differentiates diffusion-related disturbances, e.g. due to increased thickness and injury of the air:blood barrier of the alveoli. In any case, systemic hypoxaemia (lack of oxygen throughout the body) results when inadequately oxygenated blood enters the general circulation.

The onset and time course of mortality caused by the interruption of diffusional processes as a result of an acute alveolar oedema and following airway injury differ appreciably. Alveolar injury and subsequent oedema may cause death within 1 day post-exposure while airway injury causes a more protracted, delayed type onset of mortality. In animal models, this mode of action is revealed by a lingering type of lung injury and mortality delayed in onset. Time–mortality relationships in mice and rats exposed to hydrogen chloride gas or aerosol, at concentrations in the range of the respective LC_{50}, showed both phases, i.e. the delayed mortality typical for airway irritants and the early mortality typical for lower (alveolar) respiratory tract irritants (Fig. 7.1, top panel).[2] Onset of mortality following a 30 min exposure of rats to sulphur dioxide gas did not cause any immediate mortality but elicited a marked delayed mortality. A reciprocal relationship of the exposure dose and occurrence of mortality was observed (Fig. 7.1, middle panel). As detailed above, delayed mortality is likely to be associated with extensive airway inflammation superimposed by airway plugging and subsequent hypoxaemia. Unlike pure gases, combustion effluents often cause a biphasic type of mortality (Fig. 7.1, lower panel). In combustion toxicology, the term narcotic is used primarily in reference to asphyxiant toxicants that are capable of resulting in central nervous system depression with loss of consciousness and ultimate death. Although many asphyxiants may be produced by the combustion of materials, only carbon monoxide and hydrogen cyanide have been measured in fire effluents in

7.1 (opposite) Time–mortality relationships of mice or rats whole-body exposed to hydrogen chloride gas or aerosol at concentrations in the range of the respective LC_{50} (top panel). Similar relationships from rats nose-only exposed for 30 min to sulphur dioxide (middle panel) or wood combustion effluents (HCl data reproduced from Darmer *et al.*[2]). The different time-course patterns of the occurrence of mortality provide evidence whether death is related to irritation-related alveolar injury and subsequent acute oedema (≤ 1 day post-exposure) or upper/lower airway injury (HCl up to post-exposure day 7, SO_2 up to post-exposure day 18). Wood combustion products caused mortality due to carbon monixide intoxication (day 0, during exposure) or delayed (up to post-exposure day 19) which is attributed to the presence of irritant aldehydes.







sufficient concentrations to cause significant acute toxic effects. The immediate death was likely caused by the narcotic toxicant carbon monoxide whereas the superimposed delayed death could be attributed to irritant aldehydes.

Toxicants that reach the alveolar gas exchange region may pass the air–blood barrier and are then distributed to other organs (e.g. carbon monoxide, hydrogen cyanide, nitric oxides/nitrates). This can be very rapid as all the blood returning from the lung to the heart is subsequently distributed throughout the body. Not all materials deposited and retained in the alveolar region pass this barrier, e.g. poorly soluble soot particles. Alveolar macrophages are a mobile cell population designed to maintain this region free of particles, bacteria, cellular debris, etc., by the process of phagocytosis. Thus particles deposited at the alveolar level are engulfed by macrophages and then cleared from the lung into the stomach via the *mucociliary escalator*.

The thickness of the blood–air barrier is approximately 0.5 μm which makes this tissue barrier extremely efficient for gas transfer over a large surface area. However, these specifics make the alveolar region particularly vulnerable to toxic insult. Surface tension at the air–water interface produces forces that tend to reduce the area of the interface leading eventually to a collapse of alveoli. This is prevented by the presence of the *surfactants*. This also reduces the pressure gradient between the vascular system (which exhibits high hydrostatic pressure) and the alveolus where the pressure is sub-atmospheric, thus preventing oedema caused by leaking of plasma into the alveolus. The integrity of the delicate architecture of alveolar septae (the scaffold of connective tissue stabilising the alveolar structure) is maintained by a highly specialised structural network consisting of epithelial, interstitial and endothelial components. The maintenance of pulmonary fluid homeostasis is dependent on a complex relationship between the amount of fluid filtered by the capillaries and that drained by the lymphatic system. The capillary endothelium (ling cells of the small blood vessels) has a relatively high permeability to plasma proteins, whereas the normal alveolar epithelium is relatively impermeable to protein, preventing it from entering the alveolar space. Fluid and protein sieved by the capillary endothelium flows along the parenchymatous connective tissue (interstitium) and is drained by the lymphatic system. The amount of transvascular fluid and protein flux is determined by the hydrostatic pressure (heart), from the oncotic forces in the capillaries and interstitial space, and by the permeability of the epithelium. A balanced relationship is disrupted in many pathological states from inhalation of combustion products, with resultant oedema formation. Oedema types can be separated into two basic groups: high pressure or cardiogenic oedema and the noncardiogenic high permeability oedema. If surfactant is destroyed then a high surface tension oedema may result. The lung is relatively resistant to excess fluid accumulation, thanks to a number of oedema safety factors.[3]

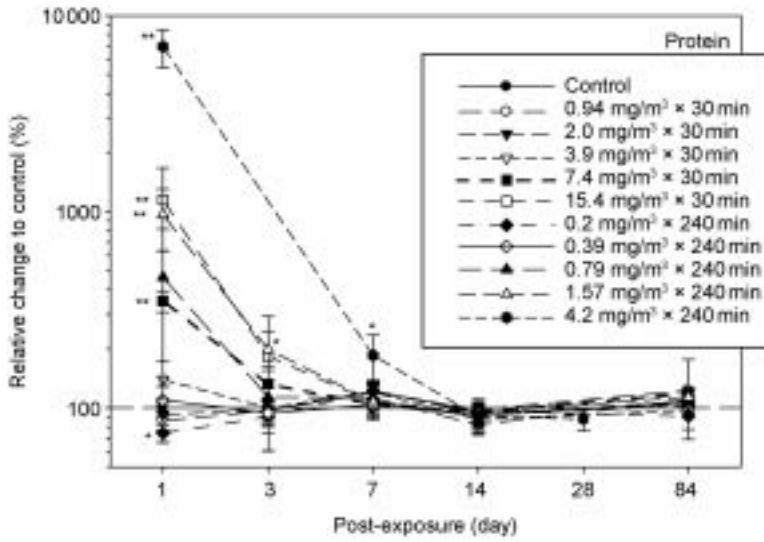
Hydrophobic chemical vapours (e.g. reactive gases such as phosgene or perfluoroisobutylene (PFIB), a product of pyrolysis of polytetrafluoroethylene

(PTFE)), when inhaled in sufficient quantities, cause alveolar barrier disruption either by surfactant dysfunction or direct cytotoxicity. Surfactant inhibition has been shown to occur following exposure to wood smoke but not cotton smoke.[4] This may then lead to lung atelectasis (collapse of the alveolus), increased *venous admixture* (non-ventilated alveoli are perfused without oxygenising the blood flowing through the lung) and oedema (alveolar flooding with the capillary fluid). Alveolar oedema occurs when the capacity of lymphatic drainage is exceeded. In severe manifestations, it interferes with pulmonary gas exchange and constitutes a grave threat to life. In contrast to airway toxicants, death occurs within 24 hours post-exposure.

The acute lung oedema is more prevalent following exposure to 'lower respiratory tract or deep lung irritants'. Experimentally this type of injury can be probed best by time-course measurements of protein in 'washed' excised lungs. The general term used for this procedure is bronchoalveolar lavage (BAL). It is a commonly used method in experimental animals to investigate and quantitate the inflammatory response at the alveolar level.[5-7] The climax of oedema formation is in the range of 15–25 hours post-exposure; however, this may be shorter at extremely high exposure doses. Dose–response and time-course measurements of protein in BAL in rats exposed to the alveolar irritant phosgene are depicted in Figs 7.2 and 7.3. These representations show that increased protein (which parallels oedema intensity) decreases rapidly following exposure (Fig. 7.2), in spite of the 70 times increase over control 1 day post-exposure, reversibility occurred within 2 post-exposure weeks. The relationship of increased protein in BAL and mortality in relation to the exposure dose (concentration × exposure duration) illustrate that marked oedema levels must be attained before lethality occurs (Fig. 7.3). Furthermore, the comparison made in Fig. 7.3 demonstrates that controlled and well-conducted animal studies deliver dose–response relationships for both lethal and sub-lethal end points. Typically, the 'point of departure' for the lethality component of the risk assessment is based on the LCt_{50} (median lethal concentration at a fixed duration of exposure) with an estimate of the highest non-lethal level which is the LCt_{01}. A conservative estimate for the highest non-lethal level has been to take one-third of the LCt_{50}. (The LCt_{50} is the median lethal concentration per minute which is the product of the concentration of a toxic component and the exposure time causing lethality in 50% of test animals.) Sub-lethal end points focus on the most critical disabling outcome leading to incapacitation or irreversible effects. Thus, these 'points of departure' constitute important starting points for risk characterisation and assessment.

7.2.2 Deposition of inhaled fire effluents within the respiratory tract

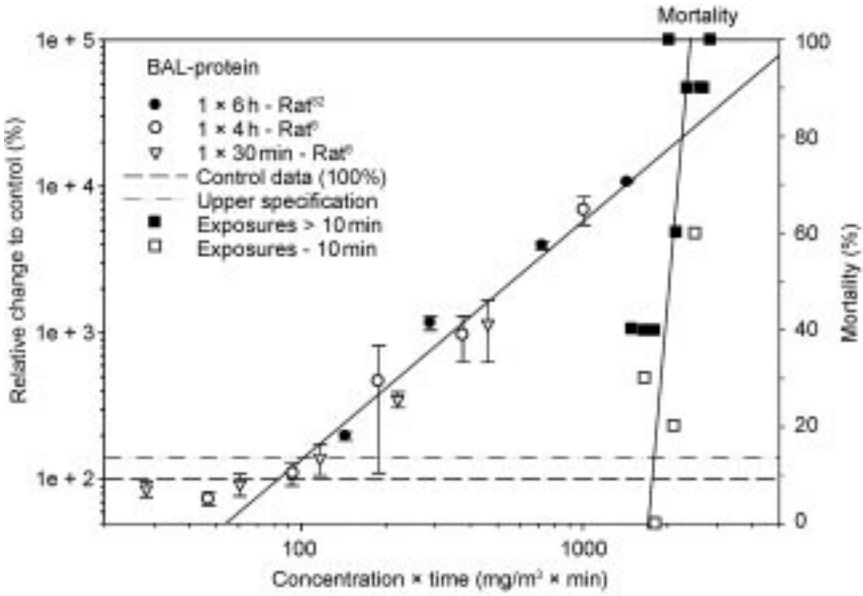
A variety of physical and/or physicochemical properties of combustion effluents determine which 'compartment' of the respiratory tract receives the highest dose



7.2 Concentration-dependence and time-course changes of protein concentrations (an early index of acute lung oedema) in the bronchoalveolar lavage fluid of rats nose-only exposed to phosgene gas for either 30 or 240 min. The magnitude of protein in BAL fluid is clearly *Ct* dependent. Data represent group means ± SDs. Asterisks denote statistical significance to nose-only air-exposed controls (* $P < 0.05$, ** $P < 0.01$, $n = 6$). Rats elaborating BAL fluid-protein levels as high as 70 times the control recovered within 14 days post-exposure. Late onset squelae did not occur. This finding is consistent with a reactive, lipophilic irritant gas causing injury at the alveolar and not at the airway level.

and, accordingly, exhibits the most critical toxic response. There are five significant mechanisms by which particles may deposit in the respiratory tract: impaction, sedimentation, Brownian diffusion, interception and electrostatic precipitation. Impaction is the main deposit mechanism for particles having diameters $\geq 0.5\ \mu$m (predominant in larger airways). Sedimentation is deposited due to gravity (predominant in smaller airways). Diffusion is the major mechanism for submicron-sized particles where bulk air flow is low or absent (bronchioles and alveoli). However, extremely small particles of nanometre dimensions may also deposit by diffusion in the upper respiratory tract. Although particles released during combustion may be nanosized (<0.1 μm in at least one dimension), the high concentrations required in acute combustion inhalation toxicity studies are conducive to particle coagulation and agglomeration (Fig. 7.2). To minimise the chance of misleading artefacts, the conventions called for by contemporary testing standards must be carefully observed.

Retention factors of gases may differ appreciably from one gas to another and are dependent on ventilation and body activity, the duration of exposure and the gas concentration. Therefore, in regard to the inhaled dose, default assumptions



7.3 Dose (*Ct*)-dependence of protein concentrations in the bronchoalveolar lavage fluid on the first post-exposure day (climax of alveolar oedema, see also Fig. 7.2). Rats were nose-only exposed to phosgene gas at various *Ct* products. Data were from different exposure durations (30 min to 6 hours) and were expressed relative to controls (= 100%). The steep curve represents the dose–mortality relationship. Comparison of both relationships demonstrates that a precipitous mortality occurs when BAL fluid-protein exceeds approximately 100 times the control.

are difficult to make for gases and caution is advised when doing so. The localisation of deposition and retention gases within the respiratory tract may vary due to the factors explained below. Among the most typical responses to reactive, irritant gases is damage to the conducting airways. The following categorisation scheme of gases has been proposed:[8]

- *Category I gases* are highly water-soluble and/or reactive and thereby interact with the surface liquid/tissue of the upper respiratory tract. The deposition of these gases is ventilation dependent and the fraction exhaled is relatively low. Examples of Category I gases are hydrogen fluoride, hydrogen chloride, formaldehyde, and volatile organic acids and esters. Hydrophobic gases (e.g. PFIB, phosgene) may follow this paradigm: however, they are retained in the lower respiratory tract.
- *Category II gases* are moderately water soluble and slowly metabolised in respiratory tract tissue. Category II gases include ozone, sulphur dioxide, xylene and propanol.
- *Category III* gases are relatively water insoluble and non-reactive in the extrathoracic and tracheobronchial surface liquid and tissue. Therefore,

relatively small doses reach these regions. The uptake of Category III gases is predominantly in the pulmonary region and is *perfusion* rather than *ventilation* limited. Typical Category III gases include chlorofluoroalkanes, propellants and narcotic gases.

The end result is that gas molecules partition between the two media: air and blood during the adsorptive phase and blood and other tissues during the distribution phase. As the contact of the inspired gas with blood continues in the alveoli, more molecules dissolve in blood until they reach equilibrium. The ratio of the concentration of chemical in the blood and the chemical in the gas phase is constant. This solubility ratio is called the *blood-to-gas partition coefficient* and is unique for each gas.

7.2.3 Phase-interactions in mixtures of combustion effluents

Specific patterns of enhanced local deposition within different regions of the respiratory tract are important in defining a non-uniform lung dose, since the latter depends on the surface density of deposition. Non-uniformity implies that the initial dose delivered to specific sites of the respiratory tract may be greater than that occurring if a uniform density of surface deposit is assumed. This is especially important for inhaled particles (deposition according to aerodynamic particle size) and gases/vapours (deposition according to water solubility and chemical reactivity) that affect the tissue of direct contact. Partition between the vapour phase and particle-associated phase may further affect the deposition pattern of volatile substances, based on their Henry's law constant.

Smoke is a complex heterogeneous, dynamic aerosol comprising liquid or solid particles suspended in a gas. Constituents of these particles can evaporate to the gas phase and gas phase constituents can deposit on particles. The matrix of the condensate (e.g. condensation aerosols of low volatility, soot particles) might not only protect reactive chemicals from hydrolysis, but may also act as *a transport shuttle* for agents into the deeper lung which otherwise had been retained in the less vulnerable upper airways. Such a configuration may enhance synergistically the critical dose of reactive substances at the most vulnerable location of the respiratory tract, the alveolar region. However, owing to the intricate methodological problems involved in the phase-specific analytical determination of analytes in combustion atmospheres, for simplicity, analytical procedures often focus on total concentrations rather than phase-specific concentrations. Nonetheless, these aspects are not only important for the hazard identification of mixtures of toxicants originating from combustion sources, but are also required to select the correct metric of exposure. In fact, acute inhalation toxicity studies should be based on mass concentrations which are the primary metric of toxicity. Thus, gas, vapour and aerosol concentrations should be expressed using a mass per volume metric, such as mg/l or mg/m^3. This allows

for a direct comparison of test components regardless of their physical state. The use of volumetric gas units (ppmV) is further complicated by their dependence on ambient pressure and temperature. To adjust for this disparity, calculators that perform mass↔volumetric unit conversions can be found on the Internet, such as: http://www.lenntech.com/calculators/converter-parts-per-million.htm or http://www.ccohs.caoshanswers/chemicals/convert.html.

The focus of hazard identification procedures of fire effluents is to simulate high level exposure patterns likely to elicit acute inhalation toxicity in humans. While paying most attention to survival, likelihood of occurrence of irreversible effects and impairment of escape (incapacitation), limited emphasis has been given in these models to the possible superimposing effects of modifying factors, e.g. heat stress, smoke obscuration and oxygen vitiation. Testing complex smoke mixtures in bench-scale tests can lead to conditions not necessarily realistic to real fires, especially when the substances interact at high concentrations prior to dilution. Owing to the dynamic nature of smoke, its chemical composition changes with time as does the absolute and relative concentration of smoke's constituents in the gas and particle phases. The equilibrium between gas and particle-phase is almost instant. Thus, from the perspective of hazard identification of combustion atmospheres, the highly dynamic gas-phase particle equilibrium, as well as the rapid growth of particles at high concentrations due to coagulation and agglomeration, needs to be appreciated. For isocyanates, a systematic empirical analysis of these aspects has recently been published.[9,10]

7.2.4 Cumulative summation approaches – toxic equivalency factors

As detailed above, the 'site of initial deposition' within the respiratory tract as well as the ensuing characteristic injury controls the type and extent of lung toxicity that occurs. Thus, simple 'dose addition' may not necessarily result in 'toxic response addition' even if the primary mode of action, such as irritancy, appears to be similar. Nonetheless, over the past decades, attempts have been made to simplify complex combustion exposure mixtures by approaches attempting to accumulate ostensibly identical chemical or physical principles. In this context it must be recognised that the applicability of both dose addition and response addition can be evaluated by appropriate toxicity testing that produces dose–response data for the whole mixture and its component chemicals. Any use of the additivity formulas to obtain estimates of mixture toxicity extrapolated beyond the range of actual mixture data should be accompanied by a description of the evidence supporting the additivity assumptions, i.e. commonality of toxicity for dose addition and toxicologic independence for response addition.

Despite these basic paradigms, attempts have been made to establish a common denominator for irritant inorganic gases, the 'smoke corrosivity'. The

irritant potency of organic aldehydes is commonly markedly higher than that of acids; however, this has been neglected. Acid gas emissions may indeed be of relevance for 'property protection' due to corrosion; however, the relationship between acidity of smoke (following the capture of smoke to obtain dilute aqueous solutions) with smoke toxicity or fire hazard appears to be ill-founded. Water-soluble, reactive irritant gases range from upper to lower respiratory tract irritants, with remarkable differences in their acute lethal toxic potencies. For example, the solubility and rate of hydrolysis of phosgene ($COCl_2$) favours its penetration into the lower respiratory tract, including the layers constituting the alveolar blood-barrier and reactions with nucleophilic molecules predominate in hydrolysis. The more proximal airways are protected against phosgene by reactions with components of the mucous layer lining the airways. In contrast, irritant gases such as hydrogen chloride are preferentially retained in upper and central airways. The difference in mode of action is reflected by the difference in LCt_{50} values. The LCt_{50} of phosgene is 1741 mg/m^3 min[11] while that of hydrogen chloride gas and aerosol in rats is 211 545 and 254 970 mg/m^3 min, respectively.[2,12]

These considerations demonstrate that a composite metric, such as 'acidity' or 'corrosivity' cannot serve as a meaningful cumulative surrogate for irritant smoke toxicity. Amino-moieties in the non-protonated and protonated forms may affect smoke chemistry, type and site of injury, and eventually bioavailability. Cationic structures from protonated amines may manifest a higher degree of pulmonary toxicity than 'acids' because of possible interactions with surfactant. Hence, the arbitrarily selected 'acidity' or 'corrosivity' metric appears to be meaningless, if not irrelevant, with regard to hazard identification.

Similar approaches for 'dose addition' have been used to simplify risk assessment procedures of complex mixtures using toxic equivalency factor approaches.[13,14] This cumulative total toxicant concept has also often been applied to isocyanates (chemicals with an R–N=C=O moiety) detected as products of thermolysis of polyurethanes. Again, such approaches do not consider the phase-dependent dose metric of exposure, the site-of-deposition specific toxic mechanisms, or the difference in toxic potencies of various types of aliphatic and aromatic isocyanates. As already alluded to above, differences in the acute lethal toxic potencies of irritant gases are governed by the predominant location of deposition and/or retention within the respiratory tract, which cannot be predicted by simple dose addition. Nitrogenous components from polymers can be converted to a range of components of varying toxic potencies. Depending on the fuel chemistry and fire conditions, these may include the upper respiratory tract irritant ammonia (NH_3), isocyanic acid (which is likely to be converted to NH_3), the airway irritant methyl isocyanate (MIC), the alveolar irritant nitrogen dioxide (NO_2) or diisocyanate aerosols (e.g. methyl diphenyl diisocyanate, MDI) to mention but a few. All of them have

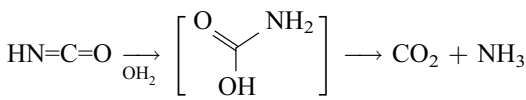
distinctly different LCt_{50} values. The LCt_{50} values of ammonia, methyl isocyanate, nitrogen dioxide and respirable methyl diphenyl diisocyanate aerosol are ≈700 000 mg/m^3 min (60 min exposure),[15] ≈7200 mg/m^3 min (120 min exposure),[16] 7600–12 000 mg/m^3 min (30 min exposure)[17,18] and 88 320 mg/m^3 min (240 min exposure; Pauluhn, unpublished data), respectively. In all cases male rats were more susceptible than female rats, which is a common finding for substances causing lethality by respiratory tract irritation.

Hence, respiratory tract irritants such as isocyanates probably differ in toxic potency due to factors beyond inherent reactivity of the R—NCO functional group, contingent on properties which include factors, such as electrophilicity and lipophilicity, steric hindrance, physical phase and other factors. Therefore, caution is advised when using simplified dose addition methods.

Recently, isocyanic acid vapour (HNCO) has been found in fire effluents. Isocyanic acid can readily be generated by the thermolysis of urea moieties which then may either trimerise to isocyanuric acid, a 1,3,5-triazine derivative, or, especially in the presence of humidity, be rapidly hydrolysed (via the unstable carbamic acid) to carbon dioxide and ammonia.

Formation: $H_2N—CO—NH_2$ (urea) → NH_3 + HN=C=O

Degradation:



These considerations are of ultimate importance for a toxicological assessment of isocyanic acid because it is amenable to spontaneous decomposition at the point of entry, i.e. the upper respiratory tract. This means it is likely to be as toxic as ammonia (which actually means non-toxic). This provides further evidence to support the view that the summation of functional moieties cannot readily be translated to the toxicity, or response addition likely to be caused within the respiratory tract, in the absence of confirmatory animal experiments.

In summary, although there are a number of modifying and influencing factors, any comprehensive framework that seeks to predict and explain the toxic effects of complex combustion atmospheres must take into account the key mechanisms of toxicity, the specific characteristics of key toxic components, the potential points at which these toxic mechanisms may interact, and the dose-dependence of both the mechanisms of toxicity and the mechanisms of interaction. These have to be disentangled from physicochemical interactions (atmosphere related) and biological perspective. At present, this objective can only be achieved by animal testing which integrates all variables in their entirety.

7.3 Bioassays

7.3.1 Available data – weight of evidence

With regard to the acute inhalation toxicity of irritant gases and asphyxiants a wealth of information has been generated in experimental animals during the past decades.[17] However, species selection, mode of exposure and inhalation chamber operation principles, analytical characterisation of test atmospheres, and length of post-exposure periods may differ remarkably from one study to another. The emphasis of past studies was on accidental exposures using short exposure periods in the range of 5 to 60 min. Especially in whole-body inhalation chambers, the equilibrium concentration (t_{95}) may not have been attained during short exposure periods or state-of-the-art analytical procedures applied to compare 'actual' with 'nominal' exposure concentration. The heterogeneity of exposure atmospheres within whole-body exposure systems has often not received any particular attention but may occur when gases are heavier or lighter than air. Especially for water-soluble, reactive gases, wall losses and hydrolysis require exposure concentrations to be defined as analytically confirmed 'actual breathing zone concentrations' rather than nominal concentrations.

Small rodents may experience an instant, reflexively induced transient depression of respiration when exposed to high concentrations of respiratory tract irritants after onset of exposure. Much (if not most) inhalation toxicity data of major toxicants in combustion atmospheres have been generated prior to the existence of internationally harmonised testing guidelines, such as the OECD#403.[19] Accordingly, variability of data across different laboratories appears to be highly contingent on the laboratory-specific method used. Owing to these limitations many of the concentration $\times$ time toxicity relationships (effect $= C^n t$; for details see Section 7.6.2) reported may have been influenced by pre-guideline study designs and ill-controlled methodological factors. Therefore, 'biological variability' needs to be clearly separated from 'methodological variability' and study results need to be selected using a science-based weight-of-evidence rather than precautionary 'lowest value' approaches.

7.3.2 Hypothesis-based *in vivo* animal exposure studies

It is desirable to model mathematically the effects caused by common toxicants from fire and, therefore, obviate the use of large numbers of laboratory animals in smoke toxicology testing. Accordingly, to date, the use of animal bioassays to evaluate the relative toxic potency of combustion products from materials has decreased to a minimum. Indiscriminate testing in experimental animals for the purpose of generating 'numerical toxicity data' is not recommended. However, with regard to hazard identification and risk assessment and follow-up risk management actions, the potential pitfalls and shortcomings of animal-free procedures have to be considered. Smoke atmospheres evolved from materials

are highly dependent on the combustion condition and the procedures used to collect and analyse metastable, dynamic atmospheres. Key components may readily be identified for known products; however, they may not receive the due attention when unexpected toxic entities are released or formed *de novo* under specific conditions. While most analytical procedures attempt to collect atmospheres close to the source (in order to minimise losses of analytes), inhalation toxicity tests focus on 'aged and stable' atmospheres that people may endure at some distance from actual fires. Hence, prior to animal exposure, atmospheres are conditioned to tolerable temperatures and oxygen content. The robustness of predicted toxicity data from 'analytical tests' depends on the parameters chosen and, therefore, requires some validation/verification with empirical data from bioassays. These assays need to be designed to integrate the toxic potency of fire effluents in their entirety with consideration of whether the key conclusions drawn from analytical-mathematical procedures are verified or refuted. Accordingly, the bioassay provides a means to judge whether the great number of minority components contained in smoke bear any significant acute threat to health or not. Moreover, the integrated bioassay is the only way to verify that the methods used in mathematical modelling were adequate or whether they need to be further refined and improved.

Acute inhalation toxicity is defined as the total of adverse effects associated with a single, uninterrupted exposure of non-fasted healthy young adult animals (preferably rats) by inhalation over a short period of time (30 min for combustion effluents) to an adequately generated and characterised atmosphere.[17,20]

Following this paradigm, the first step in this testing strategy is the modelling of toxicological effects and to determine what constitutes the exposure dose associated with a given response and which component causes the most critical acute health outcome. Consequently, toxicologists categorise components as asphyxiants, upper or lower respiratory tract irritants or yet unidentified constituents causing an unexpected/unusual toxicity. In addition to commonly determined end points (clinical observations, body weights, carboxyhaemoglobin), the extent of sensory irritation and especially the most critical site of local respiratory tract injury should be demonstrated either by physiological methods, by BAL, or histopathology. External concentrations of carbon monoxide/hydrogen chloride and blood carboxyhaemoglobin (COHb)/cyanide levels are useful to compare the external and internal exposure dose of key toxicants. Current testing guidelines for the determination of acute inhalation toxicity give preference to the nose-only mode of exposure.

7.3.3 Toxicological interactions in mixtures from combustion sources

Interior materials presently in use may contain halogen and nitrogenous moieties, which can react during combustion or pyrolysis to form the corres-

ponding halogen acid gases and nitrogenous components which may be converted, *inter alia*, to ammonia, nitrogen oxides and/or hydrogen cyanide. As shown in Section 7.8, their formation is highly dependent on the type of combustion (fire stage). The interaction of combustion gases has extensively been studied in rats in multiple combinations and animal models which included hydrogen fluoride, hydrogen chloride, nitrogen dioxide, hydrogen cyanide, carbon monoxide, carbon dioxide and oxygen vitiation.[17,18,21–29]

An antagonistic toxicological effect was observed when animals were exposed to nitrogen dioxide and hydrogen cyanide. The explanation for this antagonistic effect is believed to be due to the production of methaemoglobin (which can be effective as an endogenous cyanide antidote) by nitrite ions formed from the dissociation of nitrous acid in the blood. The nitrous acid is generated by the reaction of nitrogen dioxide and water in the lung.[18] Although the binary combinations of nitrogen dioxide and carbon dioxide showed that the toxicity of nitrogen dioxide doubled, the tertiary gas combination studies with hydrogen cyanide, nitrogen dioxide and carbon dioxide indicated that carbon dioxide did not increase the toxicity of the mixture (carbon dioxide increases the inhaled dose by the stimulation of ventilation). Possibly, this augmentation has further increased the protective dose of the nitrogen dioxide. This increased 'protective' effect of carbon dioxide is probably due to the greater amount of methaemoglobin produced.

The additive oxygen-depriving effects of nitrites (methaemoglobin formation) and carbon monoxide – which is subsumed under the term 'anoxic anoxia' – and oxygen depletion '*hypoxemic anoxia*' can synergistically increase the lethal toxic potency of carbon monoxide and hydrogen cyanide in combustion gases. Cyanide blocks the mitochondrial utilisation of oxygen and leads to *histotoxic* or *cytotoxic* anoxia, i.e. its mode of action differs from the former types of anoxia. Thus, exposure to both carbon monoxide and hydrogen cyanide in sufficiently high concentrations can result in reduced oxygen delivery to organs sufficient to produce unconsciousness ('narcosis') or death in minutes with few, if any, premonitory signs. The primary target organs from hypoxia are those with the highest aerobic metabolism and oxygen demand. Accordingly, the brain, the respiratory and the cardiovascular systems are most susceptible. Owing to the interrelationship of hypoxia and narcosis, the term 'asphyxiant gases' is also used. Nonetheless, the principally different mechanisms involved in the toxicity of hydrogen cyanide and carbon monoxide need to be reiterated: the toxic effects of cyanide ions in humans and animals are generally similar and are believed to result from inactivation of cytochrome oxidase and inhibition of cellular respiration and consequent histotoxic anoxia. Conversely, the predominant toxic mechanism of carbon monoxide is the strong binding to the carrier protein haemoglobin relative to oxygen. It is obvious that the specific antagonist to carbon monoxide is pure oxygen. Advantage can be taken of the mass law to accelerate the rate of conversion of carboxy- to oxyhaemoglobin *in vivo* by increasing the inhaled partial pressure of oxygen.

7.3.4 Composite reciprocal addition approach for estimation of acute toxicity of combustion atmospheres

For the sake of simplicity, most regulations propose composite reciprocal methods based on simple addition of the key critical components of the most hazardous substances to determine the hazard of a mixture.[30,31] Ideal conditions require these components to produce additive acute toxicity by a common mechanism which can be shown by parallel regression lines of dose–response relationships.

$$\frac{1}{\mathrm{LCt}_{50\mathrm{mixture}}} = \sum_{i}^{n} \frac{f_i}{\mathrm{LCt}_{50i}}$$

where f_i is the fraction of substance i in the mixture atmosphere. A comparable time-adjusted measurement is the LCt_{50} which relates to median lethal concentration (C) with the exposure duration (t). It is often expressed in terms of mg/m^3 min. The non-lethal threshold concentrations (LCt_{01}) (estimated LCt_{01} causing mortality of 1%) is the starting point in risk assessment designed to prevent mortality from occurring. ICt_{50} is the term sometimes used for non-lethal outcomes referring to incapacitation.

The advised approach to lower complexity is to reduce the number of variables, i.e., to consider fewer components, fewer hazardous end points and fewer exposure scenarios in the risk assessment process. A major simplification is to consider only those components of smoke mixtures that, based on the summation rules in the mixture, have contributed to toxic hazard. Hence, the key component approach is based on the identification of the critical components for each effect class, as a worst case, i.e. the component with the lowest weighted f_i/LCt_{50}. Effect classes could be stratified by end points likely to impair escape (upper respiratory tract irritation), irreversible or lethal effects (substantial airway and alveolar irritation) or systemic toxicity (e.g. narcosis). *De facto*, any lesser level of effect is then controlled as well. This has the virtue of being simple and understandable even by non-experts and would entail a minimum of bureaucracy. Similar approaches have been proposed elsewhere.[32] Toxic addition methods have a common place in combustion toxicology.[17,21–24,29]

Fractional concentrations are expedient when referring to atmospheres generated under highly controlled conditions. In combustion toxicology, tube-furnace methods may provide the most controlled means to produce stable equilibrium concentrations in inhalation chambers by incremental combustion of test materials over a fixed duration of exposure.[33–35] However, modified approaches have to be used to accommodate real-fire situations where the intensity and composition of emissions change over time. For many components released from fires, Haber's Law may not apply in its strict sense (toxic effect $C^n \times t$ with $n = 1$).[36]

Simple summation methods have limitations with regard to dosimetry or toxic effects because interactions cannot be demonstrated. Despite some minor interactive effects, mixture toxicity appears to approximate the toxicity of the most toxic component of the mixture when: (1) components of the mixture affect different target organs and/or operate via different modes of toxic action and (2) components of the mixture affect the same target organ but through different modes of action and/or at different locations. For the locally acting respiratory tract toxicants this means that the site of initial deposition is most important for the acute effect to occur. The interaction between substances in terms of toxicity has been thoroughly reviewed.[37] Sensory irritation-mediated processes may not be fully additive because of competitive agonism. It was shown that the degree of sensory irritation of a mixture of irritant aldehydes is stronger than that of the individual aldehydes but less than that of the sum of the individual irritant potencies, which is basically a result of competition for a common receptor.[38]

To date inhalation toxicology primarily focuses on individual agents, even though single agents, in isolation from other agents that might influence risks, rarely, if ever, affect people. There is a considerable body of literature on the inhalation toxicology of mixtures; however, our understanding of the significance of exposure to compounds contained in mixtures, in contrast to single component exposures, is relatively sparse. Inhalation toxicity studies of mixtures inherently are difficult, and the science of studying mixtures is not refined or codified highly. This has resulted in multiple experimental approaches both with regard to exposure methodologies and the selection of biomarkers to define the exposure intensity (or dose) and associated effect (or response). In the context of inhalation studies, the definition of the metrics of dose is particularly complex and the analyte most readily available due to practicability and expedience may not necessarily be the most relevant one to understand the critical pathomechanism(s) of the mixture or the most critical constituent contained in it. This issue is complicated even further due to the many possible physical interactions and chemical reactions. The specific facets associated with independence models of combined actions and dose addition of non-interacting chemicals in a mixture have been reviewed in detail elsewhere.[39,40] Scientifically, one must acknowledge that toxic effects of single chemicals are never observed in isolation, but always in the context of biological and environmental mixtures. Only by exaggerating dose can we presume to test effects of single agents or specific mixtures. Dose exaggeration, however, confounds any generalisation of results beyond the experimental conditions.

7.3.5 Limitations of animal-free toxicity tests

Mathematical modelling of the acute inhalation toxic potency of a combustion atmosphere is based on the yield of an incriminated toxicant and its acute toxic

potency. It further assumes that no interactions (either toxicological or physicochemical) occur and that the fire stage chosen to determine the yield is somewhat similar to that endured by people similarly exposed to combustion atmospheres. So far, the degree to which the particles present in smoke (soot and condensation aerosols) act as 'vectors' concentrating and enhancing the delivery of toxic components to the distal airways is not well defined or considered. This circumstance may challenge results obtained under idealised conditions, e.g. studies with single gases, in that way that 'upper and lower respiratory irritants' may become indistinguishable. Therefore, the bottom-up modelling approach should involve at least some acute inhalation testing in experimental animals to verify that the simplifications used for modelling do not lead to erroneous conclusions in safety assessment.

In brief, the anticipated key components and their yields are characterised under the conditions of the test, followed by an estimation of the median acute lethal toxicity (LC_{50}) using the composite reciprocal addition approach or modifications thereof. It is recommended that a stable equilibrium concentration is tested over a period of 30 min. The approach presented in Section 7.8 utilises two exposures relative to the modelled LC_{50} of the combustion atmosphere as a whole. Such an acute validating bioassay utilises a minimum of 10–20 rats in total. Not all materials should be indiscriminately tested in such bioassays. Preferentially the focus should be on the validation/falsification of theoretical modelling.

Suffice to say, toxicity is the study of the adverse effects of chemicals (or natural substances) on living organisms. Toxicity cannot be revealed and quantified by analytical methodologies alone since toxicity (or hazard identification) comprises numerous aspects which cannot be addressed in any holistic manner by the former. These shortcomings include the metric and spectrum of toxic dose, type, onset and mechanisms causing the most critical toxic effects and interactions, whether adverse effects are reversible or not and how the findings from animal models can be translated to the benefit of humans. Exposure intensities may be estimated by measuring biodosimeters that integrate the internal exposure. Hence, data from animal bioassays may provide invaluable evidence to human risk assessment and rationalisation of possible intervention measures for treatments in fire victims.

7.3.6 *In vitro* exposure of cells and tissues

While alternative *in vitro* procedures have extensively been used to examine the 'acute toxic effects' of cigarette smoke,[41–44] the principal differences of *in vitro* and *in vivo* bioassays have to be thoughtfully acknowledged. *In vitro* assays do not allow measurement of physiological responses to occur following injury (permeability or high surface tension lung oedema, recruitment of inflammatory cells that orchestrate further progression of disease, lung remodelling, including

obliterating bronchiolitis associated with delayed effects, interactions of multiple toxic mechanisms, and extrapulmonary toxicity to mention but a few). Physical principles of gas transfer as a result of convection, advection and partitioning, the mechanisms of particle deposition and the active surface area of contact within the mammalian respiratory tract with the exposure atmosphere are entirely different in small cell culture systems. Therefore, in *in vitro* systems, the cause of seemingly different potencies of airborne toxicants may either be attributable to differences in gas solubility and extraction efficacies (which eventually determined the cellular dose) or true differences in toxic potencies. In addition to culture factors,[43] the dosimetry of cells becomes increasingly complex for heterogeneous, complex mixtures consisting of insoluble particles (soot), soluble toxicants adhering to particles, and highly soluble/low insoluble volatile toxicants.

Comparison of responses in cultured alveolar macrophages in regard to function, viability or cellular adherence with similar data from acute lethality whole animal studies demonstrated that there is no correlation between the *in vitro* cytotoxicity and the whole animal toxicity. For instance, polyalkylene glycols have been shown that the molecular weight is the most critical determinant of pulmonary toxicity. This favours the hypothesis that their molecular weight-dependent interference with lung surfactant through physical mechanisms leads to a site-specific toxicity. Investigations of the effects of these chemicals on various types of cells grown in suspension culture failed to confirm any molecular weight-dependent toxicity in *in vitro* systems.[45] Therefore, *in vitro* systems are of value to compare selected end points of interest in cellular systems of different susceptibility. However, this objective is achieved best when the principal mode of action is direct cytotoxicity. Hence, the 'acute toxic effects' observed in current *in vitro* systems focus on 'pre-selected end points of interest' rather than integrating adverse responses in their entirety. Furthermore, one has to keep in mind that the physicochemical properties of smoke must be maintained within narrow limits in order not to lose control over dosimetry of smoke components delivered to the cell. Accordingly, the physics involved in the delivery of dose to cells *in vitro* is different from that occurring within the intact respiratory tract.

However, as long as the focus is on *in vitro* bioassays for genotoxicity and cytotoxicity or other highly specific end points, these shortcomings can be partially overcome. Models of acute effects on tissue damage have also been addressed by the analysis of products of lipid peroxidation and cellular degradation products.[46] Most *in vitro* assays focus on the release of pro-inflammatory mediators and oxidative stress. The time-course of recruitment of inflammatory cells that orchestrate further the inflammatory response *in vivo* or physiological sequelae cannot be reliably addressed in these models. However, this limitation can be considered to be an advantage for mechanistic studies focusing on key end points only. Owing to the difficulty of judging the impact of

protective layers (lining fluids, mucus and surfactant), imbalances of oxidants and antioxidants and between proteases and antiproteases, the quantitative outcome in humans is too complex to predict.

An accurate assessment of the pulmonary toxicity of combustion effluents in a simplified *in vitro* system is a challenging experimental endeavour. This complexity is further increased due to the numerous toxicants contained in such complex mixtures and their delivery to the respective target tissue *in vivo*, *in vitro* or *ex vivo* model (e.g. isolated perfused lung, lung slices). The complexity and heterogeneity of the respiratory tract, the mechanisms involved in the deposition of volatile and non-volatile components in respiratory tract-specific air flow rates and surface areas (submersed cultures, exposure at air–liquid interface), and the dependence of toxic pulmonary effects on biochemical and physiological mechanisms, make any quantitative assessments difficult. Despite recent advances and perspectives, quantitative aspects of inhalation toxicology in small rodents continue to be the mainstay of toxicological assessments.

A variety of *in vitro* lung epithelial cell models, and primary cultured alveolar epithelial cells, when grown to monolayer status, offer new opportunity to clarify some of the mechanisms involved in pathophysiological pathways. While continuous cell lines show potential, primary cultured alveolar epithelial cell models from rat and human origins may be of greater use, by virtue of their universally tight intercellular junctions that discriminate between the different transport kinetics of the various toxicants. Nevertheless, the relevance of using these reconstructed barriers to represent the complex disposition of intact lungs may still be debatable. Meanwhile, the intermediate *ex vivo* model of the isolated perfused lung (IPL) appears to resolve some deficiencies of these commonly experienced *in vitro* models. However, the major limitation of *ex vivo* lung models is the short viable period of 2–3 h and the likely absence of tracheobronchial circulation. Direct dosing into the trachea of IPL preparations lacks the benefits of conditioning of inhaled atmospheres. While controlling lung-regional distributions, the response to injury or systemic toxicity cannot be modelled.[47]

The selection of *in vitro* systems has to be guided by the known, reasonably well-characterised differential deposition of substances along the airways (for gases, largely driven by solubility and reactivity; for particles, largely driven by aerodynamic particle size) relative to the profile of cells along the respiratory tract. However, a complex mixture of particles, gas- and vapour-phase components is rapidly diluted and dispersed after emission and undergoes dynamic changes in its physicochemical properties because of shifts in vapour-particle distributions, sorption and desorption of vapour-phase components on the surfaces of the ducting or test system, and chemical reactions. Initially, it would seem reasonable that representative cell types be selected for regions of the lung. Obviously, not all the approximate 45 cell types of the respiratory tract could be evaluated but not all cells are accessible anyway. In general, *in vitro*

models appear to be a useful supplement to *in vivo* methods. These methods could serve the basic research community as a 'tier 1' tool to provide information on the relative toxicity that would guide the selection of subsequent steps. As detailed by Aufderheide,[43] state-of-the-art *in vitro* approaches require highly controlled exposures of cells at the air–liquid interface and elaborate technologies for smoke characterisation. However, the more complex mode of action elicited by asphyxiants cannot be modelled in these assays.

In summary, *in vitro* studies using cells and tissues from humans and laboratory animals allow observations to be made at a level of detail for which observations cannot be readily made in intact laboratory animals or people, for example, the influence of toxicants on the production and release of specific cellular mediators from defined cell populations. The related disadvantage is that the observations must be extrapolated to the intact mammal, which has a complex array of feedback mechanisms that modulate interactions at all levels of organisation in the body. While studies with isolated cells or tissues can be used as the first step within a tiered screening system to identify and rank potential toxicants and may give insight into mechanisms of action (if known), the heterogeneity of the respiratory tract and the variety of systemic or localised toxic effects that may occur following exposure to combustion effluents preclude the indiscriminate use of such tests for as-yet unknown materials. Hence, *in vitro* assay systems may be used to complement standard animal evaluations to provide further insight into the pathogenesis of a variety of lung lesions.[48]

7.4 Exposure systems for the study of inhalation toxicity

Acute inhalation toxicology testing technologies have improved significantly over time, both in terms of well-defined animal exposure and test atmosphere characterisation. Especially for short-term inhalation studies, exposure paradigms have shifted from whole-body to nose-only modes with novel procedures that minimise the re-breathing of atmospheres, attainment of inhalation chamber concentration equilibrium and optimised uniformity (i.e. degree of dynamic mixing) of flows within an inhalation chamber. The availability of computer-supported real-time monitoring devices and increased analytical sensitivity allows for better attainment of a uniform, spatial dispersion and temporal stability of test atmospheres in an inhalation chamber. In combustion toxicity testing, there are two basic types of exposure systems, based on how the test material is delivered: static, with no flow of test atmosphere into the chamber and dynamic, with a single-pass flow-through system. This dependence on available technologies when exposing experimental animals is somewhat unique to inhalation toxicology. Dynamic low through-tube furnace methods, e.g. according to the DIN 53436, have been shown to meet these objectives, namely to provide a rapid attainment of temporally stable test atmospheres.[33–35,49–51]

7.4.1 Inhalation chamber operation

In this section some of the most common inhalation bioassay procedures are succinctly summarised. For a more comprehensive overview of the various approaches used in inhalation combustion toxicology the reader is referred to the comprehensive review by Kaplan *et al.*[52]

Static exposure systems

In a static system, the test atmosphere is produced by introducing a finite amount of smoke into a closed exposure chamber. The test animals remain exposed in a closed system for the duration of test without any replacement of air. The difficulties with this type of system are the depletion of oxygen, rising temperature and carbon dioxide concentration, and decreasing toxic effluent concentration, over time. Additional shortcomings of static systems are that the analytical characterisation of chamber concentrations is usually limited because sampling affects the concentration of the material inside the chamber. Decay of toxicant concentration in the chamber also results from the deposition on surfaces by various aerosol-removing mechanisms, absorption of vapours on the surfaces, as well as uptake by the animals.[53] Thus, especially in combustion toxicology studies, the particular disadvantages of static inhalation chambers are that the combustion atmospheres vary with time and that they cannot be diluted with secondary air in order to maintain viable conditions. This may, in certain circumstances, render the interpretation of the outcome of the test difficult, because test results are predetermined by the depletion of oxygen or by high levels of carbon dioxide.

Dynamic exposure systems

In dynamic systems, the test atmosphere is continuously delivered to and exhausted from the animal exposure chamber in a flow-through manner; test material is not re-circulated. After an initial rise, the chamber concentration will approach and maintain a stable equilibrium concentration, if the generation rate is constant. This stable concentration is usually reproducible after careful test runs have been made. Prediction of the equilibrium concentration requires accurate information on generation rate, losses of test material in various parts of the system, inhalation chamber volume and flow rates. In the dynamic system, temperature and relative humidity are well regulated, oxygen is replenished and/or substituted in a controlled manner. The dose delivered to the animal is easier to determine from stable equilibrium concentrations. Ideally, the exposure is to an inhalation chamber steady-state concentration which facilitates repeated measurements of gaseous agents, condensate and soot by different equipment.

Conditioning of atmospheres and chamber steady state

The animals should be exposed in inhalation equipment designed to sustain a dynamic air flow that ensures an adequate air exchange of at least 2–3 times the respiratory minute volume of animals exposed (i.e. at least 0.5 l/min per exposure port for rats). Each exposure port should have identical exposure conditions with an oxygen concentration of at least 18% and carbon dioxide concentration not exceeding 1%. Five per cent carbon dioxide has been shown to affect the threshold for deaths due to hypoxia, i.e. this concentration caused death in animals at oxygen concentrations which in the absence of carbon dioxide would not be lethal.[26] Prior to entering a dynamic inhalation chamber combustion atmospheres need to be conditioned to obtain tenable conditions for experimental animals, this means the temperature should be at normal room temperature. The time to 95% atmosphere equilibrium (t_{95}) in minutes is calculated using the following simplified formula:

$$t_{95}(\text{min}) = 3 \times \left(\frac{\text{chamber volume}}{\text{chamber air flow}}\right)$$

The time to attain steady state should be negligible relative to the duration of exposure.

7.4.2 Nose-only mode of exposure

A dynamic inhalation system with suitable control of all inhalation chamber parameters is generally used for acute inhalation toxicity studies. The preferred mode of exposure is nose-only (which includes head-only, nose-only or snout-only). Reasons for this preference have been detailed elsewhere.[34,50,53] In brief, nose-only exposed animals are readily accessible for specific physiological measurements (e.g. respiratory function, body temperature) or the collection of blood, if applicable. When an animal is confined in a restraining tube for nose-only exposure; however, the observation of its behaviour and physical condition is somewhat restricted. Subtle clinical signs may be obscured due to impaired locomotion and limited capability to observe specific neurobehavioural responses.

7.4.3 Whole-body exposure technique

Animals should be tested with inhalation equipment designed to sustain a dynamic air flow of at least 10 air changes per hour. All animals should be individually housed to preclude them from breathing through the fur of their cage mates, thus reducing their exposure. To ensure stability of a chamber atmosphere, the total 'volume' of the test animals should not exceed 5% of the chamber volume. Maintenance of slight negative pressure inside the chamber

will prevent leakage of test article into the surrounding area. The exposure of experimental animals to combustion effluents in larger whole body chambers requires more stringent technical control measures than in the highly dynamic, smaller nose-only chambers.[53] Owing to their higher volume and lower air exchange rate, the time required to attain inhalation chamber steady state (t_{95}) is commonly appreciably longer in whole-body chambers than in dynamic nose-only chambers. In the former this may lead to a different ageing profile of atmospheres (particle coagulation and agglomeration), dynamics of condensate formation and/or losses due to the transport of smoke and adsorption onto chamber surfaces with a resultant disproportionation in the composition of phases (aerosols/vapours). Within larger chambers the location of taking samples for analytical characterisations of atmospheres and that of actual animal exposure must be carefully controlled and the time to attain the t_{95} relative to the exposure period must be negligible in order to produce meaningful empirical data.

7.4.4 DIN 53436 tube furnace combustion model

Laboratory-scale tests using the DIN 53436 tube furnace, a method the ISO TS 19700 tube furnace described in Chapter 12 has evolved from, are amenable to a 'rectangular' type of steady-state exposure pattern. Using this apparatus, combustion atmospheres are generated under specified and reproducible conditions.[35,50,51,54] Prior to entering the inhalation chamber, atmospheres are diluted with air to allow testing of atmospheres in the absence of undue oxygen depletion, excessive levels of carbon dioxide or heat stress. This also increases the availability of fire effluents for sampling and analysis. Accordingly, this methodology is capable of measuring product-specific features without the overriding effects inherent with any smoke from fire. One additional advantage of this system is that analytical exposure indices can readily be used to predict the acute lethal toxic potency of the atmospheres generated. The LC_{50} is expressed in terms of mass of material charged to the combustion device but not necessarily the amount of mass actually decomposed. Its unit is mg/l.

7.5 Principles of hazard identification and risk characterisation

Hazard identification is concerned with determining whether exposure to a substance is causally related to the incidence and/or severity of an adverse health effect. In other words, does exposure to a substance cause an adverse health effect and, if so, how bad is the health effect? Risk is not being addressed at this stage. Hazard identification is undertaken to determine whether, and to what degree, toxic effects in one setting will occur in other settings. Since exposure conditions and evaluation procedures can be rigorously controlled, it is possible

to develop quantitative assessments of exposure–response relationships. Approaches to the conduct of animal bioassays with inhaled materials are discussed in this section. Of course, the laboratory animal studies have the major disadvantages of requiring extrapolation of data from laboratory animals to people. However, toxicologists are rapidly approaching the point where such extrapolations can be made more reliable by taking into account principal toxic mechanisms and known species characteristics, as described in detail elsewhere.[55]

Epidemiological studies, beyond the advantage of directly studying humans, also have the advantage of involving real-world conditions. However, a related major difficulty is that the exposure conditions are not controlled – one must study the exposure conditions provided. The range of procedures that can be used to evaluate the health status of individuals and changes related to exposure are substantial, ranging from symptom questionnaires to sophisticated pulmonary function evaluation procedures to mortality records. Because the exposure conditions in the epidemiological studies may not be precisely defined, especially for complex atmospheres as occurring in fires, the exposure–response relationship that can be elucidated tends to be more qualitative than quantitative. Biomarkers of exposure and effect may change with the time elapsed between maximum exposure and the collection of biological specimens. Likewise, also medical interventions affect such biomarkers (e.g. carboxyhaemoglobin). It is especially difficult to establish even semi-quantitative relationships between exposure and response for more chronic types of disease end points.

Laboratory animal studies have the advantage of using carefully controlled exposure conditions matched to the experimental needs. Moreover, the range of procedures used to evaluate the 'dose of fire effluent' received by the experimental subjects can include invasive procedures as well as end-of-life observations that could not be used with people. The study of intact mammals is advantageous in that all of the body functions are subject to the complex integrated physiology that occurs in intact people. The term 'toxic hazard' is a sub-set of 'fire hazard', occurring when the hazard being considered is due to inhalation of toxic combustion products alone. As alluded to above, toxic potency is only one factor in fire hazard assessment, which also includes factors such as heat stress, smoke, obscuration and oxygen deprivation as well as those determining their exposure intensity.

The objective of bioassays has changed significantly over the last decades. At early stages, bioassays consisted of only mortality measurements at some fixed-dose levels to compare and rank product-specific properties in smoke toxicity under method-specific conditions. This led to straightforward categorisation schemes, such as 'less toxic, equally toxic, or more toxic than wood'. As smoke toxicity moved to the forefront of the fire problem, it was realised that people may be incapacitated by the fire hazards per se (heat, smoke, oxygen deprivation) long before they die from the effects of one or more of the combustion

products (generally, death has been attributed to carbon monoxide narcosis or asphyxiation).[52] This was the advent into a search for methods of assessing immediate incapacitation in laboratory animals. Correlations have been shown that both incapacitation and death from smoke asphyxiants, such as carbon monoxide and hydrogen, are high. The most important metric of exposure is accumulated dose (dose = respiratory minute ventilation × exposure duration × actual exposure concentration × retention). However, such correlations have not conclusively been established for smoke irritants, and even current hazard assessments tend to set threshold tenability concentrations rather than accumulated dose for irritant gases.

7.5.1 Objective of acute inhalation toxicity tests with fire effluents

In spite of the primary interest of identifying exposure causes that modify the ability to perform escape tasks, the starting point of defining 'acute inhalation toxicity' is the determination of the acute lethal toxic potency and to reveal key mechanisms causing lethal and significant non-lethal effects. Of all toxicity parameters, the lethality end point is the least subjective end point. Dose–response, time-course of the effect–occurrence and their progression or regression over time are important adjuncts. The increased understanding of toxic principles may prompt more diverse test procedures to reduce the uncertainties involved in the extrapolation across species, i.e. laboratory rodents to humans. It is important to recognise that the chemical decomposition, and therefore the toxicity, of the combustion products of a given material can be highly dependent on the particular decomposition condition selected.

At present, the evaluation of a chemical's acute inhalation toxicity is focused on lethality. Its determination complies with the requirements for global classification and labelling of toxic substances.[31] For the testing of fire effluents, a fixed duration of exposure of 30 min is generally considered to be appropriate. An evaluation of acute toxicity data should include the relationship, if any, between the animals' exposure to the test substance and the incidence and severity of all abnormalities, including behavioural and clinical abnormalities, the reversibility of observed abnormalities, pathology, effects on mortality and any other toxic effects. The general testing conditions called for by internationally harmonised and standardised testing procedures are closely observed.[20]

It has to be kept in mind that any given material, e.g. a piece of high/low density plastic or foam, does not, in itself, contain any inherently acutely toxic substance. Given the complexities of the thermal decomposition chemistry, it seems unlikely that the wide variety of chemical species produced at any set of test conditions, some of which may be known toxicants, while others may not have been characterised, could exactly duplicate the products of any real fire.

Hence, in combustion toxicology, the assessment of the most critical toxic hazard is most important. Hazard and risk-related issues are difficult to disentangle; i.e. whether a slowly burning material with slow release of a small concentration of a highly toxic substance or a fast burning material with rapid release of high concentrations of low toxic substances is associated with a higher risk or not.

In retrospect, the development of combustion toxicology testing procedures has probably suffered from being considered as part of 'fire testing' rather than part of 'toxicology'. The philosophies behind the development and, especially, the interpretation of test results in the two disciplines are different. In fire testing a particular property is considered to be important in fire safety; for example, the ability to ignite, surface spread of flame or smoke production. In mainstream toxicology, the nature of the toxicity, including analysis of the concentration–response relationship, is the issue of interest. If it is considered that humans are likely to show similar adverse effects to those found in laboratory animals, and then an assessment of the potential risk to health in any given situation can be made. This takes into account the likely human exposure and compares it with the effect levels seen in animals. Thus, a substance does not simply 'pass' or 'fail' its toxicology assessment, although some classification schemes do use quantitative toxicological data in such an unsophisticated way. From the regulatory standpoint, the question to be asked is not 'what is the LC_{50} of a material X, and is it below or above a value Y?' but rather 'have the major toxicants been identified, does the projected use of the material represent a potential hazard to life, what is the key component causing toxicity (mortality and morbidity), and how can this impact the causality–effect interpretations and intervention principles in fire victims?'. These questions must be answered by details of the likelihood of ignition, the speed of flame spread, the heat release and the rate of build-up of smoke and toxic gases, including oxygen depletion. Thus it can be seen that, provided a material does not produce unknown or extraordinary toxicants and its decomposition process is well understood, the true 'toxicity test' for toxic hazard may actually be an ignitability or surface spread of flame test.

The dosimetric concepts used in conventional inhalation toxicology appear to be difficult to apply in combustion toxicology because the extent of exposure in 'real-life' fires depends heavily upon the release rate of individual smoke components as well as the propagation of fire which, in themselves, provide a constantly changing environment of exposure. Therefore, in combustion toxicology, the concept of 'fractional effective dose' per 'increment of duration of exposure' may be a more appropriate means for hazard assessment than assuming a 'total dose' per 'entire duration of exposure' which has traditionally been used for single-component inhalation tests.[17]

Another unreasonable expectation surrounding combustion toxicology in general, and the combustion apparatus in particular, is a requirement for the test

to be a hazard evaluation over and above a toxicology assessment. This does not occur in other fields of toxicology, where qualitative and quantitative toxicology data are generated. The risk which the chemical or product may present is considered after the toxicological investigation, not as part of the investigation. The hazard is first defined, i.e. can lethality or other serious toxicity occur? If so, by which agent is it caused and at what concentration? Are modifying factors present that increase toxicity? In this context, one major paradigm in toxicology is the establishment of both the concentration–effect relationship and the concentration × duration of exposure (Ct) effect relationship which provides the basis of hazard characterisation and assessment. The risk, i.e. the probability of the hazard occurring, can then be estimated taking into account the physical properties of the product in its end use configuration. For combustion of materials, this requires several essential prerequisites, for example, the ignition and propagation of fire and the likelihood of exposure. These aspects, however, are beyond the scope of the process of toxicological hazard identification.

7.5.2 Acute inhalation toxicity and potency of fire effluents

Discrepancies in common acute inhalation toxicity and combustion toxicity have to be recognised. Exposure intensity (or dose) is defined as the actual breathing zone concentration of a particular chemical species in common inhalation toxicology whereas in combustion toxicology it is defined by the nominal charge or mass loss of a given material and the total volume/air flow rate through combustion and exposure system. Although the material's toxic potency may be ranked based on nominal descriptors (which inherently are highly dependent on the method used) adverse health effects are contingent upon the accumulated factional dose over time to which animals/subjects are exposed.

Considerations on the relative yields and kind of toxic effluent between different fire conditions (see Chapter 14) have challenged the relevance of material-specific toxicity data as the 'fire stage' appears to drive the toxic potency of fire effluents more than 'material' per se. Indeed, modern methodologies of fire engineering may reliably predict and define the prevailing fire stage, material-specific configurations, for instance cables, fillings, insulations, decorative materials, furniture or carpets. However, such microenvironments may lead to a different or unexpected decomposition of materials. Therefore, if not advised otherwise, the 'intrinsic acute inhalation toxicity' should be determined under 'representative worst-case conditions', leading to reasonable yields of potentially toxic fire effluents. The outcome of tests can then be used to minimise materials' combustion toxicity at their developmental stage. Principles of bioassay procedures have been published.[33,49,56–58]

Dynamic tube furnace rat bioassays using the DIN 53436 test method have shown that the acute lethal toxic potencies (LC_{50}) of different materials tested in a 30 min exposure bioassay ranged from ≈5 mg/l to approximately 100 mg/l, i.e.

the toxic potency of materials differed approximately 20-fold.[50] This analysis supports a concept of 'key toxicants' rather than a bottom-up summation approach of all constituents determined. The most abundant narcotic/asphyxic toxicant is considered to be carbon monoxide.[52] In laboratory models, especially under oxygen vitiated conditions, high concentrations of hydrogen cyanide may also be emitted. The release of inorganic irritants is highly material-specific while that of carbonaceous irritants (aldehydes) occurs commonly when organic materials are thermally decomposed. It was shown that irritant-related lethality occurred in only a minority of animal studies;[50,58] however, empirical data show that they may cause significant morbidity. Irritant gases of toxicological concern include hydrogen chloride, hydrogen bromide, hydrogen fluoride, a range of aliphatic aldehydes, nitrogen dioxide and sulphur dioxide.

Based on the Globally Harmonized System of Classification and Labelling of Chemicals[31] the classification bands from toxic (Category II) to harmful (Category IV) cover a range of 10 for dusts and mists (Cat II: $\leq$0.5 mg/l; III: $\leq$2 mg/l; IV: $\leq$5 mg/l). To make exposure to 'dusts and mists' possible, the liquid/solid phase requires active mechanical dispersion and, therefore, might be somewhat comparable to the emission process that follows ignition and fire growth. Thus, the outcomes from combustion tests can be transpose Globally Harmonized System boundaries to toxicity-equivalent. However, an arbitrary scaling is required as the metric characterising toxicity and exposure duration in combustion toxicology are defined differently in the Globally Harmonized System (GHS: 4 h, combustion toxicology: 0.5 h). The comparison based on toxic outcome and adapted classification boundaries shows a matching relationship, providing a means to rank materials based on lethal toxic potency.[59]

In combustion toxicology, substances producing LC_{50} values in the $\leq$Category II range should trigger in depth considerations on the nature of toxicity and associated risks. Bioassay procedures are particularly useful to identify potencies up to and including Category III. Recognising the need to protect animal welfare, testing of animals in Category IV equivalent ranges (equal or less toxic than combustion effluents from wood) should be discouraged and should be considered only when there is strong likelihood that results of such a test would have a direct relevance for protecting human health.

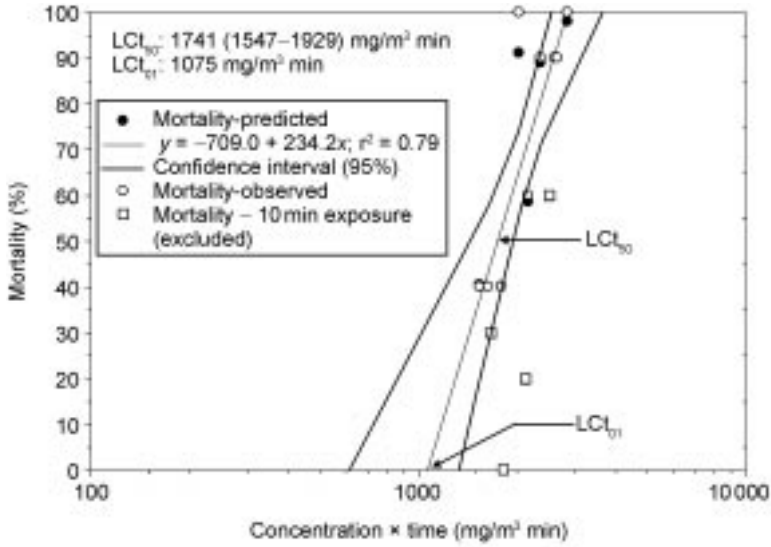
7.6 Inhalation toxicity tests with fire effluents: end points

In addition to lethal end points (LC_{50}, LCt_{50} or percentages thereof), specific regulatory requirements may also demand sub-lethal end points, such as extent of lung injury and irreversible effects, potency of eye and respiratory tract irritation; neurophysiological changes leading to impairment of escape or incapacitation.

It is still a matter of conjecture whether the incapacitation models in use truly simulate the factors involved in the impairment/disability for escape of humans. To reflect better what is actually measured, the term 'intoxication' or 'sub-lethal reversible/irreversible effect' appear to be more apt. Comprehensive mathematical engineering models have been developed over time to better define the 'time of exposure' required to attain a 'defined degree of incapacitation'.[60] However, these models become increasingly complex when all biological parameters of interest are addressed. Quantitative approaches are complicated further because the accumulated internal dose depends primarily on the species' respiratory minute ventilation and numerous modifying factors. These include, for example, body activity, respiratory acidosis/alkalosis due to the presence of acidic/alkaline fire effluents, hypoxaemia (oxygen deprivation), high concentrations of carbon dioxide (which acts as breathing stimulus), the presence of irritants which may either increase or decrease the ventilation, gas-specific uptake factors (Category I–III gases, see above), and gas–particle interactions. In recognising the strength and weaknesses of animal bioassays, in the light of changing animal welfare regulations, the current use of animal models is focused on the validation of novel modelling procedures or novel product entities with the potential to emit unusual fire effluents.

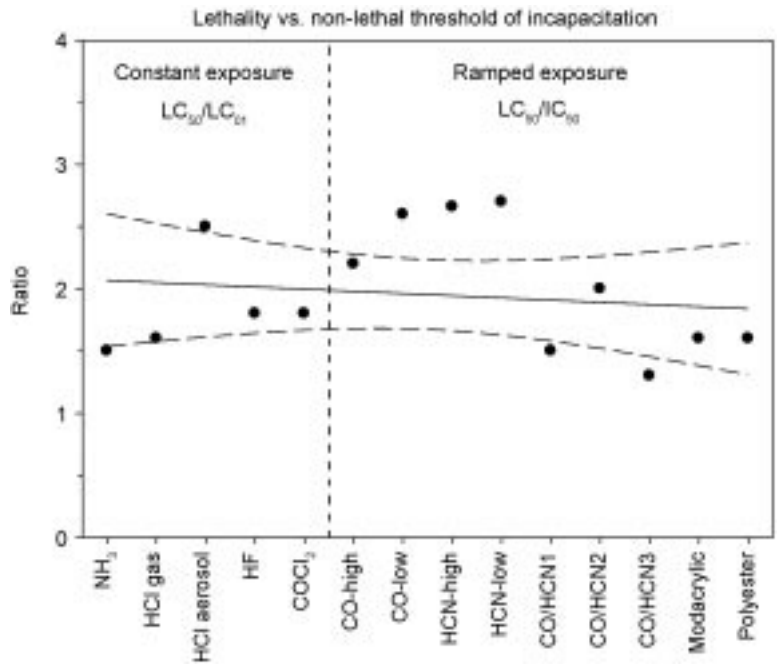
7.6.1 Median lethal concentration (LC_{50}) and fractional percentages

Concentration–response/effect relationships are commonly described by cumulative frequency distributions, mathematically represented by sigmoid curves. Such relationships are assumed to be characteristic for a specific effect and species. The term 'median lethal concentration' (LC_{50}) is suggested as a measure of acute lethal toxic potency by the inhalation route. The LC_{50} is defined as the concentration that kills half of a suitably large number of animals exposed for a specified duration. Determinations of the LC_{50} (or LCt_{50}) require a mathematical description of the concentration–response curve which can be suitably transformed into a linear function by using a concentration ($\log_{10}$)-cumulative mortality (probability percentages transformed into probits) relationship as illustrated in Fig. 7.4. The abscissa represents the product of the concentration of phosgene $\times$ exposure duration. The apparent higher tolerance following an exposure of 10 min was due to an irritant-related transient depression in ventilation (see Fig. 7.11 below). Probit values at 0 and 100% cumulative mortality are undefined (infinite). However, mathematical algorithms ('correction according to Bliss') provide a means to use these values for dose–response analyses.[61] If this relationship is established for various fixed exposure durations of exposure the *Ct* response relationships can be established. Alternative procedures are detailed in the following section.



7.4 Observed (empirical) and predicted (Bliss-corrected)[61] mortality data to estimate the indices of acute lethal potency (LCt_{50}, LCt_{01}) based on probit analysis. Rats were nose-only exposed to phosgene gas (five male and five female rats per group combined) versus *Ct* products from 30, 60 or 240 min exposures. Mortality data from 10 min exposures (filled squares) were excluded from the regression analysis.

From this relationship, fractional toxicity levels (LC_{01}, LC_{10}, …) can be estimated (see Fig. 7.4). The non-lethal threshold concentration (LC_{01}), which is the highest exposure level that does not cause lethality, is the starting point to estimate the 'Acute Exposure Guideline Level-3' (guidance values for once in a lifetime accidental exposure as used in emergency response planning) for the lethality end point.[62] The LC_{01} can also be derived by the LC_{50} value divided by 3, in cases where the exposure–response curve is steep. There is an apparent relationship of the LC_{01} and the concentration causing incapacitation (Fig. 7.5; suffixes 1, 2, 3 represent different ratios of carbon monoxide to hydrogen cyanide; published data[2,15,22,23,63,64]) as suggested by the comparison the LC_{50}/LC_{01} and LC_{50}/IC_{50} ratios. In spite of the remarkable differences in toxic mode of actions, toxic potency, and end point measurements, the LC_{01} appears to reflect what occurs at the IC_{50}. Independent whether the LC_{50}/LC_{01} or LC_{50}/IC_{50} ratio is taken, incapacitation appears to occur in the range of $\approx LC_{50}/2$. Regardless of different slopes, the time-adjusted LC_{50} and -LC_{01} relationships of lower to upper respiratory tract irritants follow this paradigm (Fig. 7.6). In the absence of specific empirical data, the highest exposure level that does not impair escape is one-third the LC_{01} value (default). In any case, experimental approaches that characterise such concentration–response relationships are considered superior for the estimation of the LC_{01} than approaches using fixed



7.5 Comparison of LC_{50}/LC_{01} and LC_{50}/IC_{50} ratios from published acute inhalation studies in rats with pure substances (irritants, asphyxiants) and combustion atmospheres. This graphical representation demonstrates an apparent constant relationship of narcosis and impending death (LC_{01}–LC_{50}) and incapacitation (IC_{50}).

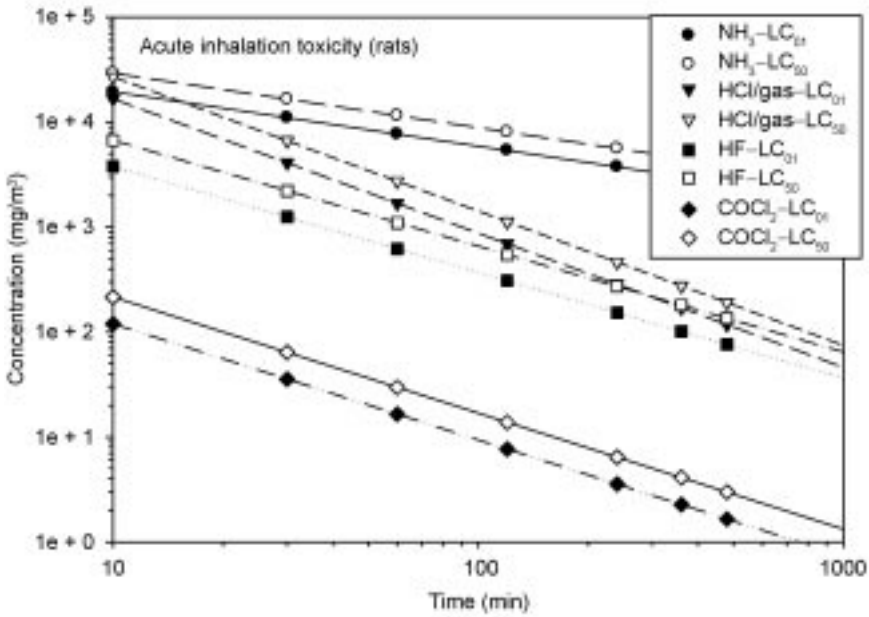
default assumptions. The disability to perform a controlled escape function of humans can have multiple causes which are difficult to duplicate in animal bioassays. Consequently, the lethality threshold concentration (LC_{01}) appears to be experimentally more expedient and robust as the point of departure to estimate the upper threshold of incapacitation than attempting to simulate the respective human behavior in rodent bioassays.

7.6.2 Concentration × time concepts

When experimental/mathematical procedures require the estimation of median lethal concentration values from multiple exposure durations (LCt_{50}) this is accomplished by the *Ct* protocol combining the exposure concentration (*C*), exposure time (*t*) and the toxic load exponent (*n*) from all exposure groups using the following equation:

$$k = C^n \times t$$

where *k* is a numerical constant. This equation can be generalised using a two variate surface plot relating toxicity (mortality) and time as follows:

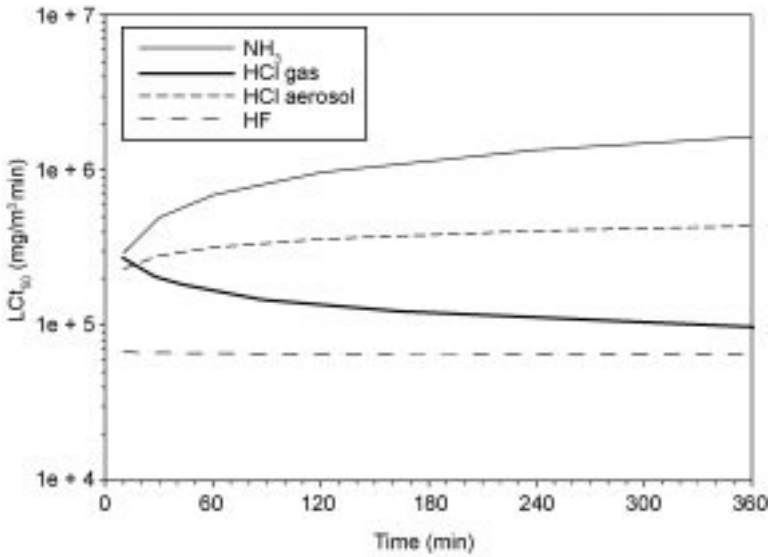


7.6 Concentration–time relationships of LC_{50} and LC_{01} values calculated by the toxic load model for upper/lower respiratory tract irritants. In spite the range of irritant gases considered the LC_{50} to LC_{01} relationship appears to be fairly constant which is consistent with the analysis depicted in Fig. 7.5.

$$y = b_0 + b_1 \log(C) + b_2 \log(t)$$

where $n = b_1/b_2$.[36] Here, y is either the probit or the normit value and b_0, b_1 and b_2 are empirically derived constants. It should be recognised that C does not have inherent exponential properties, but t might have such properties because toxicity, under non-ideal conditions, is a function of at least two independent timescales, one being the half-life of the rate-determining step of the intoxication, and the other being the intensity of exposure. When sufficient data are available, the empirical constants shown above can be suitably solved mathematically by iterative mathematical procedures combining all Ct relationships evaluated in one single matrix. From the constants of the two variate surface plot, the respective LCt_{50} and LCt_{01} (or any other values), including their confidence intervals, can be readily estimated. This empirical relationship must be derived from experimental values and is therefore limited by the availability experimental data.

Ct relationships of LCt_{50} values obtained at different exposure durations are dependent on n. The LCt_{50}–time relationships shown in Fig. 7.7 support the notion that Ct relationships are fairly constant when exposure durations exceed $\approx$30 min; however, they may decrease or increase at shorter exposure durations. Increased LCt_{50} values (less toxicity) may be related to dosimetric factors, i.e.

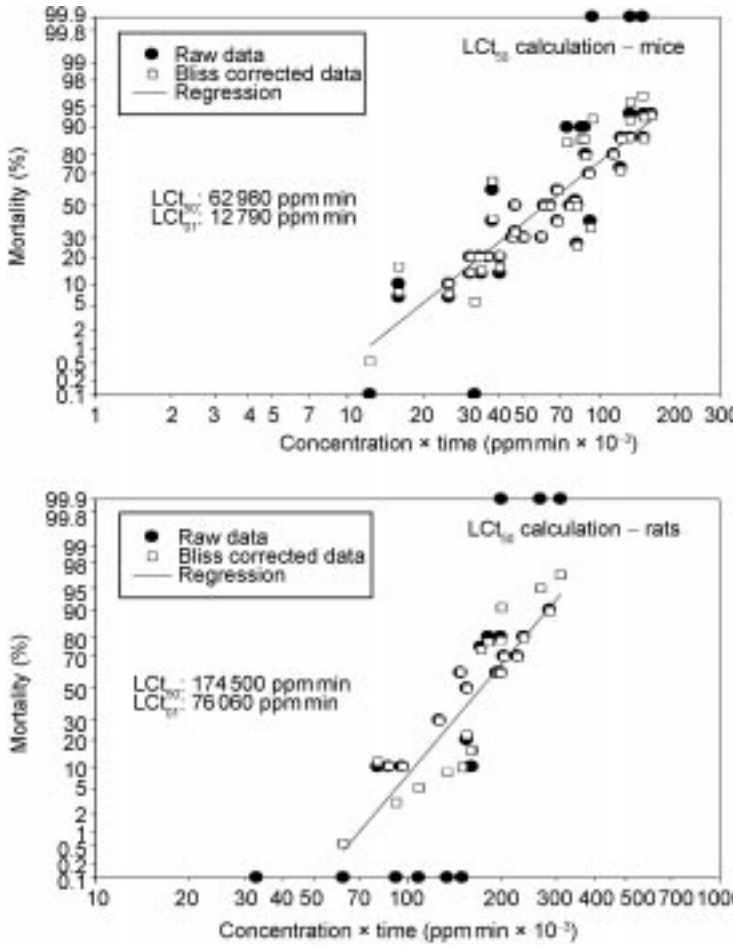


7.7 LCt_{50} versus time relationships of selected respiratory tract irritants in rats using empirical data calculated by the toxic load model. No time-dependence was found for hydrogen fluoride while for hydrogen chloride gas and aerosol/ammonia LCt_{50} values at short exposure durations (< 30 min) were higher (lower toxicity) or lower (higher toxicity), respectively. Such effects may occur owing to irritation-related changes in ventilation (reduced uptake of toxicant) or adaptive mechanisms emerging following extended exposure (e.g. increased mucus production).

transient depression in respiration and the lower dose inhaled. Alternatively, t_{95} of the inhalation chamber had not been attained. Conversely, decreased LCt_{50} values (higher toxicity) are likely to be caused by rate of delivery phenomena which means that the high dose rate will temporarily overwhelm the constitutive detoxification and compensation mechanisms, so increasing toxicity. In summary, the experimental approaches that characterise *Ct* response relationships at very short durations may duplicate the human exposure profiles to fire effluents best; however, owing to methodological and animal-specific factors they appear to be most prone to experimental shortcomings.

7.6.3 Species differences

The unifying principle of merging median lethal concentration values from multiple exposure durations can be achieved by LCt_{50} values; i.e. LC_{50} values are normalised to 1 min exposure durations. Based on compiled hydrogen chloride data,[65] the ratio of the LCt_{50} to LCt_{01} is ≈ 2 and ≈ 5 for rats and mice, respectively (Fig. 7.8). In these bioassays the LCt_{50} value in mice was approximately 2 times lower than that in rats. These findings may challenge the consistency and relevance of data from small rodent studies for humans.

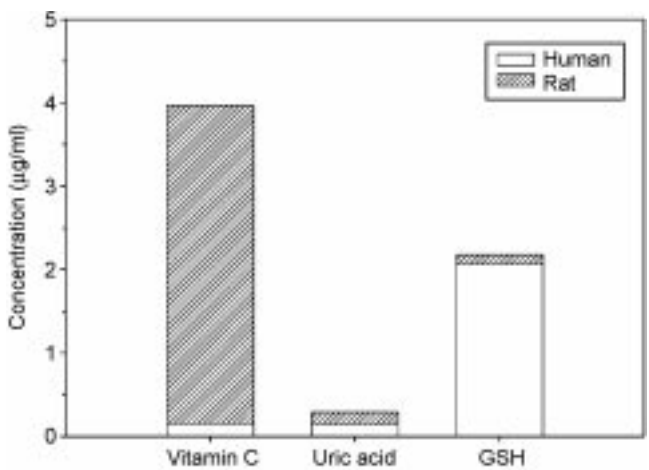


7.8 Compilation and analysis of *Ct* – mortality relationships of mice (left panel) and rats (right panel) exposed to hydrogen chloride (data were from NRC[65]). The LCt_{50} and LCt_{01} values were calculated according to Rosiello *et al.*[61]

Using mice as a toxicity model has certain shortcomings, some of which will be addressed. With regard to lung anatomy, the parenchyma of the mouse lung occupies a smaller fraction of the total lung than that of the rat but more than of the human (mouse, 18%; rat, 24%; human, 12% lung volume). The airways constitute a large percentage of the lung in mice (11%) compared with rats (5.7%). Two other significant features of the mouse lung are the thinness of the respiratory epithelium and the relatively large airway lumen. Exactly what significance these anatomical features of the mouse lung have for lung function is speculative.[66] For sensory irritation studies mice are preferred because they change their breathing patterns more rapidly. The resultant depression in respiration is more stable with continued exposure than in rats which often

develop tolerance during the course of exposure. The kinetics of 'loading' in mice is much faster than in humans (breathing frequency mouse: ≈300 breaths/min, humans: ≈20 breaths/min).[67] Owing to the small thermal inertia of mice (approx. 25 g body mass), mice respond to irritant stresses by a rapid drop in body temperature and, secondarily, many other physiological parameters.[4,68] This 'mouse-specific' susceptibility can be a disadvantage in inhalation toxicity testing as the uncertainty involved in the extrapolation from smaller mice is certainly greater than that from rats. This difference in toxic potency of hydrogen chloride in these two species matches the higher ventilation of mice as compared with rats (mouse, 1.49 ± 0.37 l/kg min; rat, 0.83 ± 0.43 l/kg min).[67] In either species, hydrogen chloride elicits a typical type of mortality delayed in onset, independent whether the exposure is to the gas phase or aerosol phase of hydrogen chloride (see Fig. 7.1). Accordingly, inhaled dose- and species-specific adjustments are required when extrapolating from one species to another.

Large species differences exist in the BAL fluid concentrations of antioxidants.[69] These may lead to differences in species susceptibilities as a result of inhalation exposures to reactive, irritant chemicals that are detoxified by antioxidant nucleophils, such as glutathione (GSH), contained in the fluids lining the airways of the respiratory tract. The content of GSH in human airway lining fluids is 140-fold higher than in plasma.[70] In regard to antioxidants, ascorbic acid (vitamin C), uric acid and GSH, have been detected in BAL fluids which are compared for humans and rodents in Fig. 7.9.[71] Humans have high levels of uric acid (most efficient antioxidant against inhaled ozone), and GSH,



7.9 Concentrations of selected extracellular antioxidant substances in BAL fluid in humans and rats (data from Slade *et al.*[69]). Major species differences exist between rats and humans for ascorbic acid (vitamin C) and glutathione (GSH).

and low levels of ascorbic acid, while rats have high levels of ascorbic acid and undetectable levels of uric acid. Glutathione was not detected in any nasal lavage samples, although it was present in BAL fluids. Hence, any localised depletion of a scavenging agent (GSH) at the site of initial contact may affect susceptibility. Co-exposure to fire effluents depleting local GSH concentrations may exacerbate toxic injury. For instance, published evidence demonstrates that the potent respiratory tract irritant gas acrolein, an α,β-unsaturated aldehyde, interacts with free sulphhydryl groups yielding acrolein–acetylcysteine and acrolein–cysteine adducts, either by enzymatic (catalysed by glutathione *S*-transferase) or non-enzymatic reactions.[72] Conceptually, owing to the increased scavenging capacity and the lower respiratory ventilation of humans, rodent species should respond to acrolein exposures with higher sensitivity than humans (for details see Section 7.7).

7.7 Non-lethal end points

7.7.1 Respiratory tract irritation

Upper respiratory tract irritation

Measurements of breathing patterns (e.g. respiratory rate and tidal volume) prior to, during and/or shortly after exposure may provide useful information for estimating the relative irritant potency of inhaled agents and for determining whether an inhaled test article is an upper or lower respiratory tract irritant. The identification of these characteristics is important in context of hazard identification and risk assessment.

Airborne chemical sensory irritants are known to evoke a burning sensation in the eyes, nose, and throat of an exposed individual. The upper respiratory tract sensory irritation and eye irritation may cause instant burning sensations with ensuing impact on an individual's capability to have a well-controlled and coordinated escape from fires. Increased irritancy at the eye generally increase *pari passu* bronchoconstriction characterised by subjective bronchial irritation. For the irritant gases sulphur dioxide, ammonia, formaldehyde and acrolein, the threshold concentrations for eye irritation were about 1½ times that for the lungs.[73] Hence, threshold concentrations based on respiratory tract irritation are implicitly protective for eye irritation.

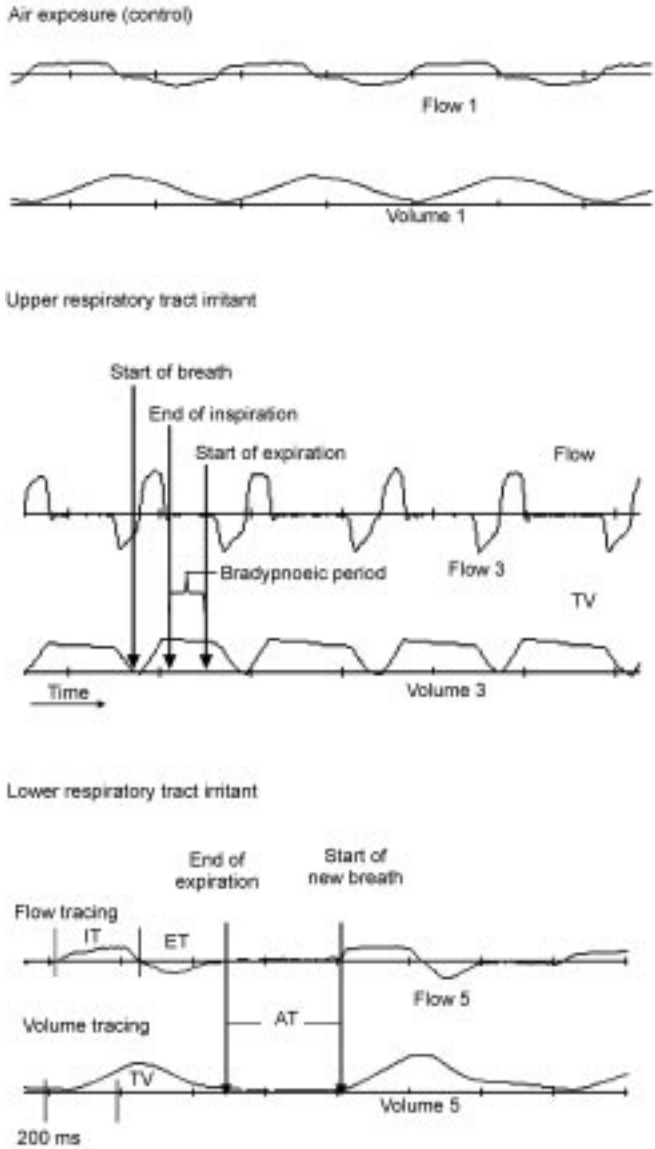
Airway and lower respiratory tract irritation may be lethal in days or sometimes weeks after exposure (see Fig. 7.1). Depending on the chemical reactivity and water solubility, an upper respiratory tract irritant at low concentration may become a lower respiratory tract irritant at higher concentration (scrubbing of gas in upper airways). This type of concentration (dose)–effect relationships need to be revealed in controlled animal bioassays.

Conventionally changes in respiratory patterns are analysed in mice as they respond more rigorously, rapidly and stable to most sensory irritants than rats.

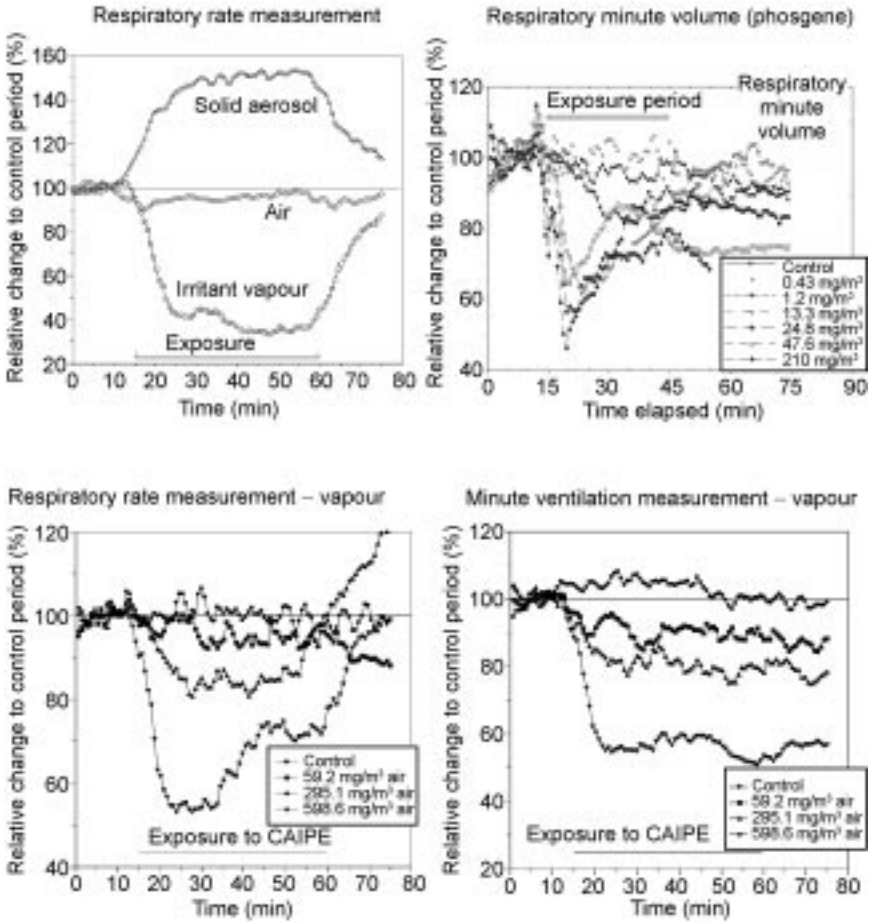
Typically, these measurements are utilised to identify the most critical site of respiratory tract irritation and to categorise a chemical as upper/lower respiratory tract sensory irritant. The breathing pattern analyses depicted in Fig. 7.10 were from measurements in 'nose-only volume displacement plethysmographs'.[5] Animals exposed to clean air show continuous flow/volume patterns (Fig. 7.10, top panel) whereas exposures to 'upper respiratory tract irritants' trigger a pause between 'end inspiration' and 'start of expiration' (Kretschmar reflex-induced bradypnoeic period; Fig. 7.10, middle panel). In contrast, 'lower respiratory tract irritants' trigger a pause between 'end expiration' and 'start of next breath' (Paintal reflex-induced apnoeic period; Fig. 7.10, lower panel). The former is a protective reflex to prevent the inhalation of toxicants, thus leading to a depression in ventilation. The latter reflex affects the ventilation of the lower respiratory tract by an increased more shallow breathing pattern (Fig. 7.10, upper left panel). The extent of lower respiratory tract irritation cannot reliably be measured by these types of functional measurements; therefore, such effects are commonly probed by bronchoalveolar lavage (see Figs 7.2 and 7.3).

Physiological measurements during the course of inhalation exposure may readily reveal species-specific responses worth considering. This includes the limited relevance of very short durations of inhalation exposure (Fig. 7.11, upper right panel). Increased tolerance occurred due to a transiently decreased ventilation and intake of test substance. Such rodent-specific changes cannot reliably be extrapolated to humans. For chemical substances causing irritation throughout the respiratory tract changes in respiratory minute volume may be more consistent than respiratory rate (Fig. 7.11, lower right and left panels). Thus, caution is advised when condensing these types of tests to one single numerical value without understanding the toxic mode of action causing the effect and whether it can be translated to a similar human response of clinical significance. Moreover, as shown for the irritant chloroformic acid isopropylester, depending on the concentration and water solubility, the response can be instant (Fig. 7.11, lower right and left panels) or more protracted. Owing to the appreciably different breathing rates of rodents and humans, the time available to exceed the buffering capacity of lining fluids may be longer in humans than in rodents.

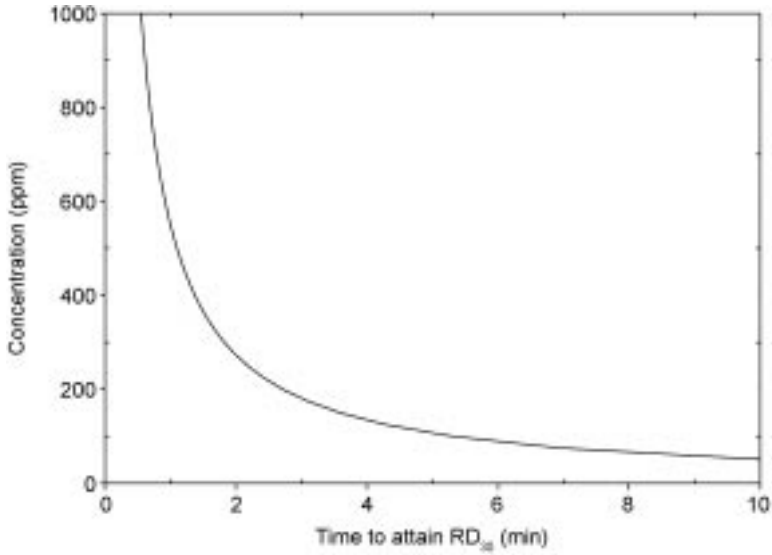
Mouse models addressing changes in respiratory rate as an index of sensory irritation have been developed. These are used to analyse concentration–response relationships yielding the RD_{50}, the concentration causing a 50% decrease in respiratory rate. This index has been shown to have a predictable relationship to sensory irritation in humans. In addition, this type of bioassay appears to be suitable to address standards for short-term exposures, such as emergency exposure limits (EELs) and short-term exposure limits (STELs). In this context, 0.1 times the RD_{50} could also be applied as a reasonable guide for the designation of irritation-based ceiling values. A value equal 0.2 times the RD_{50} has been used as a basis for STELs and 0.3 times the RD_{50} for setting



7.10 Analysis of respiratory patterns of rats in volume displacements nose-only plethysmographs. The breath structure is characterised by three phases: inspiratory time (IT), expiratory time (ET) and apnoea time (AT). These phases can be used to distinguish between upper respiratory tract irritants (bradypnea period between IT and ET as shown in the middle panel) and lower respiratory tract irritants (apnoea period between end of ET and start of new breath as shown in the lower panel). Such pauses do not occur in air only exposed rats (top panel). The integrated volume over flow of one breath is the tidal volume (TV). The product of number of breaths (respiratory rate) $\times$ TV is the respiratory minute volume.



7.11 Examples of measurements of respiratory rate and minute ventilation in small rodents in volume displacements nose-only plethysmographs. The sequence of exposure was as follows: collection of baseline data during the first 15 min of exposure to conditioned air (= 100%), then exposure to the test atmosphere for 45 or 60 min followed by a recovery period of approximately 30 min (exposure to air). Irritant vapours (reactive isocyanate) and innocuous solid particles may trigger nerve endings in the upper respiratory tract (Kretschmar reflex) and lower respiratory tract (Paintal reflex), reflexively. Accordingly, the respiratory rate may decrease or increase (left top panel). Transient reduction of inhaled dose due to reflexively reduction in ventilation (right top panel). Exposure of mice to the upper sensory irritant chloroformic acid isopropylester (CAIPE). The time to attain the plateau of decreased respiratory rate and especially minute volume is dependent on the exposure concentration.



7.12 Concentration–effect relationship showing the time required to attain a respiratory rate depression of 30% (RD_{30}) with mice exposed to hydrogen chloride during a 10 min exposure (data reproduced from Barrow *et al.*[75]). This relationship demonstrates that the early phase of exposure is clearly dependent on the rate of dose (*Ct*) delivered to the upper respiratory tract whereas at longer exposure durations the effect becomes solely concentration dependent.

EELs.[74] During the initial loading period, the *Ct*-adjusted RD_{30} appears to be a reasonable estimate for EELs. The RD_{50} and RD_{30} for a 10 min exposure period of mice to hydrogen chloride was 309 and 108 ppm, respectively.[75] The time to attain the RD_{30} was time-dependent (Fig. 7.12).

For the upper respiratory tract irritant acrolein the 30 min LC_{50} in rats was reported to be 131 ppm. The RD_{50} values in mice and rats were $\approx$1 and 6 ppm, respectively. Initial throat irritation and changes in respiration occurred in humans at 0.4 and 0.6 ppm.[72,75–78] Thus, the RD_{30} in mice below the subjective irritant threshold concentration observed in humans. *Ct*-dependent maximum threshold concentrations for emergency response were established for AEGLs. The respective threshold concentration to prevent impairment of escape in humans is 0.44 ppm for a 10 min exposure period,[79] which is a quarter of the RD_{50} in mice. This again demonstrates that extrapolations across species must be applied chemical-specific and default assumptions may not necessarily lead to relevant estimates.

Thus, attention must be paid to the similarities and dissimilarities between the test model and humans, otherwise meaningful interspecies extrapolations cannot be made. The ideal subjects for studies are people themselves, but human volunteers can only be used where the toxicological hazard is minimal, and is already reasonably well defined and accepted. It should be emphasised that the

successful completion of an inhalation study is not just the product of using an appropriate animal species, with regard to similarity to humans, but rather of carefully adjusting exposure conditions to those prevailing in humans. Even if a suitable animal model for the human respiratory tract is identified, problems in achieving a realistic exposure over the required duration of study may arise along with other problems.

Lower respiratory tract irritation

Lung lavage may provide useful quantitative information for dose-related early changes caused by lower respiratory tract irritants leading to alveolar oedema. Unlike upper respiratory tract irritants where dose-rate (concentration)-related phenomena play a more prominent role, lower respiratory tract irritation is clearly *Ct*, i.e. dose-dependent. This means, toxic effects leading to lung oedema and eventually death due to alveolar flooding with fluids from the blood capillaries follow a *Ct* relationship as already shown in Fig. 7.3. From that relationship, the non-oedema producing *Ct* relationship can be estimated. Examples have been dealt with in detail elsewhere.[11]

Analyses in blood

Analysis of arterial blood gases may be useful to assess perfusion : ventilation imbalance of the lung (hypoxia due to lung injury). Some toxic modes of action causally related to intoxication and death can be readily verified by specific determinations in blood. These include carboxyhaemoglobin formation as a result of exposure to carbon monoxide, methaemoglobin formation due to oxidant exposure, or determination of cyanide to assess the exposure intensity to hydrogen cyanide. The interrelationship of gas exposure concentration, time to incapacitation and biodosimeters has been addressed in detail elsewhere.[80]

7.7.2 Impairment of escape: incapacitation

Animal incapacitation has been considered among the most important end points as it is directly related to escape capability. A number of incapacitation models, none of which is simple, have been developed to study the toxicity of combustion products. In these models the impairment of an animal's ability to perform a normal activity or a task which the animal has been trained to perform. Methods for measurement of incapacitation include the rotorod, leg-flexion avoidance, tumble cage, motor-driven exercise wheel, inhibition of respiration and electrocardiogram. Incapacitation may also be determined visually by observations of staggering, collapse or convulsions or to escape successfully from a toxic environment. These models focus essentially on toxicants that produce a loss of consciousness by narcotic/asphyxic effects. They

may also reveal evidence of unusual behaviour as a result of neurotoxicity. Exposures leading to narcosis and lower respiratory tract irritation have been shown to be reflected best by the 'accumulated dose' metric. However, carbon monoxide is not a cumulative poison in the usual sense. Carboxyhaemoglobin is fully dissociable, and once exposure has been terminated, this complex reverts to oxyhaemoglobin, the functionally active oxygen carrying protein. In this context, instant central nervous depression leading to narcosis induced by carbon monoxide or hydrogen cyanide can also be viewed as sign of impending death. Both end points can be extended to death if the exposure dose is high enough. Accordingly, a strong relationship to the LC_{50}/LC_{01} could be demonstrated. Owing to expedience and simplicity, lethality-based end points appear to be experimentally more robust to estimate the threshold concentration leading to 'impairment of escape' than attempting to duplicate human escape behaviour in trained small laboratory rodents.

Severe upper respiratory (and eye) irritation may also lead to an impairment of escape, although by different mechanisms. Interactions with asphyxiants may occur due to the irritation-induced changes in respiration and, subsequently, inhaled dose. Concentration–effect–time relationships can readily be revealed and quantified in mice. However, for the reasons explained above, especially for the 'onset of effect period' mice may be markedly more susceptible than humans.

Collectively, extrapolation from animal species to humans is complex as the impairment of escape may involve a coordinated interplay of psychological, cognitive, memory and motor functions. A close relationship of incapacitation and lethality has been demonstrated. Therefore, incapacitation can better be assessed based on fractional lethality information and toxicity than on incapacitation data from studies addressing complex behavioural changes.[81] More recent guidance on impairment of escape for emergency response guidance recommends that in the absence of specific data (overt ocular and/or respiratory tract irritation, dyspnea, pulmonary function changes, provocation of asthma episodes, respiratory tract pathology, mild narcosis and methaemoglobin formation not exceeding 40%) one-third of the 'Acute Exposure Guideline Level-3 (lethality)' is suitable as default to assess the level at which incapacitation is likely to occur.[62] Empirical data have demonstrated that the default approach leads to a more conservative estimate (see Fig. 7.5).

7.8 Acute inhalation toxicity of combustion products: examples

The combustion of test specimens utilised the tube furnace method according to DIN 53436. The tests compiled in Table 7.1 used oxygen-depleted conditions for combustion ($CO_2/CO < 10$). A more comprehensive overview of empirical and modelled data from multiple materials has been published.[50,58,59] The

Table 7.1 Exposure parameters, carboxyhaemoglobin (COHb) concentrations in blood, and mortality in rats (five males/five females) nose-only exposed for 30 min using the DIN 53436 bioassay method

Nominal concentration (mg/l)	Weight loss (%)	Primary/ secondary air flow (l/h)	CO_2 (ppm)	CO (ppm)	HCN (ppm)	NO_x (ppm)	COHb (%)	Mortality (%)
Polyurethane foam (soft) combustion at 600 °C								
12.6	100	100/400	13 000	1800	68	15	62	0
21.1	100	100/200	18 000	2300	54	18	74	80
Polyamide foam (rigid) combustion at 600 °C								
13.0	99.4	100/1500	8 000	1700	250	9	n.d.	100
13.0	99.6	300/1300	16 000	200	22	75	7	0
Acrylonitrile-based polymeric material combustion at 600 °C								
15.0	92	100/1400	4 500	2000	123	1	45	20
22.4	90	100/900	8 000	3000	187	8	75	90
Phenylenesulphide-based polymeric material combustion at 600 °C								
18.5	31	100/1400	7 000	450	0	3	19	10
42.3	32	100/600	15 000	1400	0	8	43	100
Wood combustion at 400 °C								
26.3	≈100	100/400	12 890	3525	0	0	65	40
31.6	≈100	100/200	17 670	4184	0	76	n.d.	60
Wood–plastic–composite combustion at 400 °C								
14.5	73	100/2100	1 510	1122	0	0	25	20
23.8	68	100/1400	1 916	1649	0	0	25	90

primary air flow rate through the furnace was 100 l/h with variable post-furnace dilution air flows to condition exposure atmospheres (for details see Table 7.1). The combustion reference temperatures were 600 ºC for the synthetic polymers and 400 ºC for wood or wood–composites. One specimen was tested using a carbon dioxide:monoxide ratio of ≈80 using a primary flow rate of 300 mg/l. These testing conditions provided ventilated, oxidative combustion conditions.

In all tests oxygen levels were ≥18% in inhalation chambers. Empirical toxicological findings from animal tests with rats (LC_{50} values from 30 min exposures to combustion atmospheres from different materials) are compared with results obtained with mathematical modelling based on the analytical characterisation of atmospheres performed during the animal exposure. Two mathematical models were used. The first ('all combined') utilised the toxicity of all analytes determined during the bioassay while the other utilised the N-gas model as defined by Levin.[18] Empirical and modelled data are compared in Table 7.2. As detailed below, modelled and empirical LC_{50} values match reasonably well if the input parameters of the model were correct. This means all key toxicants were comprehensively addressed and interactions did not occur to any appreciable extent. However, in cases where analytical data were largely incorrect (problem of quantification of nitrous oxide in the presence of nitrogen tetroxide (N_2O_4) by the methods applied) or were not incorporated in the model (sulphur dioxide, aldehydes) used, the outcome of modelling was at variance with the empirically determined data. This finding strengthens the importance of bioassay cross-validation.

Exposure to polyurethane foam caused reversible clinical findings suggestive of the presence of irritants. Mortality occurred during or shortly after exposure and was causally related to carbon monoxide (essentially indicated by carboxy-haemoglobin). Polyamide foam was combusted at a similar temperature using either oxygen-depleted (100 l/h) or well-ventilated (300 l/h) conditions. This resulted in a dramatic change in the toxic profile of combustion effluents, i.e. the hydrogen cyanide-dominated asphyxic toxicity changed to minimal irritation-related (if any) toxicity. Calculation methods for the latter conditions were inappropriate because the analytical method used for nitrogen oxides did not distinguish between the less toxic nitric oxide and more toxic nitrogen dioxide.

The acrylonitrile-based polymeric material elicited clinical findings of short duration suggestive of the presence of asphyxiants. Mortality was causally related to both carbon monoxide and hydrogen cyanide. The phenylenesulphide-based polymeric material combustion inhalation toxicity was characterised by lingering respiratory distress with no immediate but marked delayed mortality occurring up to post-exposure day 14. Mortality was related to sulphur dioxide which caused airway and alveolar injury.

The toxicity of wood combustion products was indicated by lingering respiratory distess with a biphasic type of immediate and delayed mortality. Earlier studies with dry pine wood produced a similar empirical LC_{50}; with

Table 7.2 Comparison of empirically derived median lethal concentrations (LC_{50}) in rats (five males/five females) nose-only exposed for 30 min using the DIN 53436 bioassay method with modelled LC_{50} values. The yields of toxicants were determined using the DIN 53436 furnace

Test material	LC_{50} (mg/l)			Key toxicant and key mechanism
	Empirical[a]	All combined[b]	N-gas[c]	
Polyurethane foam (soft)	19	18.2	18.7	CO – asphyxia
Polyamide foam (soft)/100 l/h	7	7.0	6.5	HCN – asphyxia
Polyamide foam (soft)/300 l/h	$\gg$13	16.5	53.3	Rapidly reversible mild upper respiratory tract irritation
Acrylonitrile polymeric material	17	13.4	12.4	CO+HCN combined – asphyxia
Phenylenesulphide-based polymeric material	23	23.5	n.a.	SO_2 – distal airway irritation
Wood	26	38.6	37	Aldehydes (+particles) – airway irritation
Wood–plastic–composite	14	74	80	Aldehydes (+particles) – airway irritation

Concentrations refer to mass load concentration of furnace.
[a] LC_{50} calculated according to Rosiello *et al.*[61]
[b] LC_{50} values estimated as published elsewhere (Pauluhn),[50]
[c] N-Gas model as published by Levin *et al.*[26]

mortality up to the third post-exposure week. Mortality was related to airway and alveolar injury. Overall these data suggest that appreciable concentrations of aldehydes and particles were present in the inhalation chamber (formaldehyde: 46–131 mg/m^3, acetaldehyde: $\approx$650 mg/m^3, acrolein: 20–45 mg/m^3, total particulate matter: 480–720 mg/m^3). The combustion of a wood–plastic–composite caused mortality due to marked respiratory tract and alveolar injury. However, mortality occurred up to the first post-exposure day only. Collectively, these data suggest that appreciable concentrations of aldehydes and particles were identified (formaldehyde: up to 100 mg/m^3, propionaldehyde: up to 33 mg/m^3, acrolein: up to 97 mg/m^3, total particulate matter: up to 9832 mg/m^3). Hence, the inhalation toxicity from wood combustion appears to be causally linked to effluents causing asphyxia, viz. carbon monoxide with immediate mortality. However, survivors experienced the typical pattern caused by irritants penetrating the distal airways with associated delayed-onset mortality. The composite material generated markedly higher concentrations (yields) of aldehydes

and particulate matter. This supports the hypothesis that an appreciable amount of aldehydes, not yet fully characterised, adsorbed/partitioned onto solid or in liquid aerosol have caused this type of toxicity which is in agreement with published evidence.[7,82] The comparison of modelled LC_{50} and empirical LC_{50} values (Table 7.2) thus demonstrates that validating feedback loops are surely encouraging in reducing the uncertainty associated with animal-free prediction procures of fire hazards.

It is intriguing to recognise that the carbon monoxide-based modelled LC_{50} and empirical LC_{50} values matched for most materials tested.[50] The poorest prediction of toxicity was obtained in wood-containing materials, possibly because the combustion atmospheres were more complex and that not all aldehydes present in the atmosphere were characterised analytically. Their interaction with particulates is worthy consideration. Prediction of toxicity was appropriate for polyamide foam combustion effluents under oxygen-deprived conditions (which per se may be the key intoxication in real fires); however, at non-oxygen-depleted conditions nitrogenous moieties were apparently converted to nitrogen oxides which could not be correctly traced by the analytical methods used. These examples demonstrate that modelled data are highly contingent on the particular yield of specific toxicants and the methods selected for analysis. Minimal changes in the combustion process increased dramatically the complexity of such atmospheres. This also affected the toxic potency and the major toxic mode of action of smoke generated. In summary, these examples demonstrate that hazard identification requires careful considerations on the 'fire stage' chosen for testing as well as the selection and quantitation of critical analytes (by appropriate methodologies). Whether all analytes of potential health concern have truly been addressed can only be answered by using an integrating animal bioassay.

7.9 Conclusions

Animal toxicity tests reveal material-specific lethal or sub-lethal end points and provide a scientifically sound basis for the selection of the key components of health concerns. The characterisation of intoxication should always accompany the assessment of a material's toxic potency. These data, on a relative rather than absolute basis, are then useful for comparison of test materials for potential toxicological effects on fire tenability.

The use of animal experiments in a selective, hypothesis-based way will reduce the number of experimental animals and reserve their use to where it benefits the hazard identification and risk characterisation process. As shown for wood-related combustion products, integrating controlled animal exposures provide an important feedback loop whether the analytical procedures, end points and simplifications chosen for modelling meet the desired precision or not. This enables results from small-scale or larger-scale fire tests to be interpreted

sensibly and removes much of the criticism of the so-called 'animal-free combustion toxicity tests' relying solely on analytical methods with their inherent shortcomings of not being able to integrate different toxic effects. Especially when used to characterise the 'analytical toxicity' of unknown materials, animal-free approaches cannot identify with certainty new components or unexpected interactions of components. Animal-free methodologies for the study of the modifying effects by combustion-derived (nano-) particles have not been established yet.[83] This also means that the toxicological data in their entirety should not be reduced to one single numerical value. Rather they should be considered along with other information addressing the likelihood and intensity of exposure relative to physical fire threats and the resultant most critical mode of toxic action. Consequently, animal toxicity data provide a means to verify modelling procedures in the way that materials do not produce unknown toxicants and its decomposition process is understood. As a consequence, under safety aspects, it appears wise to consider established *in vivo* inhalation procedures to be indispensable as essential supplementary tools for hazard and risk assessment with respect to the systemic and pulmonary toxicity of complex combustion atmospheres, especially when regarding quantitative aspects of risk characterisation and health-related trigger values derived from them.

7.10 Future trends

The focus of the toxicology of combustion effluents is on substances from thermal degradation caused by accidental, acute exposures and to which extent humans may encounter inhalation exposures to airborne toxicants in concentrations/doses high enough to be detrimental to health. So far, toxicologists may pay relative little attention to fire-specific aspects, such as the emission characteristics and yield, transport phenomena, interactions of gas phase with liquid/solid phases, formation of new chemical entities, ageing processes and interactions. Each phase may follow its own dynamics and some of the emitted constituents may have ephemeral life-times which limit human inhalation exposure. As already indicated by more recent publications[9,10] these interactions need to be addressed with increased experimental sophistication in future research. Increased refinements on the emission characteristics will surely enable fire engineers to develop more refined mathematical models that will better predict the extent of human exposure. The inherent approach of toxicology is to characterise hazards and risks from a quantitative and qualitative perspective. This means, in a holistic approach the often fluctuating external exposure must be linked to an integrated total internal exposure dose causally related to the toxic effect of highest concern. The nature of effect, including critical potentiating factors, their reversibility and health significance need to be better characterised. Future research may disentangle the complex interrelationship of dose-related phenomena from substance-specific phenomena.

Although difficult to reliably transpose the dose–effect relationships established *in vitro* systems to human exposure, highly controlled, refined *in vitro* systems may increase the understanding as to how biological systems interact with substances in isolation and in complex smoke mixtures. To accomplish this objective, the complexity of defining the interrelationship of biomarkers of exposure and adverse effects must be overcome.

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8

Application of human and animal exposure studies to human fire safety

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Abstract: Toxic hazards to people in fires depend upon the main physiological and pathological effects of exposure to toxic fire effluents and the mechanisms whereby they impair escape and cause incapacitation and death. This chapter first considers how the development of the main toxic hazards (consisting of irritancy and asphyxiation) have been evaluated from studies of fire incidents and fire victims, and experimental studies of mechanisms of incapacitation using non-human primates and rodents. The advantages and limitations of using humans and each different animal species for measurement of sensory irritant, pulmonary irritant and asphxyxiant potencies to predict effects in humans are examined.

The effects of fire gas exposures are found to be largely explainable in terms of the additive effects of a small number of key irritant and asphxyiant gases, so that it has been possible to develop and validate calculation models for time to incapacitation and lethality using a set of chemical time–concentration composition data for these gases.

For bench-scale rodent toxicity tests the toxicity of fire effluents varies over two orders of magnitude as a function of material being burnt and the fire conditions. In general oxidative pyrolysis and under-ventilated combustion produce the most toxic effluents while well-ventilated flaming produces the least toxic effluents. An exception is the nanoparticles produced by fluoropolymers, which under certain non-flaming decomposition conditions show a toxic potency several orders of magnitude higher than that from other materials.

Key words: N-gas models, toxic potency of fire gases, RD_{50}, LC_{50}, combustion product toxicity, fire effluent toxicity, PTFE fume toxicity, nanoparticle toxicity.

8.1 Introduction

In order to be able to evaluate toxic hazards to people in fires it is necessary to determine the main physiological and pathological effects of exposure to toxic fire effluents and the mechanisms whereby they impair escape and cause incapacitation and death. It is then necessary to identify the main toxic species responsible for these effects and the relationships between exposure concentration, dose and severity for each toxic species individually, and in the combinations occurring in fire effluents.

This chapter examines how these issues have been addressed using a combination of fire incident investigation, studies of effects on humans of individual toxic gases in industrial accidents and experimental studies on humans, non-human primates and rodents involving individual toxic gases, specific toxic gas mixtures and fire effluents from a range of materials. First considered is the general development of toxic hazard in fires, and how the main toxic hazards (consisting of irritancy and asphyxiation) have been evaluated from studies of fire incidents and fire victims, and experimental studies of mechanisms of incapacitation using non-human primates and rodents. Consideration is then given to the advantages and limitations of different approaches using humans and each different animal species for measurement of sensory irritant, pulmonary irritant and asphxyxiant potencies in terms of predicted effects in humans.

A detailed examination is then made of how studies on non-human primates and rodents have been used to evaluate sensory irritancy of fire effluents, and to establish that the overall physiological and pathological effects of fire effluent mixtures from the vast majority of materials can be explained in terms of a small number of key asphyxiant gases and irritants. Consideration is then given to the development and validation of fractional effective dose (FED) N-gas models enabling lethal toxic potency for fire effluents to rats (LC_{50} concentrations) from materials to be calculated accurately from chemical analysis of effluent atmospheres, without the need for animal exposures. Two exceptions are also discussed for which unpredicted toxic effects have been measured in animal studies that were not predicted from chemical analysis.

The contributions to overall toxic potency from different individual chemical species in effluent mixtures from different materials decomposed under non-flaming and flaming combustion conditions (well-ventilated, vitiated (under-ventilated) and post-flashover vitiated) are then examined. The range of lethal toxic potencies to rats for individual toxic species and fire effluent mixtures under different decomposition conditions is described.

The final section outlines how data from humans, non-human primates and rodents have been used to develop FED calculation methods for the estimation of time to incapacitation for humans exposed to fire effluents in full-scale fires. These topics have been examined in detail in Chapter 3 (for effects of irritants), Chapter 4 (for effects of asphyxiants) and Chapter 19 (for toxic hazard calculation models for use with fire data).

8.2 The development of toxic hazards in fires

Once established, most growing fires in buildings (or transport) enclosures will develop over a period to time giving rise to conditions likely to be lethal to any occupants, either as result of exposure to toxic fire effluent or heat. Before lethal conditions develop, exposure to fire effluent is capable of impairing the ability

of occupants to escape and then causing incapacitation, thereby preventing escape. Once a person is incapacitated, they are likely to die some minutes later from the lethal effects of heat, toxic gases or structural failure of building elements. Thus, although the lethal effects and lethal exposure doses of fire effluents are of interest, the most important determinants of survival in fires are effects that might slow or otherwise impair escape and time to incapacitation (the point at which occupants are no longer able to save themselves).[1–4]

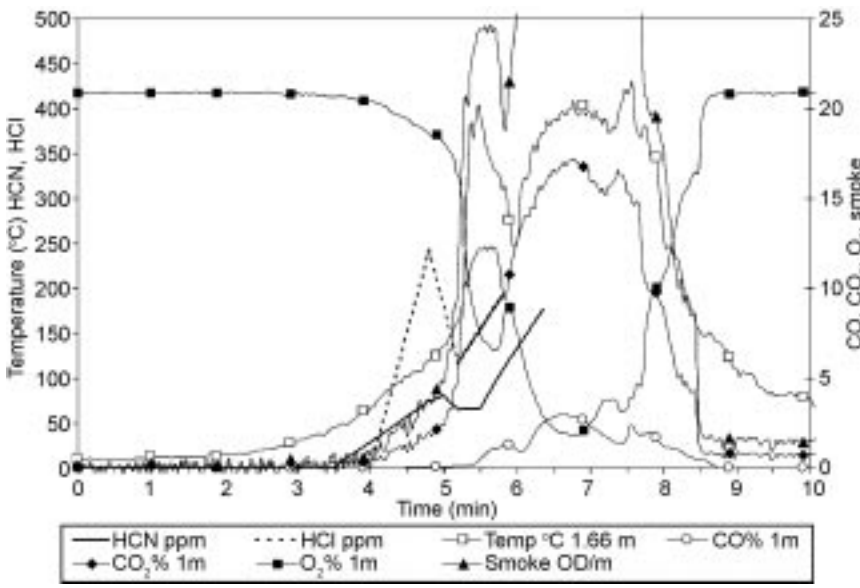
Fire hazard and fire-safety therefore depend upon the outcome of two parallel time lines: the available safe escape time (ASET), which is the time from ignition of the fire to the development of incapacitating conditions, and the required safe escape time (RSET), which is the time required for occupants to reach a place of safety.[2,5,6] Exposure to toxic fire effluent influences both these parameters, with the following hazards occurring in fires more or less in the order shown:[1]

- Behavioural effects of seeing fire or smoke (reluctance to enter smoke-logged escape routes or move past flames).
- Physiological, behavioural and pathological effects of direct exposure to optically obscure, irritant smoke:
  - Difficulty of finding escape routes and slow movement speed due to effects of smoke obscuration on visibility.
  - Further impairment of vision and eye pain due to immediate, concentration-related effect of sensory irritant smoke products on eyes – blepharospasm (reflex closure of eyes due to pain on cornea).
  - Impairment and eventual prevention of evacuation due to immediate, concentration-related painful sensory irritant effects of smoke on upper respiratory tract (mouth, nose, throat) and airways (bronchoconstriction, chest pain).
  - Uptake over a period of several minutes of asphyxiant gases leading to incapacitation and collapse once a critical exposure dose has been inhaled.
  - Incapacitation due to heat exposure or burns once a critical exposure dose of heat has been received.
  - Death during exposure at the fire scene (or after rescue, usually within a few hours) resulting from exposure to asphxiant gases, exacerbated by respiratory irritancy and effects of heat or burns to respiratory tract.
  - Death during exposure at the fire scene (or within a few days of rescue) due primarily to heat exposure and/or burns.
  - Death within a few hours of rescue from lung oedema and inflammation due to inhalation of irritant fire effluent gases and particulates into the deep lung.
  - Death within a few days of rescue due to bronchopneumonia.
  - Increased risk of heart attack or stroke (usually between a few hours to several days after rescue) resulting from effects of fine particles and asphyxiant gases in blood circulation.

– Long-term health problems including neuropathology, sensitisation and reactive airways disease syndrome.

Once a victim has become trapped or incapacitated in a fire, then conditions usually become lethal within seconds to minutes because flaming fires grow exponentially, so that concentrations of smoke and toxic gases and the heat intensity increase rapidly, resulting in death either from asphyxiation or heat exposure depending upon the fire scenario. For this reason the key determinant of survival is incapacitation.

Figure 8.1 shows an example of a typical set of time–concentration curves from a full-scale fire test in a fully furnished lounge of a two-storey maisonette. The fire was started in an item of upholstered furniture in the enclosed lounge.[7] In order to estimate the time when a room occupant would be incapacitated it is necessary to consider the developing hazards from this set of toxic products (plus smoke and heat) as their concentrations vary during the fire.



8.1 Example of time–concentration curves for smoke, toxic gases and temperature in the fully furnished, domestic lounge of a two-storey maisonette during a fire started in an armchair. The enclosed lounge had PVC-framed double-glazed windows. Initially the doorway to the hall was closed, and after 5 min the fire died down. The lounge door then swung open providing an additional air supply from the remainder of the interior volume of the maisonette. This resulted in a second period of severe fire growth until the fire was extinguished after 8 min. The interior pane of the window was cracked but the outer pane remained intact. There was some charring of the PVC frame, which probably accounted for the hydrogen chloride measured during the fire. Gas measurements were at head height or 1 metre (1 m) where indicated.

In order to carry out a fire hazard analysis for any particular full-scale fire scenario, or to evaluate the safety of any particular product or material used in an occupied enclosure, it is necessary to identify the toxic species produced during combustion and their time–concentration curves during the fire. The main components of such an analysis are as follows:

- The time–concentration curves for the main toxic species, obtained from:
  - the mass burning rate of the fuel (kg/s) and its dispersal volume, to give the mass loss concentration (kg/m^3) at different locations and times during the fire;
  - the yields of each toxic product (kg/kg) from different fuels at different locations and times during the fire.
- The time–concentration and time–dose relationships for the different toxic effects of the different toxic fire products in the effluent mixture.

If these are known, it is possible to calculate whether any of the toxic hazards are likely to reach a level capable of affecting exposed subjects and in particular:

- the time at which escape is likely to be impaired and extent of impairment;
- the time of incapacitation so that escape is no longer possible;
- the time at which an exposure capable of causing significant post-exposure effects has occurred;
- the time at which a lethal exposure has occurred.

8.3 Toxicity of individual fire gases and toxic potency of different materials

A significant problem in understanding and evaluating toxic hazards in fires is to identify the range of toxic species evolved from different materials under different combustion conditions in fires, and to determine their toxic effects individually, and in combination in mixed fire effluents. In particular, are the main toxic effects of fire effluents caused by exposure to a small number of key toxic gases or are a larger number of more exotic chemical species important?

It has been known for many years that one toxic gas, carbon monoxide, is evolved at high concentrations in most fires. Rescued fire survivors often show signs of carbon monoxide intoxication, with high concentrations of carboxy-haemoglobin (%COHb) in their blood, and fire fatalities dying as a result of exposure to toxic smoke usually also have fatal or near fatal %COHb levels (see details in Chapter 4).[1,8–10] Carbon monoxide is undoubtedly of major importance as a cause of incapacitation and death in fire victims, but is it the only toxic product that needs to be considered? Measurements of the chemical composition of combustion products, including very detailed studies of tobacco smoke and effluents from a variety of polymeric materials, have shown them to contain

hundreds of different chemical products, many of which show significant toxicity[11–13] (see Chapter 14).

'Toxicity' embraces a very wide range of different injurious effects, occurring over a range of time-scales. In simple terms, and especially in the context of fire hazards, toxicity can be considered as a combination of physiology and pathology. Physiological effects of toxic fire effluents occur over short timescales of seconds to minutes, and are important in determining incapacitation and death during and immediately after fires. Pathological effects generally develop over longer timescales of hours to years. In the context of fire survival, the most important considerations are the physiological effects of fire effluents at the fire scene and to a lesser extent the more rapidly developing acute pathological effects usually occurring a few hours or days after exposure in fire survivors. The acute physiological effects of asphyxiant gases, such as carbon monoxide, on the heart and brain are therefore of considerable importance in fire survival, while the potential carcinogenic effects of exposure to benzene and polycyclic aromatic hydrocarbons (PAHs) in fire effluents are not directly relevant, since carcinogenicity is considered to result from continuous exposure over a period of months or years, and requires a similar timescale to develop. For this reason, some highly toxic chemical species often present in fire atmospheres are not relevant to immediate survival. Another important consideration is the relationship between the exposure concentrations or doses presented in fire effluents and the threshold for acute physiological effects to occur. For a number of chemical species, the threshold concentrations for acute effects are several orders of magnitude higher than those occurring in fire effluent atmospheres, which therefore reduces the list of potential hazardous species that require consideration.[1,13] On the other hand, toxic effects have been observed during and after some animal exposures to fire effluent atmospheres that cannot be explained in terms of the measured chemical species present, leading to the conclusion that a number of potentially relevant toxic species remain unidentified in complex fire effluent mixtures, and/or their toxic effects have yet to be characterised.[13,14]

In the 1970s there was considerable interest in toxic hazards from fires. In the UK, analysis of fire injury and death statistics shown in Chapter 1 revealed that there had been a fourfold increases in the number of fire fatalities between the 1950s and 1970s reported as 'overcome by smoke and toxic gases' while the numbers reported as dying from exposure to heat and burns remained approximately constant.[15,16] Injuries due to smoke exposure had increased even more dramatically, and this, together with reports of various fire incidents worldwide, gave rise to concerns that fire effluents were becoming more 'toxic' due to the increased use of synthetic polymeric materials (such as polyurethane foams) in household furniture and bedding.

Two basic research approaches have been used to solve this problem and to develop methods for predicting toxic hazard in fires. For one approach attempts

are made to identify the main chemical species produced during fires, measure their yields and time–concentration curves in fires and attempt to predict overall effects on people from a knowledge of the toxic effects of each individual toxic gas and the interactions between different gases. The advantage of this method is that for a small number of gases, a significant amount of information is available on both human and animal exposure upon which to base an assessment of different effects in fires. The main weakness is that fire effluents contain complex mixtures of many hundreds of potentially toxic gases, vapours and particulates, the identities, concentrations and toxic interactions of which are only partially understood.

For the other approach toxicity is considered more in terms of the material being burned, and toxic potency is determined by exposing animals to fire effluent mixtures generated in small-scale combustion toxicity tests. The advantage of this approach is that the animals are exposed to the whole complex fire effluent mixture, so that the effects can be observed directly. The disadvantages are that the range of effects measured on animals is somewhat limited (often to simple lethality data) so that it is difficult to extrapolate to predicted effects on human survival in fires. Also, it is known that the yields of toxic products from individual materials vary considerably under different fire conditions (see Chapter 14), so that the concept of a single 'toxicity' or 'toxic potency' of a material such as wood or polyethylene is not valid. Further, since any particular toxic effluent mixture will exert a range of different effects with different time–concentration relationships, it is not very meaningful to represent the 'toxicity' of a fire effluent atmosphere in terms of a single number or entity.

Despite these limitations, a considerable amount of information has been obtained using a combination of human and animal data for individual toxic gases, in combination with data from animal exposures to fire effluent mixtures from burning materials in tests in which the yields and concentrations of toxic species have been measured. This has enabled the development of methods for predicting and evaluating toxic hazard in fires. The strength of this approach is derived not from any one particular approach, but by the combination of findings from all the different methods used.

The main issues addressed by the different research approaches are as follows:

- Identify major physiological and acute pathological effects.
- Identify major toxic chemical species important in toxic fire hazards: determine the extent to which overall toxic effects can be understood in terms of measured composition of effluent mixtures from different materials decomposed under a range of combustion conditions; determine the occurrence of any unusual or extreme toxic effects from specific materials.
- Measure concentration–dose relationships for incapacitating effects of each individual toxic species and develop physiological models for calculating time to incapacitation in humans.

- Determine interactions between individual toxic species in fire effluent atmospheres for incorporation into physiological models.
- Develop methods for the calculation of ASET times for application to fire hazard analysis.
- Examine the range and diversity of toxic hazards from combustion of different individual materials or products under different combustion conditions.

Different approaches have been used to address these issues, involving the application of various combinations of incident investigations and experiments involving human and animal exposures and chemical analysis. The main applications of different methods are summarised in Table 8.1.

8.4 Fractional effective dose methodology for hazard analysis

Some toxic effects of exposure to combustion products occur almost immediately on exposure and the severity of the effect is proportional to the concentration of the substance and its potency. This applies to visual smoke obscuration and to the painful effects of exposure to irritants. For example, irritant smoke in the eyes or nose immediately causes pain (sensory irritation), reflex closure of the eyes and breathing difficulties. The intensity of the effects is proportional to the logarithm of the exposure concentration, varying from mild eye and nasal or throat irritation to severe pain, eye closure and breathing difficulties at high concentrations.[1]

For other substances, such as asphyxiant gases, the effect depends upon the dose inhaled. The effects therefore take some time to develop and depend upon the concentration inhaled and the time over which the substance is inhaled. The effects tend to be more persistent than those of sensory irritation, since it takes some time for the toxic material inhaled to be detoxified (for example hydrogen cyanide) or expelled (for example carbon monoxide). An example of dose-dependent effects is collapse from asphyxia resulting from exposure to carbon monoxide.

In practice, a threshold concentration or exposure dose can be identified at which serious effects are predicted. This is known as the effective concentration or exposure dose for a given toxic or physiological end point (for example, the exposure dose of carbon monoxide required to cause loss of consciousness or the exposure dose of heat required to cause skin pain). For application to toxic hazard calculations, the concept of fractional effective concentration (FEC), or dose (FED), is used whereby the exposure concentration or dose at any point during a fire is expressed as a fraction of the exposure concentration or dose predicted to produce a given effect such as incapacitation or death. For example, the concentration of smoke present at any time during a fire can be expressed as

Table 8.1 Methods for evaluating toxic hazards of fire effluents

Method	Advantages and range of application	Limitations
Fire incident investigation	Enables direct evaluation of effects of accidental exposures to fire effluents on humans. When blood concentrations of CO and or HCN are measured, and if fire is recreated in a full-scale experiment, it is possible to estimate in semi-quantitative terms what subjects were exposed to and what effects occurred. Possible to speculate on key toxicants and effects.	Evaluation only after the event in fire survivors and fatalities. No detailed measurements of exposure concentrations or effects at the time. Taken in isolation the likely causes of incapacitation or death may be only speculative.
Workplace atmosphere and chemical incident investigation	Enables direct investigation of effects of workplace or accidental exposures to some individual chemical species present in fire effluents. Used for determination of upper acceptable limiting concentrations for toxic gases and concentrations considered immediately hazardous to life and health. Includes some data for most important fire gases (CO, HCN, CO_2, HCl, HBr, SO_2, formaldehyde, etc.).	Detailed data on effects of measured concentrations usually available only for low level exposures. Data from acutely hazardous exposure incidents usually limited and related only to approximate concentration estimates.
Experimental human exposures to individual fire gases at low concentrations CO, HCN,CO_2 CS gas and acid gases	Enables detailed physiological measurements of uptake and effects of low concentrations and exposure doses with development of predictive equations for individual gases: principally CO, CO_2, low oxygen hypoxia. Some limited experimental data on effects of low level exposures to other irritants such as CS gas and HCl.	Limited usually to acute exposures of healthy young men so little information on sensitivity of other groups. Limited for ethical reasons to low concentrations and minor physiological end points. Limited use in predicting important serious effects such as incapacitation. No data on interactions between mixtures.

Experimental sub-lethal exposure in primates CO, HCN, hypoxia CO_2 Acid gases Fire effluent mixtures	Enables exposure to higher concentrations and exposure doses than experimental human exposures, to study important physiological end points causing incapacitation. Possible to examine effects of combinations of individual toxic gases and interactions, and incapacitating effects of fire effluent mixtures. Large animals are similar to humans so time–concentration effects similar and useful in development of predictive equations for individual gases and interactions, especially beyond the range of human experimental exposures. Includes all asphyxiants: CO, HCN, CO_2, low oxygen hypoxia and a range of individual irritants: acrolein, hydrogen chloride. Enables detailed physiological measurement of uptake and effects (neurophysiological, behavioural, irritancy, respiratory, circulatory. Enables studies of respiratory tract pathology (lung inflammation and oedema).	Necessary to be aware of physiological differences between primates and humans, especially effects of body size, and sensitivity to noxious exposures. Difficult to extrapolate from effects in simple experiments on trained animals to effects on behaviour of humans in complex situations in large buildings.
Experimental sub-lethal and lethal exposures in rats and mice	Enables detailed studies of pathological mechanisms and lethality for individual toxic gases and fire effluent mixtures, involving larger numbers of animals for measurement of toxicity end points (RD_{50} and LC_{50}). Mouse RD_{50} good model for evaluation of sensory irritation. Rat LC_{50} indicates approximate lethal exposure doses of lung irritants likely in humans. Useful for revealing and evaluating unpredicted toxic effects and mechanisms for specific fire effluent mixtures. Enables exposures to toxic effluents from a wide range of materials decomposed under different combustion conditions. Enables identification of key toxic species and extent to which toxic effects of fire effluent mixtures from different materials can be predicted from measured concentrations of key known toxic species.	Although basic physiology and pathology of toxic effects in all mammals, including rodents and humans, are similar, it is difficult to derive predictive calculation methods for physiological end points in humans from rodent data, owing to allometric and physiological differences. Therefore of limited use of toxic hazard calculations for humans.

a fraction of the concentration required to seriously impair escape capability. Thus FEC of smoke (FEC_{smoke}) = 1 represents a smoke concentration considered capable of seriously limiting escape capability, where FEC_{smoke} is the concentration (of smoke) present in a fire at any time divided by the concentration considered to significantly affect escape efficiency.

The exposure dose of carbon monoxide can be expressed as a fraction of the exposure dose predicted to cause incapacitation. Thus F_{Ico} (fraction of an incapacitating dose of carbon monoxide) can be expressed as:

$$F_{Ico} = \frac{\text{conc. gas present} \times \text{time}}{\text{conc.} \times \text{time for incapacitation}}$$

e.g. for exposure of 1000 ppm for 20 min

$$F_{Ico} = \frac{1000 \text{ ppm CO} \times 20 \text{ min}}{35\,000 \text{ ppm min}} = 0.57$$

Another reason for expressing the concentration or dose as a fraction of that causing the effect for each toxic product is that a fire atmosphere contains a mixture of toxic products of differing potencies. In order to sum the effects of the different effluent components, it is necessary to normalise them in terms of the effective dose. Furthermore, the concentrations of toxic products change with time during a fire, so that for constituents whose effects are dose-related, it is necessary to calculate the effective doses received, based on the concentrations averaged over short periods of time, and then integrate these over successive periods. The aim is to calculate the time at which the summed effective doses reach unity, at which point the end point (such as incapacitation) is predicted to occur. The general FED equation is therefore:

$$\text{FED} = \int_{t_1}^{t_2} \sum_{i=1}^{n} \frac{C_i}{(Ct)_i} \Delta t \qquad 8.1$$

where C_i is the average concentration of a dose-related toxicant such as an asphyxiant gas 'i' over the chosen time increment; Δt is the chosen time increment, expressed in minutes (min), and $(Ct)_i$ is the specific exposure dose expressed as concentration $\times$ minutes, that would constitute an effective dose (i.e. an exposure dose producing a defined end point such as preventing an occupant's safe escape).

Effective concentrations and exposure doses for defined end points for smoke, heat and toxic effluent mixtures are presented in the following sections.

For asphyxiant gases the end point is reached when the condition of an exposed subject changes from near normal to a state of collapse, which tends to occur at a fairly well-defined exposure dose. For sensory irritation, end points are less simple to define, owing to the gradual increase in severity of effects with exposure concentration. These graded effects are represented in algorithms to predict effects on walking speed, but it is also considered reasonable to identify

tenability limits above which the intensity of effects is likely to significantly impair or prevent effective escape. Serious inflammatory effects of inhaled irritants on the lungs also appear to have a fairly well-defined threshold below which minor respiratory discomfort occurs, and above which serious, life-threatening oedema and inflammation result in severe respiratory distress, which can be fatal.[17] These issues are discussed in more detail in Chapter 3.

8.5 Similarities and differences between animal models and humans

8.5.1 General similarities among different mammalian species

Although animal models have been used to study the toxic effects of both individual fire gases (and gas combinations) and mixed fire effluent atmospheres, they are useful for the prediction of effects in humans only to the extent that the physiological and pathological effects observed in the animals, and the exposure dose and concentrations at which they occur, can be related to humans.

A variety of different animal species are used in toxicological investigations, involving different methods for measuring toxic end points, with different practical applications to the evaluation of human toxicology. In general, all mammalian tissues and organs are very similar in both structure and function. For example, at the microscopic level it is difficult to distinguish rat tissue from human and the lungs of a rat have the same basic structure and function as those in a human, with almost identical structure and innervation (nerve structure) of the airways and alveolar region. The basic functions of the blood, respiratory, cardiovascular and nervous systems are also similar in all mammals.

The main acute physiological and pathological effects observed in human fire victims and animal studies are therefore essentially the same, consisting of:

- asphyxiant effects on the cardiovascular and nervous system leading to collapse and loss of consciousness;
- acute sensory irritant effects on the eyes and respiratory tract;
- acute inflammation and lung oedema following exposure to irritant fire effluents.

With regard to asphyxiant effects, the basic physiological and pathological effects of exposure are very similar in rodents to those in humans. When mice, rats, monkeys or humans are exposed to carbon monoxide, the gas is taken up from the lung into the blood stream where it combines with haemoglobin to form carboxyhaemoglobin (COHb). As the inhaled dose increases, the percentage of haemoglobin as carboxyhaemoglobin (%COHb) increases at a rate depending upon a number of physiological variables, of which two of the most important are the volume of air inhaled each minute (minute volume) and the carbon monoxide concentration. When the %COHb reaches a critical level, the

hypoxic effect on brain function become sufficient to cause loss of consciousness, followed by coma and death if exposure continues. As this sequence of effects is the same in mice and humans, with similar effects and interactions for other asphyxiant gases, it is a fair assumption that if rats or mice are exposed to a fire effluent atmosphere containing asphyxiant gases, and show signs consistent with asphyxia, then the same basic effects can be expected to occur if humans were to be exposed to similar fire effluent mixtures, although there may be some differences in sensitivity to specific dose levels and in rates of uptake and excretion.[1,13,14,18]

With regard to sensory irritation of the eyes and upper respiratory tract, the basic effects are also very similar in rodents and humans. Both species have similar nociceptive (pain-sensitive) nerve endings in the facial skin, the lining of the nose, mouth and upper airways served by the trigeminal nerve. The epithelial linings of the cornea and the upper respiratory tract are similar, and similar physiological effects involving neurosensory pain and irritancy responses, accompanied by similar reflex reductions in breathing rate, occur in these and other mammalian species. Mice and rats can therefore be used to determine if individual acid gases, organic chemical species and fire effluent mixtures will be irritant to humans, and to some extent the likely irritant potency. Similarly, when rodents are exposed to doses of irritant gases or fire effluent mixtures over a period of time, they develop lung oedema and inflammatory effects on the linings of the airways and in the alveolar regions of the deep lung. These are the same as observed in human victims of industrial accidents and fires, so that rodents can also be used to evaluate these effects in fire effluents.[19–28] At least one example of a direct neurotoxic effect of a specific organophoshate fire effluent has been observed in rats, and is considered a potential hazard to humans.[29]

For these reasons it is considered appropriate to use rodents to examine the basic physiological and pathological effects of fire effluents from different materials to evaluate mechanisms of toxicity. However, direct extrapolation of time and dose to effects between rodents and humans can be less meaningful, so care must be exercised in using rodent data to develop predictive calculation models for human incapacitation.

8.5.2 Important differences to be considered when extrapolating from animal models to humans

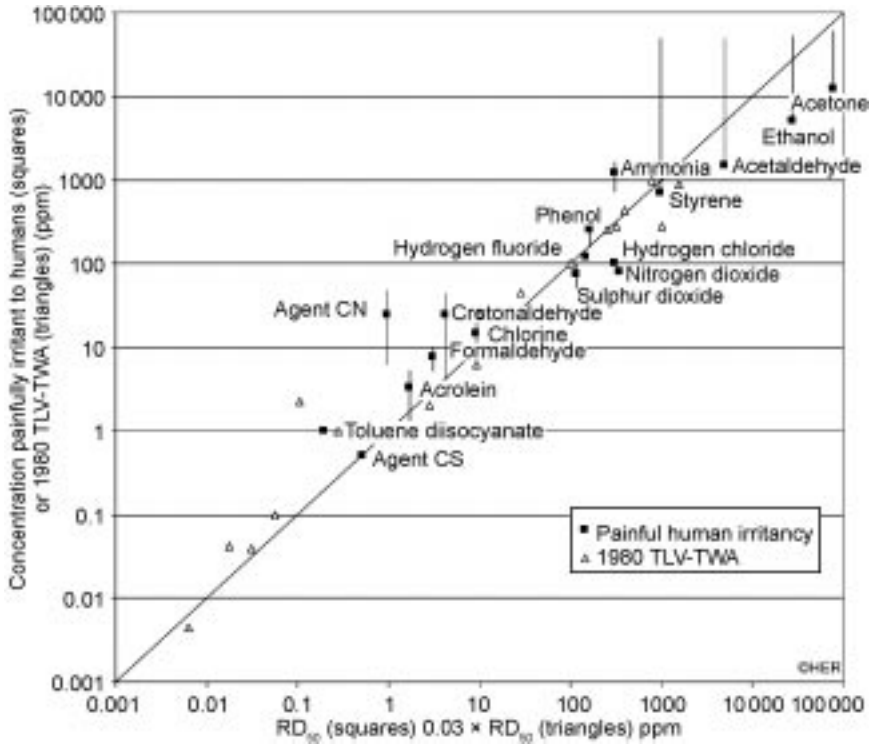
The main problems in extrapolating from animal models to humans are as follows:

- limitations on measurable parameters;
- size differences;
- body structure differences;
- biochemical and physiological differences.

Practical difficulties in using small animals such as rats and mice are the limitations on the range of physiological variables that can be readily measured. Most rodent studies on combustion products have been restricted to measurements of lethal exposure doses (LC_{50} or approximate lethal dose), or used for measuring sensory irritation (RD_{50} – concentration causing a 50% decrease in respiratory rate). Some studies have attempted to measure time to incapacitation in rodents. One method uses leg flexion shock avoidance (whereby tubed rats have one leg suspended over an electrified plate – incapacitation being taken as the time at which the rat fails to withdraw its leg).[18] Another method used with rats or mice is to place the animal in a motor-driven activity wheel. In this case incapacitation is taken as the time at which the animal fails to run in the wheel and begins to tumble.[18] This method has the advantage that the animals are actively exercising, which increases the rate of uptake of toxic gases – as occurs in humans escaping from a building fire. If the respiration of tubed rats or mice is monitored, incapacitation can also be recognised by changes in the breathing pattern. Another limitation is the difficulty of obtaining sufficient blood samples for serial measurement of blood gases. Rodents are suitable for studying lung pathology. More sophisticated physiological and behavioural studies of the effects of fire gases and fire effluents have been carried out using non-human primates (macaque monkeys and baboons).[30,31] These are more relevant to the prediction of human incapacitation and have been used to develop the more detailed predictive models of physiological and behavioural effects on humans.[1,14]

Evaluation of the sensory irritant potential of fire effluent atmospheres is one area where the respiratory rate depression reflex of rodents, especially mice, provides a useful tool.[1,19,22] As described in Chapter 3, the RD_{50} test provides a useful quantitative method for comparing the relative sensory irritant potencies of individual irritant gases and fire effluent mixtures. Although the basic effects in humans are very similar to those in mice, with the same basic reflexes involved, the test method does not rely on the mouse and human responses being identical, but rather that the intensity of the mouse response can be used as a predictive scalar for the severity of effects in humans. It has been demonstrated that most individual chemicals are highly irritant to humans at the mouse RD_{50} concentration. So this method (in conjunction with other available data) can be used to estimate concentrations of individual irritants or irritant fire effluent mixtures likely to seriously impair escape of human fire victims.

A validation of this method is shown in Fig. 8.2 which illustrates the relationship between the mouse RD_{50} concentration and reported effects in humans for a variety of common irritant chemicals. Two data sets and comparisons are plotted for the same set of chemicals. The black squares show a comparison of the concentration of each gas reported to be painfully irritant to humans plotted against the mouse RD_{50} concentration. The open triangles show a comparison between workplace maximum tolerated exposure concentrations for irritant chemicals (the 1980 workplace threshold limit values [TLV-TWA]) for this set



8.2 Relationships between two irritancy end points in humans and mice. Black squares compare mouse RD_{50} concentrations with concentrations reported to be painfully irritant to humans. Open triangles compare 0.03 × mouse RD_{50} concentration with workplace tolerance levels for irritancy (1980 TWA-TLV). Data from Purser[1] and Alarie.[19]

of chemicals (for which human tolerance levels have been set on the basis of irritancy) against 0.03 × the mouse RD_{50} concentrations. In both cases there is a reasonably good agreement between the human and mouse data, demonstrating that the mouse RD_{50} model is quite a good predictor of irritancy in humans, and that the mouse RD_{50} concentration in general represents a concentration likely to be painfully irritant to humans. For most irritants, an upper limit for tolerance in the workplace is approximately 1/30 of a concentration causing severely painful irritancy.[19] The figure also illustrates the enormous range of irritant potency for different chemicals, over approximately six orders of magnitude from the most irritant species such as toluene diisocyanate, to low potency chemicals requiring much higher concentrations to elicit a similar painfully irritant effect, such as ethanol and acetone. For the four least potent substances the reported painfully irritant concentrations for humans were reported as 'greater than', as illustrated by the range bars on the figure. Although the RD_{50} model provides an indication of the severity of effects in humans it is also necessary to use experimental and

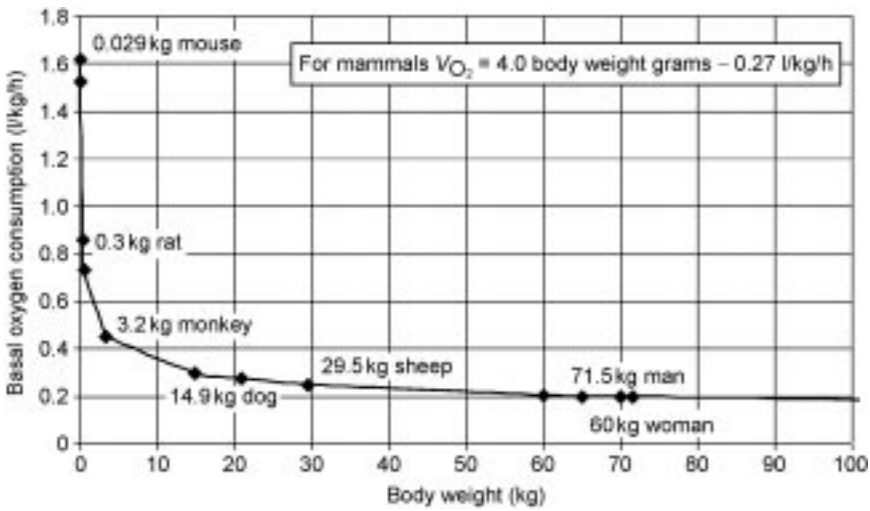
incident data from humans to estimate the severity of effects on human escape capability.

Effects of allometric relationships on rates of uptake of asphyxiant gases and time to incapacitation

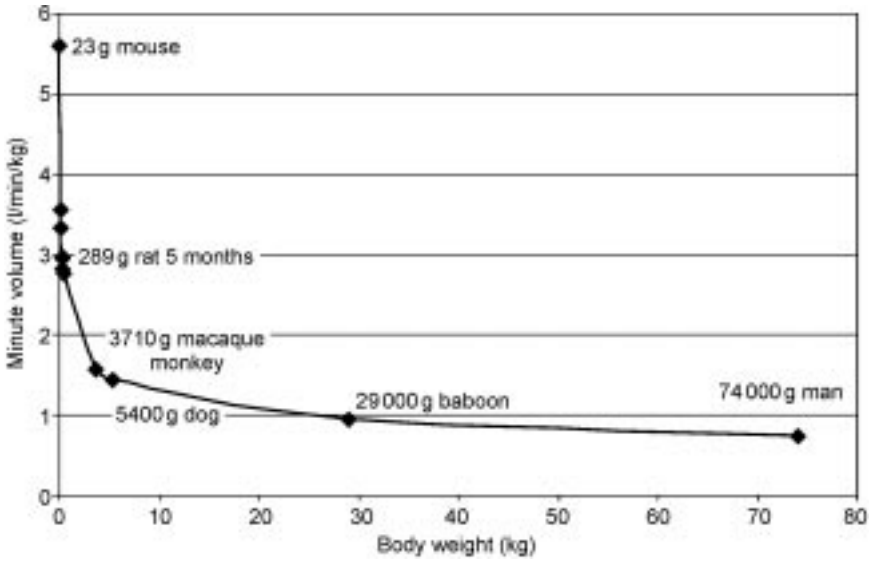
Allometric relationships (relationships between the size of each part of the animal, or each animal relative to the others) need to be considered when comparing effects in animals and humans. A basic consideration is that the rate of heat loss in mammals depends upon the body surface area/volume ratio. This means that small mammals need a high metabolic rate in order to maintain their body temperature, and therefore a high rate of oxygen consumption, as illustrated in Fig. 8.3. The body surface area per kilogram body mass of a human is approximately 4.5 times that of a rat and 2.8 times that of a 3.2 kg monkey, while the basal rate of oxygen consumption per kilogram body mass for an adult human is approximately 4.4 times that of a rat and 2.2 times that of a monkey.[32] This is reflected in the respiratory minute volume which is a major determinant of the rate of uptake of toxic gases, as shown in Fig. 8.4, which is an expression of Guyton's formula,[33] whereby:

$$\text{Volume of air breathed per minute } (V_E \text{ ml}) = 2.18 \,\text{body weight in grams}^{0.75} \qquad 8.2$$

As Fig. 8.4 shows the volume of air inhaled per minute per kg bodyweight in a mouse is greater than that in a human by the factors shown in Table 8.2. This is



8.3 Relationship between body weight and rate of oxygen consumption (mammals).



8.4 Relationship between body weight and basal respiratory minute volume (V_E) litres/minute (mammals).

reflected in large differences in the rate of uptake of carbon monoxide in rats and humans exposed to the same carbon monixde concentrations, as described in Chapter 4 (asphyxiants – Fig. 4.9).

The data demonstrate that the rate of uptake of carbon monoxide is much more rapid in the rat than in humans and monkeys, as predicted from the differences in V_E per unit body mass. At 1200 ppm carbon monixde the time to reach 40% COHb for rats is 8.76 min, compared with 32 min for monkeys and 76 min for humans. However, rats can tolerate much higher %COHb concentrations before incapacitation occurs (where incapacitation in humans and monkeys is represented by loss of consciousness, and in rats by failure of leg flexion avoidance response).

Figure 4.9 shows plots of blood carboxyhaemoglobin concentration (%COHb) against time for continuous exposures to two carbon monoxide concentrations,

Table 8.2 V_E ratios for different species

Species	V_E factor
Human	1
Baboon	1.3
Dog	1.9
Monkey	2.1
Rat	4.0
Mouse	7.5

1200 ppm and 3000 ppm in rats and humans. Also shown on the curves are predicted times to incapacitation. For rats, time to incapacitation was calculated from the fitted curve developed by Kaplan and Hartzell.[18] A single experimentally determined point is also shown for macaque monkeys exposed to 1200 ppm carbon monoxide. For humans and monkeys at rest incapacitation occurs as confusion and loss of consciousness at approximately 40%COHb,[13,34–36] while for rats incapacitation occurred at 65–76% COHb. However at 1200 ppm carbon monoxide the rat uptake curve levels off at around 65%COHb as the blood carboxyhaemoglobin concentration approaches equilibrium with the inhaled carbon monoxide concentration. In practice the true equilibrium concentration is slightly higher at around 72% COHb, so what the uptake model shows is not quite a perfect fit, as discussed in Hartzell *et al.*,[37] and the actual %COHb levels at incapacitation in rats can be somewhat higher. Also shown are calculated uptake curves for continuous exposure to 3000 ppm carbon monoxide. At this concentration 40% COHb is reached after 2.7 min in rats and incapacitation occurs at 76% COHb, which is reached much more rapidly than at 1200 ppm (after 13 min) since this is below the point at which equilibrium is reached and the uptake curve levels off. For humans, incapacitation is predicted at around 40% COHb, which is achieved after 27 min.

Based upon these data and calculations, 40% COHb in rats is reached approximately 10 times faster than in humans, which is even greater than the factor of 4 difference between the basal V_E levels. Of course the rate of uptake in humans and primates also varies with the level of activity and hence V_E, as discussed in Chapter 4, so that in practice time to incapacitation in a resting monkey is similar to that in a lightly active adult human, while a primate provides a more direct uptake model for an infant human of similar body size.

When measured time to incapacitation in rats using the avoidance response is compared with time to incapacitation using an activity wheel,[18] incapacitation occurs slightly earlier for the activity wheel. This can be explained on the basis that the animals are forced to exercise, so the rate of carbon monoxide uptake will be somewhat faster than for a rat resting in a restraining tube. Another point is that in rats there is some evidence that the physiological effects are not simply a function of the %COHb level achieved, but also of the time for which it is maintained, and this may also be true of humans.[1,38]

The differences in uptake rates and sensitivities to hypoxia between species and at different activity levels need to be borne in mind when comparing incapacitating and lethal exposure doses for asphyxiant gases. Effects in different species are often compared in terms of exposure doses, which are simply the product of exposure concentration and exposure time for a given end point (incapacitation or lethality). This of course ignores the important aspects of uptake and distribution of toxic substances in the body. A default assumption is that toxic gases obey Haber's rule, so that the Ct product for any particular end point is a constant, and the exposure dose is the same for a short exposure to a

high concentration as for an equivalent longer exposure to a lower concentration. Although this is a useful general assumption, in practice significant deviations occur for several important fire gases (especially carbon monoxide over concentrations and timescales approaching equilibrium, and also for hydrogen cyanide, low oxygen hypoxia and carbon dioxide at all concentrations).

Most combustion toxicity tests use a 30 min exposure period, so it is relevant to compare effects of exposure doses over this timescale. For carbon monoxide, deviations from linear uptake (deviation from Haber's rule) are small for exposure doses to incapacitation at carbon monoxide concentrations above 2000 ppm. Table 4.7 shows approximate *Ct* exposure doses for incapacitation and death from carbon monoxide in different species. For humans at rest the carbon monoxide exposure dose for incapacitation is around twice that in a macaque as predicted from the difference in uptake rates. But it is also approximately twice that in a rat, which is a somewhat coincidental result of the combination of more rapid uptake rates and a higher incapacitating dose threshold in the rat. Under conditions of light activity the exposure doses for incapacitation appear quite similar in all four species; however, the human data are for fast walking, while the primate data are for less vigorous intermittent movement in a shuttle box chamber. For humans there is a good database of %COHb concentrations in fatal victims of carbon monoxide poisoning (see Chapter 4) and while the mode of the distribution is around 75% COHb, survival is rare above 50% COHb. This puts the fatal exposure dose for humans at approximately 60 000–190 000 ppm min under conditions where the subject begins as active and then collapses, and up to 110 000–240 000 for subjects at rest throughout.

For hydrogen cyanide, the dynamics of uptake into the blood and dispersal throughout the body are more complex than for carbon monoxide, and incapacitation occurs for much lower *Ct* exposure doses at high exposure concentrations than for lower concentrations. For a 30 min exposure period the *Ct* exposure dose for incapacitation in a resting macaque is approximately 2610 ppm min,[1,39,40] which compares with approximately 3000 ppm min for a rat.[18] Again, it is likely that the similarity is something of a coincidence. For low oxygen hypoxia the 30 min LC_{50} concentration in rats is 5.4% (representing a depletion of 15.6%)[41,42] while around 8% O_2 (representing a depletion of 13% is fatal in humans within around 12 minutes).[43] The effects of hypoxia are non-linear, so that exposure doses for incapacitation are much smaller at high levels of depletion than at lower levels. Rats are certainly more tolerant of hypoxia than humans.

Exposure doses for lethal lung damage from irritants are not well characterised for humans, but assumed to be approximately similar to those in rodents. However, when extrapolating to humans for safety purposes it is common to apply a factor of 10 to allow for interspecies differences. Since the 30 min lethal exposure dose for hydrogen chloride in rats is 114 000 ppm min it could be considered potentially dangerous to expose humans to more than

11 400 ppm min or approximately 380 ppm. This aspect is considered in more detail in Chapter 3.

Effects of body structure differences

Other differences between rodents and humans relate to allometric differences in body structure, physiological and biochemical differences. There are significant differences between the structure and function of the upper respiratory tract between rodents and primates, including humans. Rodents have well-developed nasal passages with a larger surface area than those in primates, and are obligate nose-breathers, while primates can use both nasal and oral breathing (the latter especially under stress or exercise). This difference results in a greater absorbance of water-soluble acid gases in the upper respiratory tract of rodents than in primates. This is reflected in differences in the physiological response to inhaled acid gases as described in Chapter 3. In rodents the upper respiratory tract nociceptive (trigeminal nerve mediated) response of a marked and maintained respiratory rate depression dominates. While in human and non-human primates, although the same, mainly trigeminal-mediated, respiratory rate depression response occurs initially, this is replaced after a few seconds by a hyperventilatory response resulting from stimulation of vagal receptors in the airways and lower respiratory tract. Rats and mice inhaling an irritant atmosphere are able to reduce their respiration by up to around 90%. They appear to tolerate the resultant hypoxia well, partly by reducing their peripheral circulation (somewhat similar to the diving response in marine mammals). This constitutes a protective effect reducing the uptake of toxic gases into the lungs. Thus when rats were exposed to 3000 ppm carbon monoxide with 1000 ppm hydrogen chloride the time to incapacitation was increased from 13 min with carbon monoxide alone up to 22.2 min in the presence of hydrogen chloride. The lethal exposure time was increased from approximately 65 to 109.5 min.[37] This protective effect does not occur in primates, so that for macaque monkeys exposed to carbon monoxide in the presence of irritants, the rate of uptake was similar to that from carbon monoxide alone.[13,17] When Alarie bypassed the upper respiratory tract by introducing irritant gases via a tracheal cannula in anaesthetised mice, respiratory rate depression did not occur, but a characteristic pattern of rapid breathing and the extent of effects on the deeper lung were enhanced.[26] Malek and Alarie carried out experiments on guinea pigs forced to exercise on a wheel while inhaling irritant gases. This also resulted in enhanced toxicity.[44]

The main findings from these studies are that while the basic mechanisms of toxicity are similar in rodents and primates it is necessary to be aware of the differences when extrapolating from rodent data to primates including humans. It is considered that rodents are good models for investigating the physiological and pathological mechanisms of toxicity from fire effluent gases and fire effluents, and that quantitative data on exposure doses can also give an indica-

tion of likely incapacitating and lethal exposure doses in humans, provided allowances are made for species differences. A combination of human and primate data is considered essential to develop detailed predictive calculation methods for humans for asphyxiant fire gases. In order to estimate the sensory irritant and lung inflammatory effects of irritants (physiological, behavioural and pathological) it is necessary to use a combination of data from all available sources including human data from workplace exposures and industrial accidents, mouse RD_{50} data, physiological and behavioural studies using primates, and lung pathology studies using rodents.

8.6 Identification of toxic species in fire effluents and assessment of contributions to toxic hazards

8.6.1 Fire incident investigations, associated fire tests and pathology studies

Smoke irritants

An important source of information on toxicity and toxic hazards in fires has been fire incident investigation combined with clinical and pathological studies of fire survivors and fatalities. With regard to conditions during fire incidents, survivors surveyed in a number of studies have reported difficulty or unwillingness to enter and move through smoke, and that both smoke obscuration and irritancy are factors.[1] From the studies of Wood in the UK[45] and Bryan in the US[46,47] around 30% of people were found to turn back rather than continue through smoke-logged areas and the average smoke density at which people turned back was at a 'visibility' distance of 3 metres (0.33 OD/m, extinction coefficient 0.76). It is likely that a major factor in these behaviours was simple optical obscuration so that it is difficult to evaluate the extent of effects from irritants. Smoke from electrical fires (likely to be high in hydrogen chloride) is reported as being particularly irritant, and very low smoke levels in minor incidents have resulted in buildings being evacuated due to eye and respiratory tract irritation.

The presence of a significant content of irritants in fire effluent smoke, and its tendency to penetrate deep into the lungs are also confirmed by the occurrence of chemical pneumonitis in some fire survivors. A typical pattern in a proportion of fire survivors is a transient hypoxic crisis with low blood arterial blood oxygen concentrations developing several hours after rescue due to pulmonary oedema and inflammation. This can be fatal at this stage, or can resolve after around 24 hours. This may then progress to bronchopneumonia, which can also be fatal, or if infection is avoided recovery can be rapid. The general picture from fire incidents involving significant smoke inhalation is that while people report a slight hoarseness and productive cough for a few days

after the incident, at 3 month follow-up they are generally free of respiratory symptoms.[48]

The basic position with regard to the effects of irritants in fires is then that they are known to be present, and both sensory irritation and lung inflammation are known to occur as result of exposure to fire effluents. However studies of fire incidents do not really enable the identification of important irritant species or provide a method for predicting the severity of effects.

Asphyxiant gases

Most attention has been directed to carbon monoxide because it is always present, often at high concentrations (0.5–1%CO), in fires and because it remains in the blood during and after exposure as carboxyhaemoglobin. The presence of high %COHb levels in the blood of fire survivors and fatalities is therefore strong evidence that they have inhaled significant quantities of toxic smoke during a fire, since all fire gases tend to be present simultaneously. Also, studies of fire fatalities and human victims of accidental and deliberate carbon monoxide poisoning show similar %COHb distributions (see Chapter 4), leading to the suggestion that carbon monoxide is likely to be the major ultimate cause of death in most fires where serious burns are not present. In fact the %COHb levels in many fire victims are somewhat lower than those from carbon monoxide deaths, indicating the presence of other asphyxiants.[9] Post-mortem studies also show elevated blood cyanide concentrations in a proportion of fire victims, but elevated blood cyanide levels are always accompanied by elevated %COHb levels.[49] Because cyanide is much less stable in blood than carbon monoxide,[50] and owing to the dynamics of uptake and dispersal of cyanide in the blood, it is difficult to determine its importance in producing incapacitation at the fire scenes from post-mortem studies.[39,40] However, measurements taken during experimental house fires involving typical domestic furnishings showed hydrogen cyanide concentrations exceeding 1000 ppm which is likely to be a major factor in causing incapacitation (loss of consciousness) and thereby limiting time available for escape in many fire incidents.[7,51,52] This is supported by a study in which fresh blood samples were taken from fire survivors at the time of rescue from the fire scene, in which high blood cyande concentrations were measured,[53] and also in samples taken from the Manchester Airtours fire victims.[54]

A difficulty with regard to carbon dioxide and low oxygen hypoxia is that these gases do not leave any obvious traces in fire survivors or fatalities once removed from the fire scene. Carbon dioxide is always present at high concentrations during fire experiments, and in fire victims its main effect is to cause hyperventilation, thereby increasing the rate of uptake of other fire gases. With regard to low oxygen hypoxia the effects are more difficult to predict. During enclosure fire experiments (such as that shown in Fig. 8.1) it is generally found

that oxygen depletion at head height is relatively minor by the time victims are predicted to be severely affected by carbon monoxide and hydrogen cyanide.[1,7,51]

Oxygen concentration in upper layer fire effluent plumes can, however, be as low as 1% O_2 as well as being at temperatures of several hundred degrees centigrade. If a fire victim were to be exposed to, and inhale, an atmosphere such as this, they would be expected to collapse unconscious within seconds. A small number of reports do exist of observations that could be consistent with this effect, in which victims in fire incidents have been observed to collapse or almost collapse following inhalation of a single breath of smoke.

Other potential asphyxiant gases present in fire effluents are oxides of nitrogen (NO_x), but concentrations measured have not been high enough to make a significant contribution to asphyxia, except in specific incidents such as fires involving nitrate film.[55]

The general indications from fire incident studies and full-scale fire experiments are that a short list of asphyxiant gases is important in most fires, including carbon monoxide, hydrogen cyanide, carbon dioxide and low oxygen. Of these, carbon monoxide is present in all fires and almost always found at high concentrations in the blood of fire survivors and fatalities who have received serious smoke exposure in fires. Carbon monoxide is also likely to be the major ultimate cause of deaths during fires, but it is likely that both hydrogen cyanide and carbon monoxide are important as causes of incapacitation, while their uptake is enhanced by the presence of carbon dioxide. Irritants and simple hypoxia may be important in some fires as additional causes of hypoxia, and all may be additive with carbon monoxide as ultimate causes of deaths from asphyxia during fires. Based upon the %COHb levels in fire fatalities it is possible to estimate the fatal exposure doses of carbon monoxide for human fire victims. By comparing clinical status with measured %COHb concentrations in fire survivors it is possible to make some estimates of carbon monoxide exposure doses and %COHb concentrations causing incapacitation during fires. However, wide variations are reported in practice, as described in Chapter 4.

8.6.2 Studies using animals in conjunction with bench-scale and large-scale fire toxicity tests

Considerations related to fire models and animal models used

The majority of studies of the toxicity of fire effluent atmospheres using animals involve exposure to fire effluent atmospheres generated using bench-scale generation methods, although a few examples exist involving exposure of rodents to effluent samples taken from large-scale fires. For bench-scale experiments involving animals there are two major considerations with respect to their relevance to toxic hazards experienced by humans in full-scale fires:

- The extent to which the yields of toxic products and exposure concentrations in the bench-scale tests represent those occurring in different types and stages of full-scale fire scenarios involving human exposures.
- The extent to which the animal toxicity models used provide qualitative or quantitative data relevant to the physiological and pathological effects on human fire victims during and after exposure in fire incidents.

At the time most of the animal exposure studies were performed during the 1970s and 1980s, few attempts were made to relate the decomposition conditions and product mixes generated in small-scale combustion generation equipment with those occurring during full-scale fires. In practice, most exposures were to products generated by non-flaming oxidative decomposition of material specimens heated in air, while only a few experiments were conducted under the flaming decomposition conditions occurring in the vast majority of accidental fires involving human fire victims (see Chapter 14). Very few experiments were conducted under the vitiated flaming conditions occurring in most full-scale compartment fires. This limits the relevance of much of this work as a predictive tool for full-scale fires. However, where animal exposures were combined with measurements of the concentrations of the major fire gases, they do give some indication of the extent to which fire effluent toxicity can be expressed in terms of the small number of major fire gases, and the extent to which other atmosphere components may be important. Also, by screening a relatively large number of natural and synthetic polymeric materials, they have provided an indication of the extent to which the overall toxic potencies of fire effluent atmospheres from different materials are similar, and where more extreme or unusual toxic potency atmospheres may be produced from specific materials.

The other major limitation of many of these experiments was the toxicity model used. As described, the major toxic hazards considered important during fires are the rapidly developing physiological effects of sensory irritation and incapacitation due to effects of asphyxiants. Most animal tests involving rats and mice used simple measurements of lethality (LC_{50} concentrations), usually involving 30 min exposure periods, sometimes followed by a 14 day observation period. Such methods produced a crude average of the overall lethal toxic potency from asphyxiants during exposure and lung inflammation following exposure, giving no indication of time or exposure dose to incapacitation. They also suffer anomalies due to physiological differences between rodents and humans as discussed. For this reason, the relationships between exposure concentration and time to death, or number of deaths in any specific test, are only very approximately relevant to predicted effects in humans. Much more directly applicable to humans are the limited number of experiments involving exposure of primates to fire effluent atmospheres with detailed physiological and behavioural measurements of effects leading to incapacitation.[1,13]

8.6.3 Findings from primate exposure studies

Following the findings from the UK fire statistics of a four-fold increase between the 1950s and 1970s in deaths resulting from exposure to toxic smoke in fires, a set of experiments was carried out involving sub-lethal exposures of macaque monkeys to individual asphyxiant fire gases (carbon monoxide, carbon dioxide, hydrogen cyanide and low oxygen hypoxia) and a set of mixed fire effluent atmospheres generated from a range of polymeric materials.[13,17,30,36,39,43,56] The aim of these experiments was to investigate the physiological mechanisms by which fire effluents impede escape and cause incapacitation in human fire victims. A set of physiological parameters were measured before, during and after 30 min exposures under dynamic steady-state exposure conditions. Effluent atmospheres were generated using an early version of the ISO19700 tube furnace,[57] whereby strips of material were introduced at a constant rate into a tube furnace under a stream of air, and the effluents expelled into a mixing chamber where they were diluted with secondary air, forming an effluent atmosphere to which the animals were exposed (via a face mask or in a whole-body shuttle box chamber). Continuous measurements were made of physiological parameters indicating respiratory, cardiovascular and neurophysiological status, including respiratory flow, tidal volume and frequency, heart rate and electrocardiogram, electrocorticogram, nerve-conduction velocity and auditory-evoked potentials. Clinical signs and status of body reflexes were also monitored, and blood samples were taken at intervals for measurement of carboxyhaemoglobin and blood cyanide concentrations. Observations were continued for 14 days post-exposure and some lung pathology investigations were also carried out.

For fire effluent exposures different materials were decomposed in two sets of experiments. For the first set wood (*Pinus sylvestris*), polyacrylonitrile and flexible polyurethane foam were pyrolysed under nitrogen at 300, 600 and 900 ºC. For the second set of experiments a rigid polyurethane foam, nylon 6, polystyrene and polypropylene were decomposed under non-flaming oxidative decomposition conditions at 440–500 ºC. Polypropylene was also decomposed under flaming and pyrolytic decomposition conditions and polystyrene under pyrolysis. The fire effluent atmospheres were monitored continuously for carbon monoxide, hydrogen cyanide, carbon dioxide, oxygen smoke optical density and total particulates. Based upon these and more detailed investigations of decomposition chemistry by Woolley and Fardell,[12] the different effluent atmospheres were found to contain significant concentrations of asphyxiant gases (carbon monoxide and hydrogen cyanide), and varying concentrations of smoke particulates. Gas chromatography combined with mass spectrometry (GC-MS) investigations showed a rich mix of aliphatic and aromatic hydrocarbons generated under pyrolysis, with an additional significant content of partially oxidised species (acrolein, formaldehyde, crotonaldehyde, acetaldehyde, phenol, aliphatic acids, etc.) being formed under non-flaming oxidative decomposition

conditions. Under flaming combustion conditions the organic content was mostly consumed in the combustion process. Flexible polyurethane foam decomposed into isocyanate derived 'yellow smoke'. In addition to these experiments on resting primates two sets of experiments involved animals conditioned to carry out a behavioural task in a chamber. For these experiments the animals were conditioned to press a lever when an audible signal was sounded, after which they had a few seconds to reach the other end of the chamber where a food reward was presented for a brief period. The task was repeated at 3–5 min intervals throughout a 30 min exposure and post-exposure period.[30] The purpose was to test the animal's performance abilities during exposure and to maintain them in an active state. These behavioural experiments were carried out with exposure to different concentrations of carbon monoxide and also to fire effluent atmospheres generated from polypropylene under pyrolytic and non-flaming oxidative thermal decomposition conditions.[1]

In other experiments Hartzell and co-workers used a conditioned escape paradigm to examine effects of 5 min exposures of baboons to different concentrations of acrolein or hydrogen chloride gas. After 5 min exposure the animals were conditioned to press a lever to release the door catch and escape from the exposure chamber.[31]

The findings from the individual gas exposure experiments are summarised as follows:

- During exposure to carbon monoxide there were no physiological or behavioural effects until the blood carboxyhaemoglobin concentration reached approximately 30% COHb (for active animals) or 40% COHb (for animals at rest). The free moving animals were unaffected until they suddenly became lethargic and over a period of seconds passed through a brief period of apparent intoxication to collapse and loss of consciousness. The resting animals were unaffected until a point in time when their consciousness became impaired. At this point there was a decrease in heart rate with occasional arrhythmias, a large increase in slow-wave brain activity, a decrease in respiration and failure of withdrawal reflexes as the animals became unconscious. Loss of consciousness occurred at a threshold exposure dose of around 27 000 ppm min for free moving animals and 36 000 ppm min for resting animals.
- During exposure to hydrogen cyanide there were also no immediate effects, but after a period of a few minutes (depending upon the exposure concentration) the animals started to hyperventilate. This induced a positive feedback situation in that the increased ventilation increased the rate of uptake of hydrogen cyanide, which further stimulated respiration until the animals lost consciousness, showing similar signs to those exposed to carbon monoxide. At this point there was a large decrease in respiration, so that the rate of hydrogen cyanide uptake decreased and the blood cyanide concen-

tration levelled off. The animals sometime showed signs of recovery at this point, then passing slowly deeper into unconsciousness. Recovery was rapid within a few minutes of the end of the exposure, although whole blood cyanide concentrations showed little decrease over periods of up to an hour.[39,40] Short exposures to high hydrogen cyanide concentrations (150–200 ppm) produced incapacitation within a few minutes (*Ct* exposure dose 270 ppm min) while lower concentration 80–100 ppm required approximately 30 min to cause incapacitation (*Ct* exposure dose 2610 ppm min).[1]

- Exposure to 10% oxygen also resulted in signs of cerebral depression and lethargy throughout most of a 30 min exposure, but signs were short of loss of consciousness.
- Exposure to 5% carbon dioxide produced some minor cerebral effects, but mainly an approximate threefold increase in V_E.
- The findings from the baboon studies were that the animals were able to perform the escape behaviour efficiently up to very high concentrations of 15 000 ppm hydrogen chloride and 2780 ppm acrolein, although post-exposure signs of severe irritancy were observed at hydrogen chloride concentrations above 1000 ppm.

The findings from the studies involving exposure to fire effluent atmospheres were as follows:

- The physiological effects measured were basically the same as those of the dominant toxic gases present in the effluent atmosphere. The effects were:
  - dominated by and identical with the effects of carbon monoxide alone (e.g. wood pyrolysed at 900 ºC, flaming polypropylene);
  - dominated by and identical with the effects of hydrogen cyanide (e.g. pyrolysed polyacrylonitrile, 900 ºC, rigid polyurethane foam non-flaming oxidative decomposition); or
  - dominated by signs of sensory irritancy during exposure and lung inflammation after exposure (polyurethane foam pyrolysed at 300 ºC and 600 ºC, wood pyrolysed at 300 ºC).
  - In one case where significant concentrations of both carbon monoxide and hydrogen cyanide were present the effects were consistent with the toxicity of the two gases being additive.
  - Where both carbon monoxide and irritants were present, although there was some hyperventilation resulting from stimulation of lung irritancy receptors, the uptake of carbon monoxide was not increased. It was considered that although V_E was increased, it was likely that ventilation-perfusion ratio changes prevented increased carbon monoxide uptake.
  - When polypropylene was pyrolysed, the resultant atmosphere contained a hydrocarbon mist and a wide range of aliphatic and aromatic pyrolysis products, but the atmosphere was innocuous, producing no signs of irritancy or other toxic effects in the animals, and no disruption of the

behavioural task performance. When polypropylene was decomposed under non-flaming oxidative conditions, the resultant atmosphere also contained a smoke, but was highly irritant to the animals, producing a distinctive respiratory pattern with hyperventilation, and signs of lung oedema and inflammation some hours after exposure. Behavioural task performance was inhibited at 1.85 mg/l mass loss concentration.

– When flexible polyurethane foam was pyrolysed the particulate isocyanate-derived 'yellow smoke' was highly irritant, producing respiratory changes during exposure and lung inflammation and oedema some hours later.

The overall results of these primate studies basically confirmed and quantified the effects reported in fire fatalities and survivors, that the only important effects of exposure to fire effluents from common polymeric materials were asphyxia from the mixed asphyxiant gases present (carbon monoxide, hydrogen cyanide, carbon dioxide and low oxygen hypoxia) and irritant effects consisting mainly of sensory irritancy at the time of exposure and lung inflammation and oedema after exposure. The effects of carbon monoxide and hydrogen cyanide were found to be additive as later confirmed in experiments with rats.

The irritant effects were as might have been predicted in general terms from the chemical composition of the effluents, in that atmospheres rich in partially oxidised organic species such as unsaturated aldehydes of isocyanate-derived compounds were found to be highly irritant, while atmospheres low in organic content, or lacking partially oxidised organic species were relatively non-irritant.

Polypropylene provides a good example of this finding. When polypropylene was decomposed under nitrogen, the atmosphere formed was rich in organics, but contained no organic species containing oxygen and was non-irritant. Under non-flaming oxidative decomposition condition in air there was a high organic content to the atmosphere produced, consisting of a mixture of products, including both oxygen-containing and non-oxygen containing species. The resultant atmosphere was highly irritant. When the furnace temperature was increased to 700 ºC so that flaming combustion occurred, a 'cleaner' atmosphere was formed with a lower smoke and organic content and most of the fuel carbon released as oxides of carbon. The resulting atmosphere was of low irritancy but caused asphyxia due to the carbon monoxide content. Irritant atmospheres were produced by both wood and flexible polyurethane foam when decomposed under nitrogen, since both materials contained sufficient molecular oxygen to release significant yields of irritant compounds.

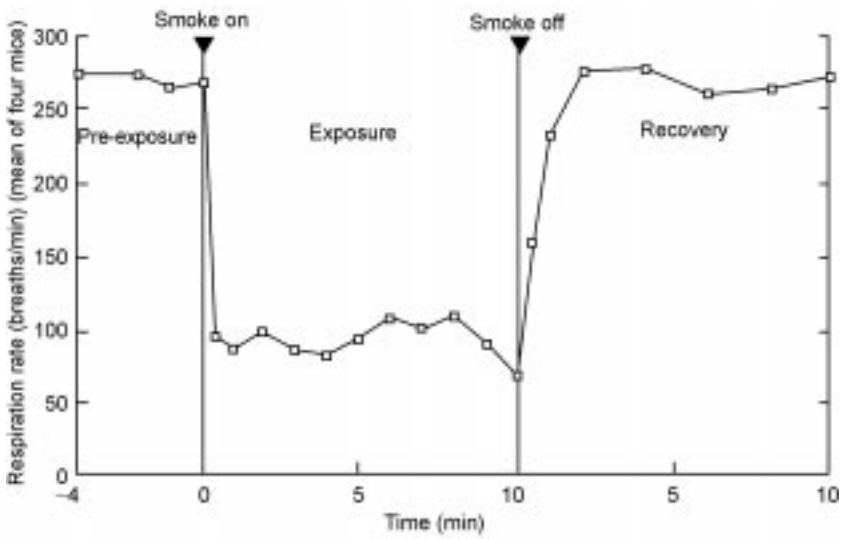
These results confirm a general principle on the relationship between thermal decomposition conditions and fire effluent composition (see Chapter 14). For all materials, the most irritant atmospheres, rich in a wide range of organic species at relatively high yields, are obtained under non-flaming oxidative decomposition conditions. For non-fire-retarded materials, well-ventilated flaming results

in efficient combustion, so that organic species are oxidised to form carbon oxides and irritants are absent or present a very low yields. Under vitiated combustion conditions the organic content increases, so that atmospheres produced by vitiated combustion are predicted to be somewhat irritant, but almost certainly much less irritant than atmospheres produced under non-flaming conditions, since both the number of species present and the yields are lower than under non-flaming oxidative decomposition conditions.[11,12] This means that if any exotic acute toxic effects are likely to occur from organic chemical species in fire effluent mixtures, they are almost certain to be found in the organic-rich effluents from non-flaming oxidative decomposition, while under flaming combustion conditions, the main toxic effects can be predicted to be those of the major asphyxiant gases, plus a degree of irritancy especially from products of vitiated combustion, or from acid gases. Although none of the materials used in the primate studies were fire-retarded, increased irritancy is to be predicted from fire-retarded materials, mainly from the acid gases released (halogen halides, sulphur oxides and phosphoric acid) under all decomposition conditions, and also because fire retardants acting in the gas phase (especially halogen fire retardants) reduce the efficiency of combustion under flaming conditions, thereby also increasing the content of potential organic irritants. The relationships between combustion conditions and toxic product yields in fires are considered in detail in Chapter 14.

The work involving sub-lethal exposures of primates to individual fire gases and fire effluent mixtures has therefore provided useful information on the mechanisms of incapacitation of human fire victims. It has also provided important quantitative information on the uptake and effects of toxic fire gases, which have been used to develop predictive methods for calculating time to incapacitation in human fire victims. However, the range of materials studied was limited to a small number typically used in domestic furnishings. In order to study the toxic effects of fire effluents from a wide variety of materials it has been necessary to use rodents animal models, as described in the next section.

8.6.4 Estimates of sensory irritant potency for natural and synthetic polymers under different fire conditions using rodents and contribution to overall irritant potency from major irritant gases

As described, the most widely used method for direct measurement of sensory irritant potency of individual chemicals in the gas phase is the mouse respiratory rate depression (RD_{50}) test. This method has also been applied in small-scale toxicity tests carried out for a range of materials. The test makes use of the reflex decrease in breathing rate when exposed to an irritant atmosphere, which is common to humans and rodents. This reflex is particularly well developed and stable in rodents, especially mice, such that the percentage decrease in breathing

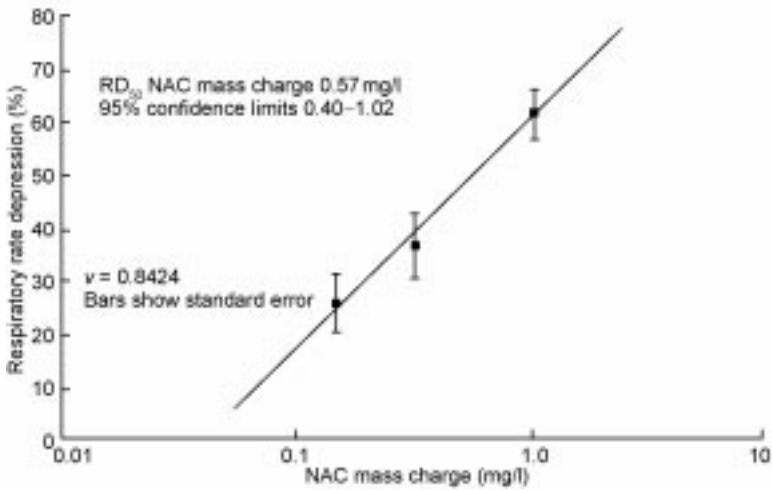


8.5 RD_{50} test: respiratory rate depression in mice exposed to thermal decomposition products from PVC cable jacket.

rate is proportional to the log of the inhaled concentration. This is illustrated in Fig. 8.5, showing results of exposure of groups of four mice to thermal decomposition products from a PVC cable jacket material at a mass loss concentration of 0.72 g/m^3 decomposed in an early version of the ISO TS19700 tube furnace[22,57] at approximately twice the RD_{50} concentration of 0.34 g/m^3. At this concentration the effects on breathing rate are almost instantaneous, the rate decreasing to around 30% of the pre-exposure level. Figure 8.6 illustrates determination of the RD_{50} concentration from the relationship between percentage respiratory rate depression and log exposure concentration for thermal decomposition products from a PVC cable insulation material. The results are expressed in terms of the nominal mass charge atmosphere concentration (NAC mass charge), which represents the mass of material introduced into the furnace per litre of diluent air.[22]

As discussed in Chapter 3 and illustrated in Fig. 8.2, the irritant potencies of different individual chemical substances cover a very wide range, approximately six orders of magnitude, and there is a good relationship between the mouse RD_{50} concentration and the severity of irritant effects in humans for different substances. The use of mouse RD_{50} data in combination with other data to predict escape impairment and incapacitation in humans is discussed in detail in Chapter 3, but an aspect considered here is the evaluation of irritancy for combustion product effluent mixtures from different materials in small-scale toxicity tests.

These studies have been carried out with two main aims. One aim has been to measure directly the irritant potency of effluent from different materials to rank



8.6 Relationship between breathing rate and log exposure concentration in mice (PVC-I).

them in comparison to each other and in relation to the irritancy of common irritant chemical species. Another aim has been to establish the extent to which the overall irritancy of fire effluent mixtures can be explained in terms of the individual chemical components present, and to develop a predictive calculation model for sensory irritant potency, so that irritant potency can be calculated from chemical analysis of a combustion atmosphere.

A default model has been developed for the estimation of irritant potency of an atmosphere based upon the fractional effective concentration concept. Sensory irritant effects occur on a continuum, increasing in severity in proportion to the log of the exposure concentration. However, it is considered feasible to recognise two important thresholds for effects on humans related to fires:

- A concentration capable of seriously impairing escape capability and movement speed.
- A concentration capable of causing incapacitation, such that the subject effectively cannot move.

For this model a concept of fractional irritant concentration (FIC) has been developed assuming that each component contributes additively to the overall irritancy of a mixture. The FIC for each component is expressed in terms of a fraction for which the numerator is the concentration of the irritant present in the atmosphere and the denominator is the concentration considered likely to impair escape capability or the concentration considered likely to cause incapacitation. In relation to predicting the overall effects of a mixture of irritants on mice the denominator would be the RD_{50} concentration for each irritant present. The overall FIC for an irritant mixture is then as follows:

$$\mathrm{FIC} = \mathrm{FIC}_{\mathrm{HCl}} + \mathrm{FIC}_{\mathrm{HBr}} + \mathrm{FIC}_{\mathrm{HF}} + \mathrm{FIC}_{\mathrm{SO_2}} + \mathrm{FIC}_{\mathrm{NO_2}} + \mathrm{FIC}_{\mathrm{CH_2CHO}} + \mathrm{FIC}_{\mathrm{CH_2O}} + \Sigma\mathrm{FIC}_x \quad 8.3$$

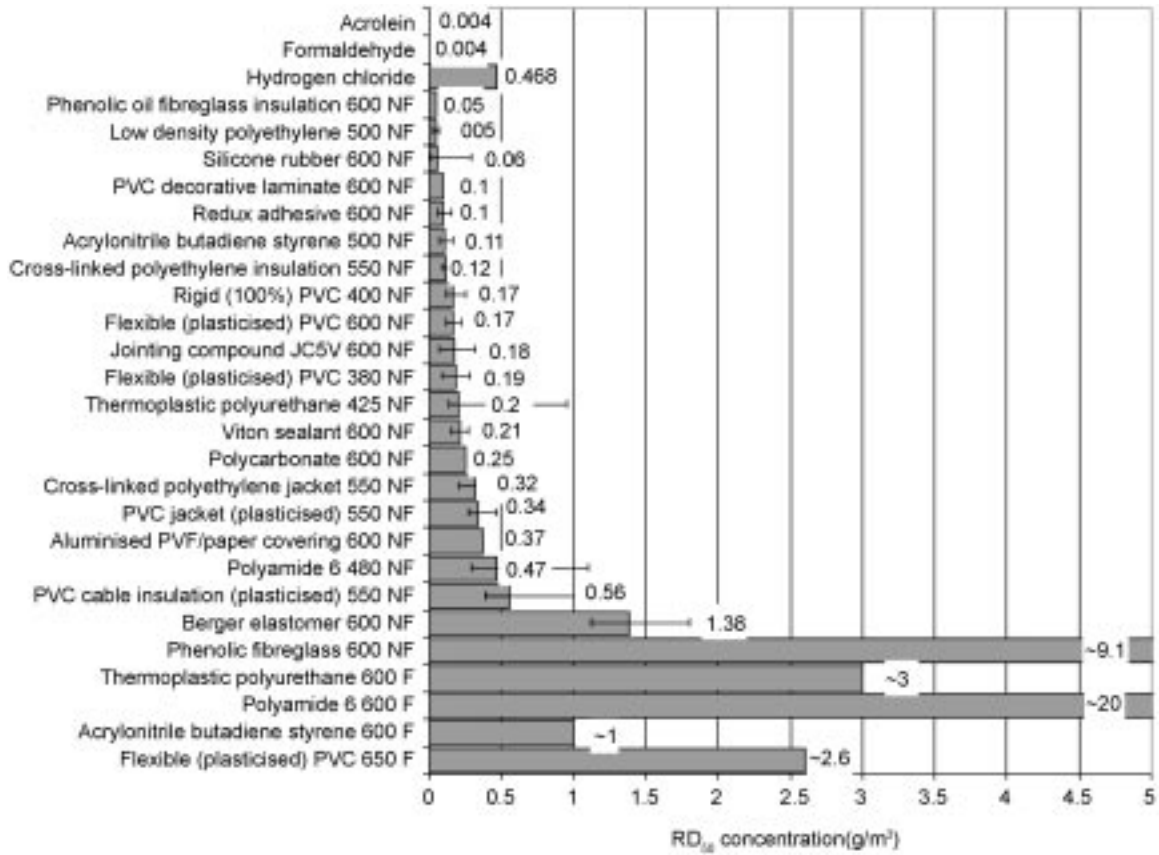
where $\Sigma\mathrm{FIC}_x$ = FICs for any other irritants present. This method is commonly used to assess the potential effects of mixtures of toxic gases for industrial hygiene purposes and has the merit that it is reasonably conservative.

Findings from combustion irritancy tests

Mouse respiratory rate depression measurements and RD_{50} determinations have been carried out by Alarie and associates for a wide range of individual chemicals.[19,23,26,58] This group has also measured mouse respiratory rate depression in combustion product atmospheres generated using the University of Pittsburgh furnace test method.[59–61] Although some interesting results were obtained, the usefulness is limited by the nature of the decomposition method. The method employed was ramp heating of a sample of material in a large crucible under a stream of air, which was used to carry the effluent through a chamber in which groups of four mice were exposed nose-only and their respiratory pattern measured. The specimen therefore passed through a number of stages involving a period of increasing non-flaming oxidative decomposition as it heated up, followed in some cases by flaming combustion if ignition occurred. Since the mass loss rate of the fuel was not measured and there was limited analysis of the atmosphere, it is difficult to relate the effects observed to the yields and concentrations of thermal decomposition products evolved. It is also difficult to relate the furnace conditions to those occurring during actual full-scale fires.[1]

Another set of experiments was carried out by Purser using an early version of the ISO 19700 tube furnace apparatus. The advantage of this method is that, as described in Chapter 14, the decomposition products are evolved continuously from a strip of material introduced into the furnace tube at a constant rate under a constant stream of air. This method enables a wide range of combustion conditions to be set up, specified in terms of continuous flaming or non-flaming behaviour and fuel/air equivalence ratio. The concentrations of effluents in the exposure chamber are maintained constant throughout and can be characterised in terms of a wide range of measured atmosphere components and the mass loss or mass charge concentration of the material under investigation. Figures 8.5 and 8.6 illustrate the results from one such set of experiments on PVC cable jacket and insulation materials.[22]

The majority of experiments performed with this method using mice use non-flaming oxidative decomposition of the test materials, but a small number of experiments were carried out under flaming conditions. The basic results are summarised in Fig. 8.7 in which the materials tested are ranked in order of irritant potency (mouse RD_{50} concentration).[14] This means that the shorter the bar, the more irritant the atmosphere. All results are expressed as concentrations



8.7 Mouse RD_{50} concentrations measured under non-flaming (NF) oxidative and flaming (F) combustion conditions for a range of materials using and early version of the ISO 19700 tube furnace method.

in g/m^3 mass loss (standard error bars are shown). The upper three bars are for individual irritants common in fire effluents, and considered as likely major individual fire effluent irritant species. The low molecular weight unsaturated aldehydes are among the most potent irritant species known to occur in fire effluents, both with measured RD_{50} concentrations of 0.004 g/m^3, while hydrogen chloride has an RD_{50} concentration of 309 ppm or 0.0468 g/m^3. Materials were decomposed in air at the furnace temperatures listed, and were all highly irritant under non-flaming oxidative thermal decomposition conditions (RD_{50} 0.05–1.38 g/m^3) except a phenolic resin/fibreglass composite material. The most irritant materials were the fumes given off by the binder oil in the fibreglass insulation blanket materials used as insulation in aircraft fuselages, low density polyethylene (LDPE, RD_{50} 0.05 g/m^3), and silicone rubber (RD_{50} 0.06 g/m^3). Plasticised PVC laminate and polypropylene were also highly irritant (RD_{50} 0.1 g/m^3). However, when several of these materials were decomposed under flaming conditions, the irritant potency was considerably reduced. For these single experimental runs under flaming conditions the results are only approximate, but were generally at least an order of magnitude less irritant than when the same materials were decomposed under non-flaming oxidative conditions.

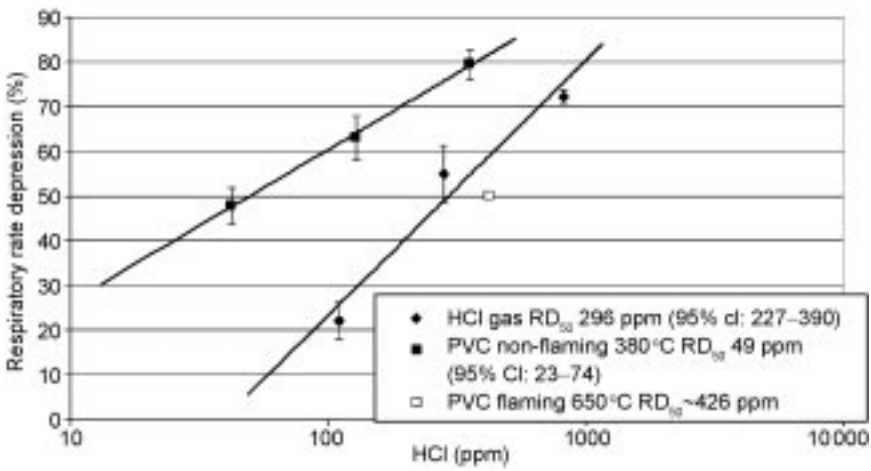
These results demonstrate that almost all materials produce highly irritant atmospheres under non-flaming oxidative thermal decomposition conditions, when high yields of organic substances including irritant species are known to occur. Under flaming conditions the irritancy is reduced although materials such as PVC remain somewhat irritant due to the release of hydrogen chloride.

Another consideration is the extent to which the observed irritancy in these atmospheres can be explained in terms of the effluent composition. Some attempt has been made to do this for a few cases using GC-MS characterisation of the atmospheres, in addition to measurements of particulates, carbon oxides and hydrogen chloride from PVC. The basic finding from the most irritant materials such as polyethylene is that approximately 30% of the mass loss is in the form of organic products, giving a mass loss concentration of total organics of around 0.015 g/m^3. The most irritant substances detected in these atmospheres are acrolein and formaldehyde, but in order to account for the observed irritant potency the total mass loss concentration of these substances would need to be 0.004 g/m^3, representing approximately 26% of the total organic mass loss. In practice the bulk of the organic mass loss is known to be in the form of low molecular weight aliphatic hydrocarbons (methane, ethane, ethene, propane, etc.), small amounts of benzene, phenol and styrene, and traces of other compounds including aldehydes, although it was not possible to carry out fully quantified organic analysis of these atmospheres it is evident that the observed irritant potency is considerably greater than can be accounted for in terms of the organic irritants detected (assuming a simple additive FIC model). It is concluded that effluent atmospheres from common polymeric materials must

contain a number of highly potent irritant compounds that remain to be identified, or that some process other than simple chemical irritancy, such as free radical activity, is involved.[1]

Another question that can be addressed is the extent to which the measured irritancy of effluents from PVC can be explained in terms of the measured hydrogen chloride, and what contribution if any is made by organic irritants. Figure 8.8 illustrates the results of a study to investigate the contribution of hydrogen chloride to the sensory irritancy of thermal decomposition products from a plasticised PVC under non-flaming oxidative thermal decomposition conditions at 380 ºC.[62] Assuming hydrogen chloride was the only irritant gas present, the RD_{50} concentration for PVC expressed in terms of hydrogen chloride concentration was 49 ppm, compared with 297 ppm measured for hydrogen chloride gas alone. This means that the mixed thermal decomposition products from the PVC were six times more irritant than could be accounted for in terms of the hydrogen chloride content of the exposure atmosphere (the difference presumably being due to the content of organic irritants in the atmosphere in addition to the hydrogen chloride). Under flaming conditions at 650 ºC an approximate 50% decrease in respiratory rate was obtained for an hydrogen chloride concentration of around 426 ppm, which is reasonably close to the hydrogen chloride RD_{50} concentration of 276 ppm, indicating that under flaming conditions the observed irritancy of PVC can be largely accounted for in terms of the hydrogen chloride evolved.

These experiments demonstrate that the mouse model is capable of measuring the overall irritant effect of a combination of chemical species in a fire effluent mixture without the need to measure them all chemically, and that



8.8 Concentration–effects relationships atmospheres containing hydrogen chloride (HCl) in different forms (bars show 95% confidence limit (cl)).

hydrogen chloride is only a minor component in the overall irritancy of PVC thermal decomposition products under non-flaming decomposition conditions. In later work an attempt was made to account for the observed irritancy by GC-MS analysis of the detectable irritants, but insufficient concentrations of known irritant species were detected to account for the severity of the observed effects. The experiments also clearly demonstrate that effluent atmospheres formed under flaming conditions are generally much less irritant than those formed under non-flaming decomposition conditions. Although there is a need for more research on the irritant potencies of mixtures of individual irritant species and to determine the contribution of individual organic irritants to the overall irritant potencies of thermal decomposition products, it is considered that the simple additive FIC model is a reasonable approach to estimating the overall irritant potencies of known mixtures in humans. Based upon the observations made in mice, primates and humans, and on the chemical analysis of fire effluent mixtures, it is likely that in full-scale flaming fires, the most important irritants are likely to be acid gases, with some contribution from the organic irritants likely to be present, particularly under vitiated combustion conditions. Although different sensory irritants stimulate the nociceptors by different biochemical mechanisms, it is likely that the effects of different chemical species will be broadly additive up to a particular level, above which the pain response is likely to reach saturation.[62]

8.6.5 Estimates of lethal toxic potency for natural and synthetic polymers under different fire conditions using rodents, and contribution to overall toxic potency from major toxic gases

Small-scale toxicity tests have been carried out for a range of materials using rats to measure LC_{50} concentrations, mainly under non-flaming oxidative decomposition conditions and well-ventilated flaming combustion conditions. These results can therefore be used to compare the generic lethal toxicity of different materials decomposed under similar conditions. The primate experiments already described have established that, at least for a limited range of materials, the main incapacitating toxic effects can be understood in terms of asphxyiant gases and irritants. Where rodent experiments have included measurement of the major toxic gases present it should also be possible to estimate the contributions to overall lethal toxic potency using LC_{50} data in rats for each gas. In order to do this it has been necessary to obtain data on the lethal exposure doses of each individual toxic gas and their interactions in mixtures. These data have been used to develop calculation models to allow for the interactions between the different toxic gas mixtures present. The basic models used for this are called N-gas FED models and are described in the next section. Because the standard exposure period for combustion toxicity experiments is

30 min, the N-gas models use 30 min LC_{50} concentrations for the gases considered. This also includes deaths both during exposure and during a 14 day post-exposure period, which is important for gases causing lung inflammation.

N-gas models for predicting lethality (LC_{50} concentrations) in rats following a 30 min exposure

The main concepts in these models are similar, but they differ somewhat in terms of which factors are considered and in the ways the various interactions are handled. The models estimate the FED for lethality for rats in terms of the concentration of each toxic gas present, expressed as a fraction of the LC_{50} concentration. The basic concept is that fractions of lethal doses of almost all gases are directly additive. Thus if half the lethal 30 min concentration of carbon monoxide is present with half the 30 min lethal concentration of hydrogen cyanide, then exposure of rats to this mixture for 30 min will on average result in the deaths of half the animals. Deaths are considered both during exposure and over a post-exposure observation period of up to 14 days. It is considered that in terms of overall lethality, the effects of asphyxiant gases (carbon monoxide, hydrogen cyanide and low oxygen hypoxia) are additive with the effects of irritant gases (acid gases such as hydrogen chloride and nitrogen dioxide and organic irritants such as formaldehyde). It is recognised that carbon dioxide modifies the toxicity of other gases and this is treated differently in different models. It is also recognised that nitrogen dioxide has some protective effect against hydrogen cyanide toxicity due to methaemoglobin formation (see Chapter 4).

Levin's N-gas model for predicting FED for lethality in rats

The N-gas model developed by Levin *et al*.[41,42,63] is based upon a number of LC_{50} experiments on individual asphyxiant and irritant gases, and experiments on various concentration mixtures of two or even three gases. The key precepts of the model are as follows:

- Fractions of lethal doses of almost all gases are directly additive.
- Based upon combination experiments of carbon monoxide and carbon dioxide it is considered that carbon dioxide enhances the lethal toxicity of carbon monoxide, with a maximum effect at a concentration of 5% carbon dioxide. Above 5% carbon dioxide the enhancement of carbon monoxide toxicity decreases. This effect is handled in the N-gas equation by the use of constants m and b, which represent the slope and intercepts of the combination gas toxicity curve.[63]
- In a more recent version of the model, the corrective terms are added for the protective effect of nitrogen dioxide on hydrogen cyanide toxicity.[42] Versions of the model are also considered for predicting deaths during exposure and combined deaths during and after exposure.

Table 8.3 Constants and LC_{50} concentrations for gases used in the Levin N-gas model

Gas	LC_{50} concentrations for 30 min exposures plus 14 days post-exposure period
For $[CO_2] \leq 5\%$	$m = -18$ and $b = 122\,000$
For $[CO_2] > 5\%$	$m = 23$ and $b = -38\,600$
Hypoxia – oxygen depletion	$21 - 5.4 = 15.6\%$ depletion
HCN	150 ppm
HCl	3700 ppm
HBr	3000 ppm
NO_2	200 ppm

The current version of the N-gas model[42] for total deaths (during and after exposure) is as follows:

$$\text{FED} = \frac{m\ [\text{CO}]}{[\text{CO}_2] - b} + \frac{21 - [\text{O}_2]}{21 - \text{LC}_{50}\ \text{O}_2} + \left(\frac{[\text{HCN}]}{\text{LC}_{50}\ \text{HCN}} \times \frac{0.4[\text{NO}_2]}{\text{LC}_{50}\ \text{NO}_2}\right) + \frac{0.4[\text{NO}_2]}{\text{LC}_{50}\ \text{NO}_2} + \frac{[\text{HCl}]}{\text{LC}_{50}\ \text{HCl}} + \frac{[\text{HBr}]}{\text{LC}_{50}\ \text{HBr}} \quad 8.4$$

The constants for Equation 8.4 are given in Table 8.3.

The N-gas equation works reasonably well and is based upon some very comprehensive experimental data obtained from rats for key gas interactions. However, although carbon dioxide has been shown to exert synergistic effects on the toxicity of several other gases, a carbon dioxide correction is applied only to carbon monoxide, on the basis that carbon monoxide is likely to be the major toxic gas present. Also, the correction of hydrogen cyanide toxicity for the protective effect of nitrogen dioxide as expressed in the equation works only for the case of 200 ppm nitrogen dioxide. As the term is currently expressed a low level or no nitrogen dioxide would negate hydrogen cyanide toxicity, which is incorrect, while a higher level than 200 ppm would enhance it, which is also incorrect. In practice nitrogen dioxide is present at low concentrations during fires and the major oxide species is nitric oxide.[55] Another problem is that in fire gas atmospheres organic irritants can be major causes of lung inflammation and death, and these are omitted from the analysis. The effect of low oxygen hypoxia is also assumed to be linearly related to decreased oxygen concentration, when in practice it is known to be non-linear (Chapter 4).

Purser model for predicting FED for lethality in rats

The Purser rat lethality model[1] is based upon the same general concepts as the N-gas model and makes use of the rat LC_{50} data for individual gases and gas

interactions obtained mainly by Levin *et al.*[41,42,63] and Hartzell *et al.*[64] The key precepts of the model are as follows:

- Fractions of lethal doses of all gases except carbon dioxide are directly additive.
- The main effect of carbon dioxide is considered to be a multiplicatory effect on the rate of uptake of other gases depending upon the extent of carbon dioxide-driven hyperventilation. In addition it is considered that once animals are incapacitated, carbon dioxide induced respiratory acidosis enhances the metabolic acidosis already present, providing an additive toxicity factor.
- Low oxygen hypoxia is usually a minor factor in small-scale rodent toxicity experiments and can be ignored unless oxygen concentrations are allowed to decrease below 12%. At low levels an additive term can be used. An exponential functions has been developed to allow for the effects of oxygen at low concentrations.
- A correction for the protective effect of nitric oxide and nitrogen dioxide on hydrogen cyanide toxicity due to methaemoglobin formation can be made if necessary and for the additive effect of other nitriles present.
- It is considered important to make allowance for the effect of all inorganic acid gases present and for organic irritants.

The estimated FED for lethality in rats for a 30 min exposure and defined set of toxic gas concentrations is calculated as follows:

$$\text{FED} = \left(\frac{[\text{CO}]}{\text{LC}_{50}\ \text{CO}} + \frac{[\text{CN}] - [\text{NO}_x]}{\text{LC}_{50}\ \text{HCN}} + \frac{[\text{each acid gas}]}{\text{LC}_{50}\ \text{each gas}} + \frac{[\text{each organic irritant}]}{\text{LC}_{50}\ \text{each organic irritant}} \right) \times V_{\text{CO}_2} + A + \frac{1}{\text{hypoxia function}} \qquad 8.5$$

where: V_{CO_2} is a multiplication factor for CO_2-driven hyperventilation $= 1 + (\exp(0.14 \times [\text{CO}_2]) - 1)/2$, A is an acidosis factor $= ([\text{CO}_2] \times 0.05) - 0.02$, hypoxia function $= \exp(8.13 - 0.54 \times [21 - \text{O}_2])$, [CN] represents the concentration of cyanide, and [NO_x] represents the summed concentration of NO and NO_2.

Where data on organic irritant concentrations are absent it is recommended that a contribution to the overall FED should be derived from an estimate of the total yield of organic products. The FED component for organic irritants (FED_{org}) is then estimated as:

$$\text{FED}_{\text{org}} = \frac{\text{mass loss concentration of organic material} \times \text{\% carbon present as organic carbon}}{35}$$

FED_{org} is then substituted for the organic irritant term in Equation 8.5.

If these data are unavailable, an FED_{org} of 0.35 should be used for non-flaming decomposition and 0.105 for vitiated or inefficient combustion, with

Table 8.4 LC_{50} concentrations for gases used in the Purser LC_{50} FED N-gas model

Gas	LC_{50} concentrations for 30 min exposures plus 14 days post-exposure period (ppm)
CO	5400
HCN	165
HCl	3800
HF	2900
HBr	3000
SO_2	400
NO_2	170
Hypoxia (using function)	$21 - 5.4 = 15.6\%$ depletion

0.035 for well-ventilated combustion at the LC_{50} mass loss concentration for the material or product under test. If the concentrations of the irritants present and their lethal exposure doses are known, then the equation can be solved fully. Where unknown irritants are present the equation enables the maximum LC_{50} to be predicted based upon the asphyxiant gases and a generic expression for overall irritants. The LC_{50} concentration values used for the Purser LC_{50} FED model are shown in Table 8.4.

Application of LC_{50} N-gas models to rat lethality data from small-scale combustion toxicity tests

A number of different combustion toxicity test methods have been used with rats, mostly in the 1970s and 1980s to estimate the lethal toxic potency of the effluents from a range of different natural and synthetic polymeric materials. Unfortunately few of these had involved LC_{50} concentration measurements in combination with comprehensive measurement of the chemical composition of the atmospheres or the mass loss concentrations of the materials tested. Also, few have been conducted under conditions that can be readily correlated with those in full-scale fires, and for most methods the composition of the test atmosphere and the decomposition conditions change continuously during a test run. Issues relating to the test decomposition conditions are discussed in detail in Chapter 14, but three methods used have provided some data that can be used to determine LC_{50} concentrations under reasonably constant and well-defined combustion conditions coupled with measurements of the concentrations of at least a few of the major toxic gases. Where these data are used to indicate the possible LC_{50} concentrations in full-scale fires it is essential to examine carefully the relationship between the decomposition conditions in the test and those in the large-scale fire scenarios of interest. However, in order to examine

the validity of the rat lethality LC_{50} N-gas models, the exact decomposition conditions are less important. The main requirement is that a mixed fire effluent of constant composition is produced containing a reasonably typical mix of fire effluent gases and particulates, including those used in the model.

Probably the largest database of rat lethality data for different materials was generated using the University of Pittsburgh toxicity test method.[59,60] Unfortunately, as already mentioned, the method involved ramp heating of a static sample under a stream of air and is of limited value, because the conditions, identities and yields of products change continuously throughout the test exposure as the specimen is heated and the decomposition mode changes from non-flaming to flaming. The effluent composition and sample mass measurements are also limited and the animals are not retained for a 14 day post-exposure observation period.

More useful are the results obtained by Levin *et al.*[65] using the then National Bureau of Standards cup furnace method ('Pott's Pot') (see Chapter 12). This method involved decomposing samples of different mass in a crucible furnace under non-flaming oxidative thermal decomposition conditions at a temperature 25 ºC below the auto-ignition temperature of the specimen and also under flaming conditions at 25 ºC above the auto-ignition temperature. The effluent generated from the crucible passed directly into an enclosed 200 litre volume chamber to which groups of six rats were exposed nose-only. Exposure began as the sample was dropped into the crucible furnace, so in practice the composition of the test atmosphere to which the rats were exposed was not constant but increased in concentration for a period as the specimen was decomposed. For flaming exposures there was also a period during which products of non-flaming decomposition were generated before ignition occurred, but this was usually quite short. Exposure concentrations of the major asphyxiant gases (carbon monoxide, carbon dioxide, oxygen and hydrogen cyanide) were measured continuously and the stated exposure concentrations were averaged over the 30 min exposure period. Animal deaths were scored during the exposure period plus a 30 min post-exposure period (scored as within exposure deaths) and also for the exposure period plus a 14 day post-exposure period. In general this means that within-exposure period deaths are likely to be due primarily to the effects of asphyxiant gases, while exposure plus 14 days includes both asphyxiant deaths occurring during and immediately after exposure and deaths resulting primarily from lung oedema and inflammation caused by irritants, which typically occur over a period of a few hours after exposure to 14 days. The test material exposure concentrations are reported on a mass charge basis.

For a more recent set of experiments the crucible furnace was replaced by a radiant furnace, which is the basis for the current NIST toxicity test method.[66] For this method the specimen, in the form of a flat strip, is irradiated from above by two angled radiant heaters. The effluent rises through a slit between the heaters into the enclosed 200 litre chamber, while replacement air circulates

back into the air space between the sample and the heater via two slits at each end of the heated area. The main decomposition mode is flaming combustion, and as with the crucible furnace method the initial decomposition is under non-flaming conditions until the specimen ignites, followed by a period of flaming until the specimen is extinguished, and a subsequent period during which off-gassing may occur from any residue. The basic exposure procedure is the same as for the cup furnace method, involving a total 30 min exposure period over which the gas concentrations are averaged. The mass loss rate of the specimen is also measured and the exposure concentrations are reported on both a mass charge and mass loss basis.

Another method for which some useful rat lethality data have been generated is the DIN 53436 tube furnace method.[67,68] This method represents an early version of the concept used for the ISO 19700 test method, in which the sample in the form of a strip is decomposed continuously in a stream of air, producing a dynamic steady-state decomposition condition with a constant atmosphere composition to which the rats are exposed nose-only over a 30 min period (plus 14 day post-exposure observation period). This method has mostly been used for non-flaming decomposition, although some flaming decomposition experiments have been performed.[69] Unfortunately the test atmosphere composition measurements made were somewhat limited.

For the NBS cup-furnace method and the NIST radiant method, the flaming combustion conditions vary somewhat depending upon the size and behaviour of the specimen. In relation to the description of fire types in Chapter 2 the combustion conditions in these tests can be classified approximately based upon the carbon dioxide:carbon monoxide ratios obtained. In practice (for non-fire retarded materials), for different materials and specimen masses they vary over a range from well-ventilated, through an equivalence ratio of around unity, to slightly vitiated combustion conditions. For the DIN 53436 experiments the conditions were generally rather vitiated flaming, at high furnace temperatures more or less simulating post-flashover vitiated combustion conditions.

In the following section use has been made of data from these tests to compare measured rat LC_{50} concentrations (exposure plus 14 days) with LC_{50} concentrations calculated from the measured atmosphere compositions using the Levin N-gas LC_{50} calculation method and the Purser LC_{50} calculation method. The materials tested, together with the actual measured and calculated LC_{50} concentrations are listed in Table 8.5.

Figure 8.9 shows the actual measured rat LC_{50} concentrations plotted against those calculated using the Levin (N-gas) method. Linear regression lines have been fitted for the non-flaming and for the flaming data. The 'perfect fit' 45 line is marked for comparison. The results show a reasonably good relationship between the actual rat LC_{50} concentrations and those calculated using the Levin N-gas LC_{50} calculation method ($R^2 = 0.6913$) for materials decomposed under flaming conditions. The fit is improved if one outlier (flaming polystyrene) is

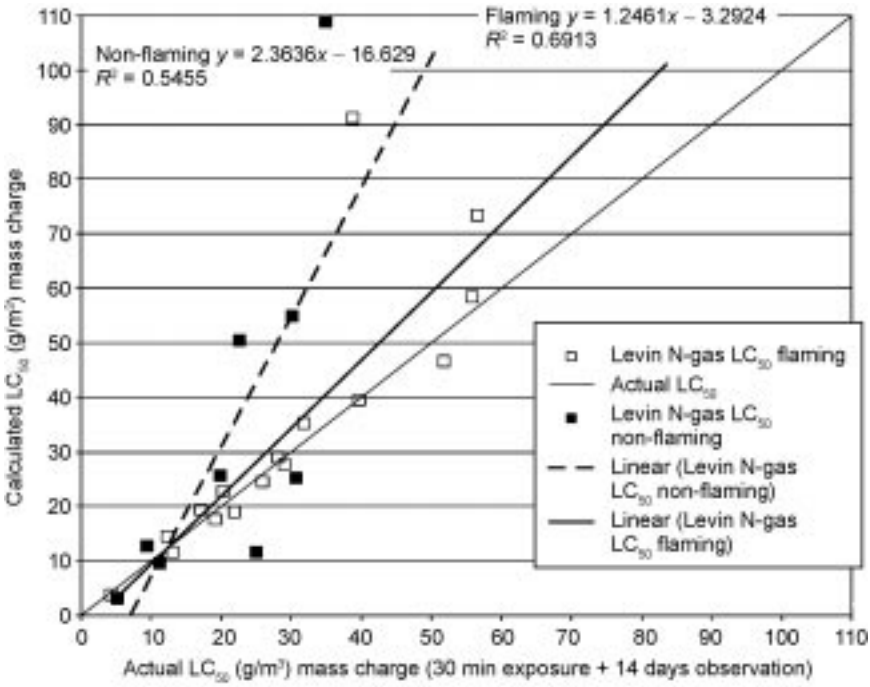
Table 8.5 LC_{50} concentrations (exposure plus 14 days, mass charge) for materials tested in the NBS cup furnace, NIST radiant and DIN 53436 apparatus

	Non-flaming LC_{50}			Flaming LC_{50}		
	Acutal	Purser	Levin	Actual	Purser	Levin
NBS cup furnace						
Acrylonitrile butadiene styrene (ABS)	30.9	20.8	25.0	19.3	17.0	17.4
Douglas fir (DFIR)	22.8	25.8	50.2	39.8	40.9	39.2
Flexible polyurethane foam (FPU)	35.0	30.3	108.6	20.3	21.3	22.5
Modacrylic (MOD)	5.3	2.8	2.9	4.4	2.9	3.5
Polyphenylsulphone (PPS)	9.5	8.3	12.6	–	–	–
Polystyrene (PS)	–	–	–	38.9	32.1	91.0
Polytetrafluoroethylene (PTFE)	–		–	–	–	–
Polyvinylchloride (PVC)	20.0	21.4	25.4	17.3	17.3	17.4
Polyvinylchloride/zinc ferrocyanide (PVCZ)	11.3	9.2	9.3	–	–	–
Red oak (REDO)	30.3	35.0	54.6	56.8	60.4	73.2
Rigid polyurethane foam (RPU)	–	–	–	13.3	11.0	11.4
Wool	25.1	10.6	11.3	28.2	25.2	28.8
NIST radiant furnace						
Douglas fire rad (DFIRrad)				56.0	58.9	58.3
Rigid polyurethane foam (RPUrad)				22.0	16.8	18.7
Flexible polyurethane foam (FPUrad)				52.0	46.3	46.4
PVC (PVCrad)				26.0	22.8	24.4
Vinyl fabric (VFrad)				32.0	32.4	35.0
Melamine (Melrad)				12.5	14.4	14.2
DIN tube furnace 850 °C						
Scot's pine (*Pinus sylvestris*) (SP)				29.2	23.9	27.4

removed ($R^2 = 0.9392$). For non-flaming decomposition data the fit is not very good ($R^2 = 0.5455$).

Figure 8.10 shows the results for the Purser LC_{50} calculation method plotted against the same rat LC_{50} data. The results show a good fit for the flaming data ($R^2 = 0.9707$) and a reasonably good fit for the non-flaming data ($R^2 = 0.7004$).

The models are intended to be general, and therefore applicable to all forms of combustion atmosphere (both flaming and non-flaming). Pooling the non-flaming and flaming data gives the results shown in Fig. 8.11 for the two different calculation models. The overall findings are that both models provide reasonably good predictions of actual rat LC_{50} concentrations using measured concentrations of a small number of key toxic gases as input data. This is especially true for flaming decomposition, for which the composition of the atmospheres is much less complex than under non-flaming conditions, consisting mainly of the common asphxyiant gases (for polymers containing C, H, O and N), with the addition of some irritant acid gases (for polymers

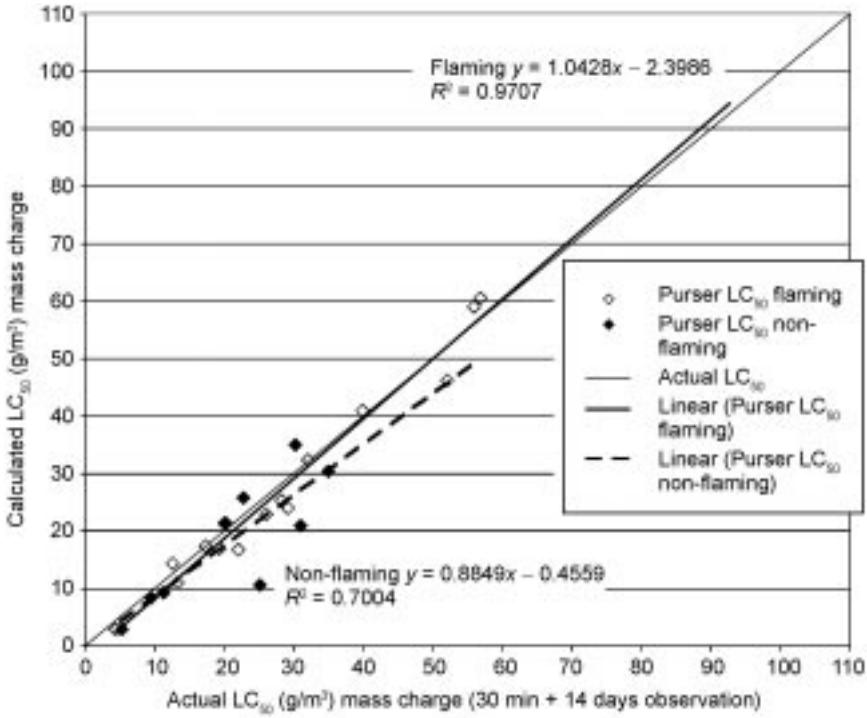


8.9 LC_{50} concentrations calculated using the Levin N-gas model compared with measured rat LC_{50} concentrations for different materials decomposed under non-flaming and flaming combustion conditions.

containing N, F, Cl, Br, P or S). Since both models are based primarily on an additive fractional effective dose concept, it also demonstrates that the toxic effects of these gases are primarily additive, and in particular that the lethal effects of the asphyxiant gases during exposure can be considered approximately additive with the lethal effects of irritants on the lung during the post-exposure period up to 14 days (but mainly during the first 48 hours after exposure).

This is important because it demonstrates that for a wide range of materials (with two exceptions), the toxic effects of fire effluent mixtures can be predicted from this small set of gases using relatively simple additive models, and that (especially for flaming combustion conditions) there is no evidence for any major unknown acute toxic effects other than the asphyxiant and irritant effects predicted from these few mixed gases. These results therefore confirm the more detailed findings from the primate work for a much wider range of materials tests.

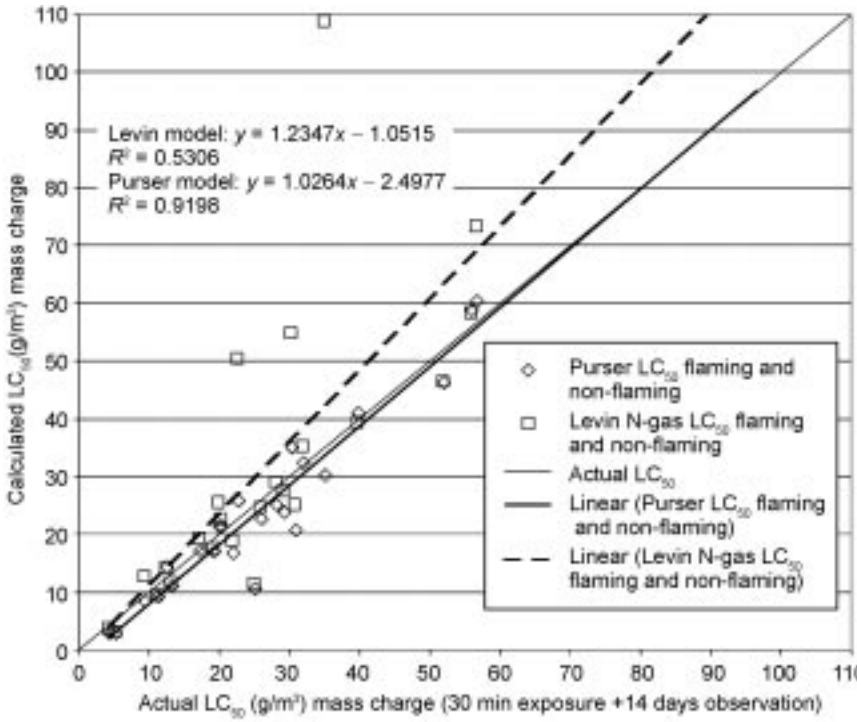
Comparing the two models in more detail, the Levin N-gas model is more empirically based upon a detailed and very valuable set of 30 min rat LC_{50} studies of the effects of individual fire gases and different gases mixtures, to which a set of additive FED fractions were fitted and functions generated to derive constants for the effects of carbon dioxide and interactions between nitrogen dioxide and



8.10 LC_{50} concentrations calculated using the Purser LC_{50} model compared with measured rat LC_{50} concentrations for different materials decomposed under non-flaming and flaming combustion conditions.

hydrogen cyanide. The Purser model also assumes basic additivity between the FEDs of the main toxic gases, but differs from the Levin model in attempting to use a more physiologically based approach. The main differences between the models are the treatment of carbon dioxide, low oxygen hypoxia and organic irritants. The Purser model gives more weight to the effect of carbon dioxide on V_E, whereby increasing hyperventilation at higher carbon dioxide concentrations increases the rate of uptake of the other toxic gases. On the other hand less weight is applied to the hypoxic effects of oxygen depletion, which is arranged to have little effect until oxygen concentrations approach 5–6%, as observed experimentally. To some extent the greater weight given to hypoxia in the Levin model compensates for the lower weight given to carbon dioxide in terms of the predicted effects of the models.

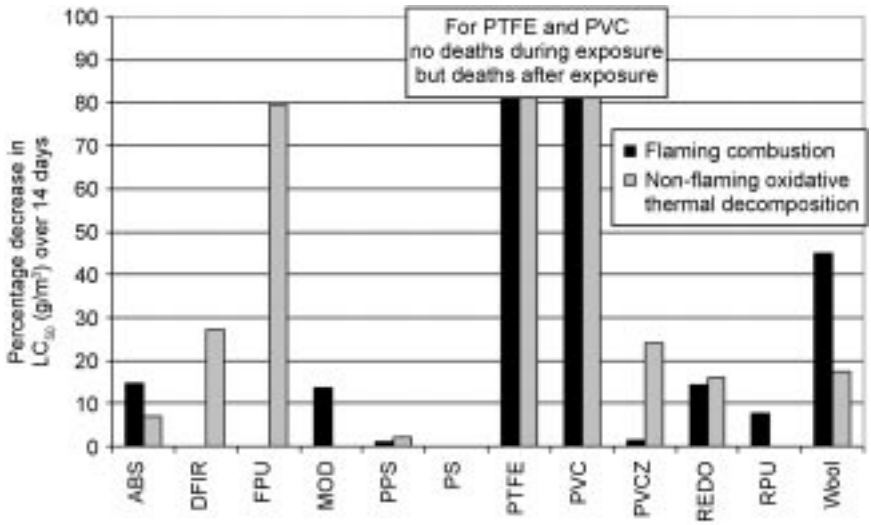
Another fairly important difference between the models is that the Levin model ignores the effects of organic irritants. Based upon both observed effects in humans and primates, and the results in the rats and mice (particularly the post-exposure deaths), it is evident that the mixed organic irritants produced, particularly under non-flaming oxidative thermal decomposition conditions (but



8.11 LC_{50} concentrations calculated using the Levin N-gas and Purser LC_{50} models compared with measured rat LC_{50} concentrations for different materials using pooled data for both non-flaming and flaming combustion conditions.

also to some extent under vitiated flaming combustion conditions), make an important contribution to overall lethal toxicity. This is particularly the case where the organic atmosphere component is high in relation to that of the asphxyiant gases. Unfortunately, it is difficult to obtain fully quantitative measurements of the concentrations of all the potentially irritant organic compounds in fire effluent mixtures, and as already stated, based upon the mouse irritancy studies, it is considered that a number of important irritant species remain unidentified. Such GC-MS studies as have been performed have shown that the mix of compound formed under specific decomposition conditions is often relatively similar for different materials, containing a range of species common to most materials, with the addition of a number of species more specifically related to the molecular structure of the material. On this basis, the approach taken for the Purser model is to use a generic term for the total organic content of the atmosphere, calculated from the organic fuel mass loss multiplied by the fraction of fuel carbon present in the form of organic carbon.

This term accounts for most of the differences between the LC_{50} concentrations predicted by the Levin and Purser models, giving a better fit to the data



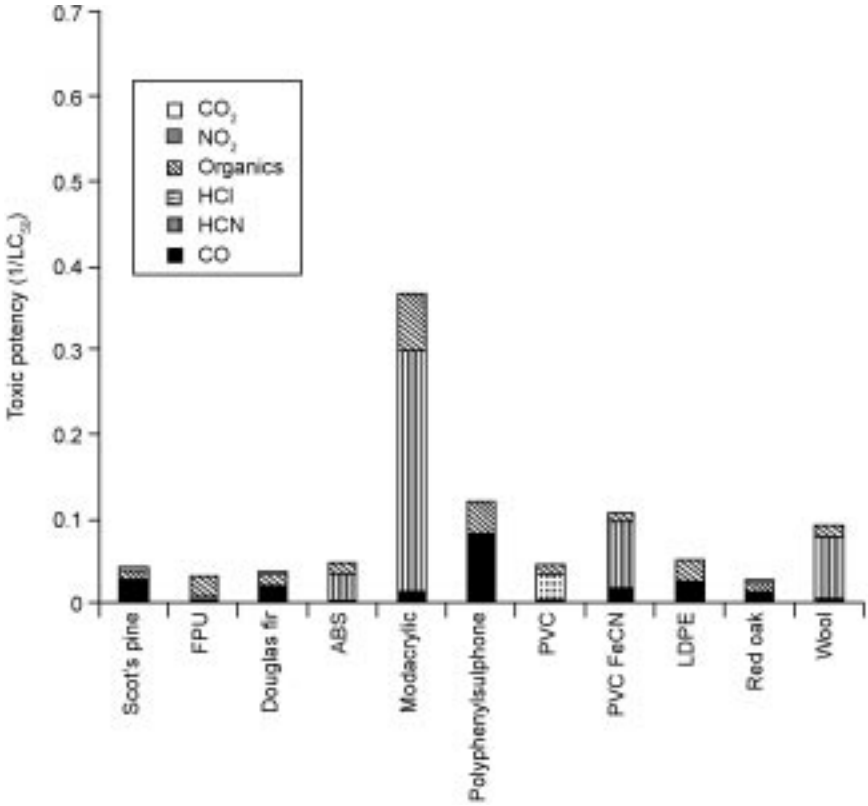
8.12 Percentage decrease in LC_{50} concentration (i.e. increase in toxicity) over the 14 day post-exposure period. (See materials listing in Table 8.5.)

for the Purser model especially for non-flaming decomposition conditions, for which approximately a third of the observed toxicity can be attributed to the effects of organic irritants on the lung. For these experiments carried out on rats, the effect of organic irritants is much lower under flaming conditions, with the exception of polystyrene, which produces a dense smoke under flaming conditions that is rich in particulates and organic irritants including styrene monomer. However, most of these experiments were conducted under relatively efficient combustion conditions, and it is considered that at higher equivalence ratios the contribution from organic irritants might be somewhat increased.

An indication of the extent to which organic irritants contributed to overall toxicity in the NBS cup furnace experiments is given in Fig. 8.12. This shows the percentage decrease in LC_{50} (i.e. increase in toxicity) between exposure plus 30 min and exposure plus 14 days. This represents the increase in toxicity resulting from post-exposure toxic effects, which are mainly lung inflammation caused by inhalation of irritants. The results show that for most materials, the toxicity increased significantly during the post-exposure period under non-flaming decomposition conditions, and also for a number of materials under flaming decomposition conditions.

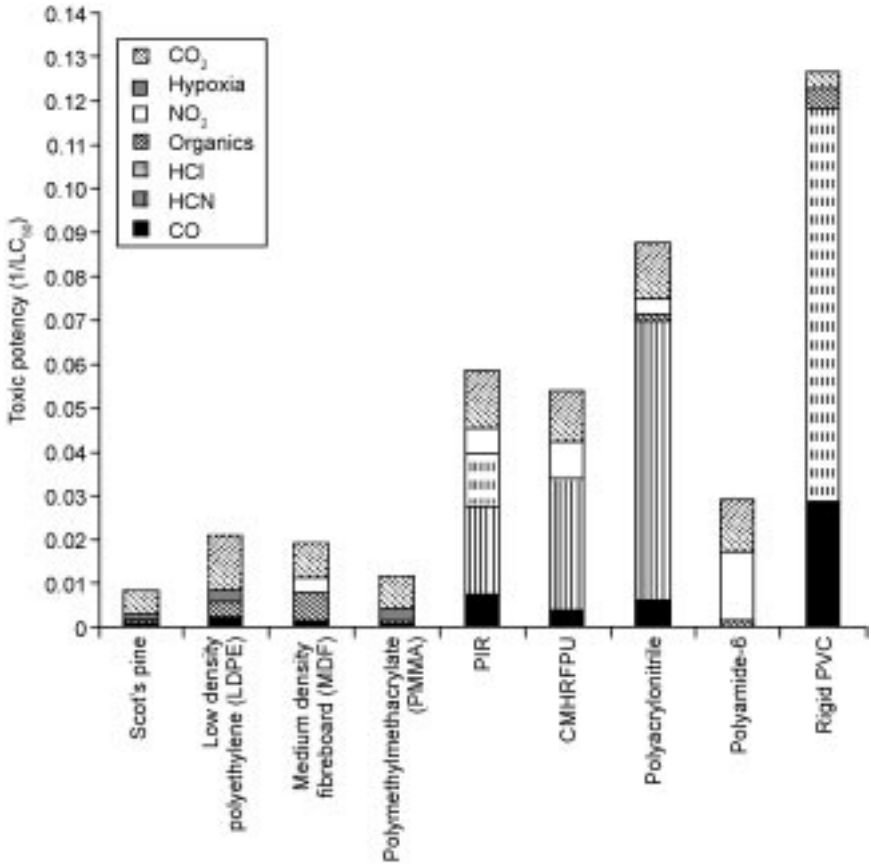
Contribution of different toxic gases to overall lethal toxic potency from different materials

Figures 8.13–8.16 illustrate the extent to which different toxic species contribute to the overall toxic potency of different materials for the main different fire



8.13 Toxic potencies ($1/LC_{50}$) and contributions from different toxic atmosphere components under non-flaming oxidative thermal decomposition conditions.

types described in Chapter 14. The materials for which results are shown in Figs 8.13–8.16 are as follows: acryolonitrile butadiene styrene (ABS), combustion modified high resilience flexible polyurethane foam (CMHRFPU), Douglas fir, low density polyethylene (LDPE), medium density fibreboard (MDF), modacrylic, polyacrylonitrile (PAN), polyamide 6, polyisocyanurate (PIR), polymethylmethacrylate (PMMA), polyphenylsulfone, polystyrene, poly(vinyl chloride) (PVC) flexible and rigid, polyvinylchloride/zincferrocyanide PVCFeCN, Red oak, Scots pine, flexible polyurethane (FPU), wool. The contributions from different chemical species are calculated using the Purser LC_{50} FED model. The chemical atmosphere composition data are from the NBS cup furnace and ISO19700 tube furnace.[55,70] Figure 8.13 shows the results for non-flaming oxidative thermal decomposition (mostly NBS cup furnace data). The data are plotted as toxic potency ($1/LC_{50}$), so that the higher the bar the greater the toxicity. The shading then illustrates the contribution to the overall toxic potency from each atmosphere component.



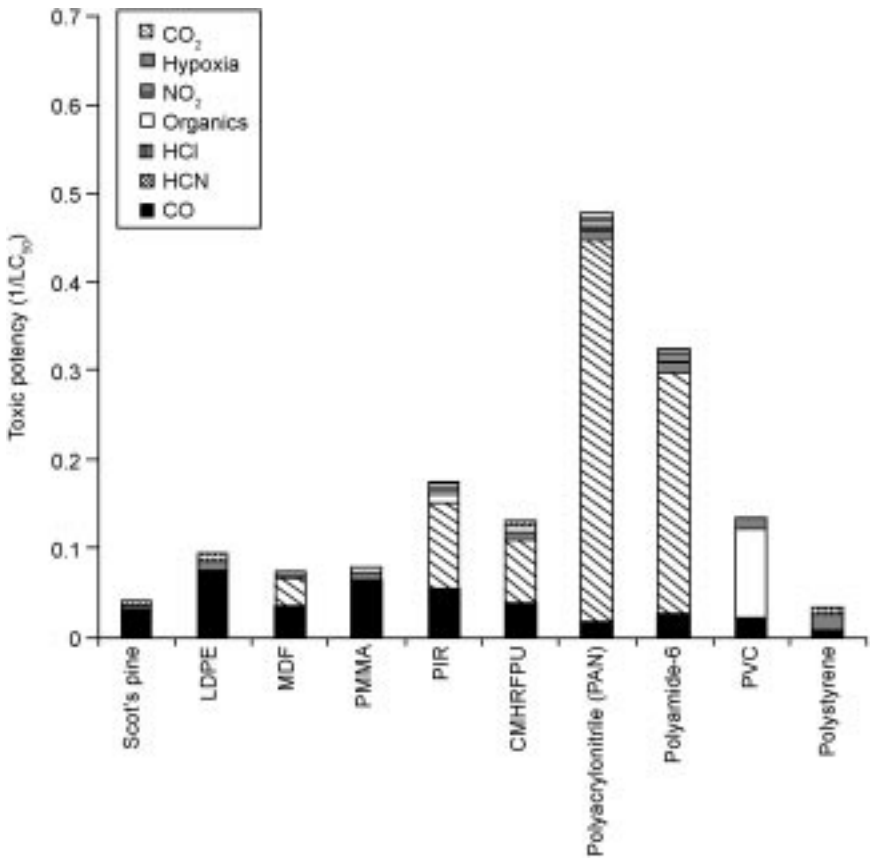
8.14 Toxic potencies ($1/LC_{50}$) and contributions from different toxic atmosphere components under well-ventilated flaming combustion conditions.

Under non-flaming oxidative thermal decomposition conditions toxic potencies are relatively high, ranging from 0.029 to 0.37 (LC_{50} 34.8–3.8 g/m^3). The main toxic components are hydrogen cyanide, with a small contribution from nitrogen dioxide (for nitrogen-containing polymers), carbon monoxide and organic irritants for most materials, and hydrogen chloride (for PVC).

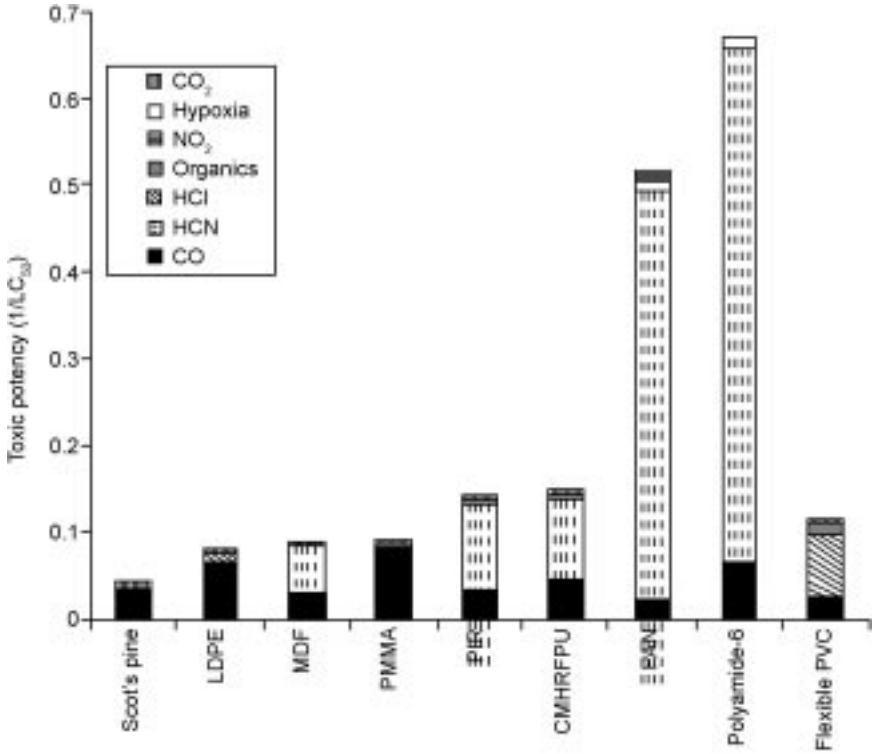
For well-ventilated flaming the yields of toxic products are low, so that toxic potencies are generally low. The results in Fig. 8.14 are therefore plotted at a scale five times higher than those for non-flaming decomposition. The overall potencies range from around 0.008 to 0.13 (LC_{50} 118–7.9 g/m^3). A variety of different components contribute to the overall potencies, but for well-ventilated combustion carbon dioxide is always important as a cause of hyperventilation. In this sense it is not directly toxic itself, but magnifies the toxicity of the other components by increasing their rate of uptake. It also has a direct toxic effect at

high concentrations owing to acidosis. For nitrogen-containing materials hydrogen cyanide is important, but nitrogen dioxide also makes a contribution, since the yields of nitrogen oxides are highest under well-ventilated combustion conditions. Carbon monoxide is also important for some materials, and for materials containing chorine, both carbon monoxide and hydrogen chloride are significant components of the overall toxicity (due to inefficient combustion resulting from the gas phase effect of chlorine). Hypoxia and organic irritants also make a contribution at high mass loss concentrations.

As compartment fires grow the combustion conditions become increasingly vitiated (see Chapter 14). Not only does the overall fuel mass loss concentration in the fire effluent increase, but the yields of toxic gases per unit fuel mass consumed increase considerably (Fig. 8.15). The overall toxic potencies are therefore considerably higher than under well-ventilated combustion conditions (0.03–0.48) (LC_{50} 30.8-2.1). Carbon monoxide is a significant toxic component



8.15 Toxic potencies ($1/LC_{50}$) and contributions from different toxic atmosphere components for under-ventilated flaming combustion conditions.



8.16 Toxic potencies ($1/LC_{50}$) and contributions from different toxic atmosphere components for post-flashover under-ventilated flaming combustion conditions.

in all cases, with a contribution from carbon dioxide and organic irritants. For nitrogen-containing materials the toxicity is dominated by hydrogen cyanide, with a small contribution from nitrogen dioxide, and for PVC hydrogen chloride and carbon monoxide are the main toxic components with a small contribution from organic irritants. Polystyrene toxicity is heavily influenced by irritant organic particulates.

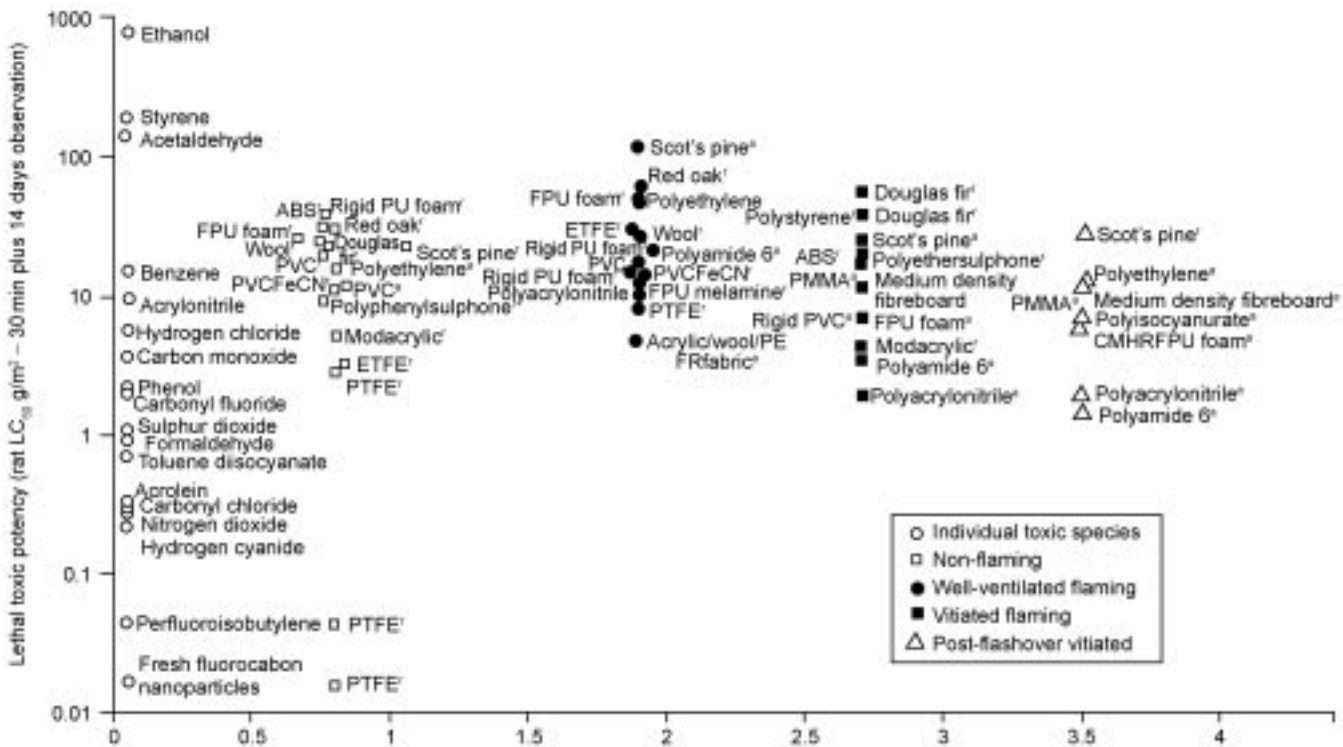
Under post-flashover vitiated combustion conditions (Fig. 8.16) the toxic potencies and patterns are similar to those under vitiated combustion conditions, but yields of carbon monoxide and hydrogen cyanide can be somewhat higher, so that toxic potencies for this set of materials range from 0.04 to 0.67 (LC_{50} 23.9–2 g/m^3). Two types of materials, fluoropolymers and certain phosphorus-containing materials, show toxic effects that cannot be accounted for in terms of simple asphyxiant gases and organic irritants.

Thermal decomposition and combustion products from fluoropolymers show a great range of toxic potencies, depending upon the precise thermal decomposition or combustion conditions. A detailed account is given in Purser.[71] At

decomposition temperatures above 650 ºC under both non-flaming and flaming decomposition conditions, lethal toxicity results from post-exposure airway and lung inflammation which can be explained in terms for the known major toxic products, including carbonyl fluoride, which hydrolyses to form hydrogen fluoride, and per-fluororisobutylene. As shown in Fig. 8.17, this results in a mass loss LC_{50} of between approximately 1 and 8 g/m^3. Below approximately 400 ºC fluoropolymers are relatively stable so that significant decomposition and toxicity do not occur, but between 400 and 650 ºC under specific conditions, a highly toxic, ultrafine particulate is produced with a very high toxic potency if inhaled. Freshly formed particulates are approximately 0.01 μm (10 nm) in diameter, and thus in the nanoparticle size range. When inhaled they penetrate into the deep lung interstitium, where an inflammatory reaction starts to occur within a few minutes. This is fatal to rats over periods of hours to days following exposure. The mechanism of toxicity is not fully understood, and may be a simple function of the particle size, or may be partly related to active surface chemistry of the particles (stable free radicals have been detected on the particle surface), and partly as a result of the particle size favouring delivery to and uptake by the lung interstitial cells.

Similar effects have since been reported for many types of ultrafine particles, particularly those containing different transition metals, which are known to become involved in oxidation reactions involving free radical formation. However, fluoropolymer particulate has a much higher toxic potency than other ultrafine particulates, with an LC_{50} concentration of 0.017 g/m^3. The fluoropolymer particulate is composed of a high molecular weight PTFE condensate. The ultrafine particulate rapidly condenses into agglomerates within a minute or so, with a particle size approximately ten times greater. This larger particulate is harmless, so the conditions of generation and exposure are critical to the atmosphere composition and toxicity. Extreme toxic potency has been observed under conditions where a fluoropolymer such as PTFE or tetrafluoroethylene/hexafluoropropylene copolymer (FEP) is heated for several hours at temperatures around 420 ºC under a stream of air, with rats exposed to the fresh particulate stream. Other conditions resulting in extreme toxicity involve heating at temperature between 450 and 650 ºC in an enclosed space (such as the NBS cup furnace apparatus), such that particulate fume is formed, released into the atmosphere and then recirculated back through a heated zone. In this way the ultrafine toxic fume is formed and continuously regenerated in the hot zone, so that the rats are exposed continuously to freshly generated toxic fumes.

It is therefore considered that extreme toxic effects are most likely to occur when fluoropolymers are decomposed within this temperature window of 400–650 ºC, under conditions where recirculation into a heated zone may occur. The extreme toxicity particulate is not formed from fluoropolymers containing hydrogen in the molecular structure, such as ETFE (ethylene tetrafluoroethylene copolymer). The extreme toxicity resulting from these nanoparticles released



8.17 Range of lethal toxic potencies (LC_{50} – 30 min exposure plus 14 days observation) for individual toxic species found in fire effluents and fire effluent mixtures from a range of materials ([r] rat LC_{50} data; [a] LC_{50} calculated from analytical data).

from fluoropolymers and other sources does raise potential toxicity issues for other materials formulated with nanoparticle additives if these nanoparticles are released in fire effluents.

Another unusual toxic effect has been observed for materials containing phosphorus and a trimethyolol propane polyol.[29,72] When decomposed thermally these materials form a caged biphosphorus ester in the gas phase, which has been found to cause epileptic-type seizures in rats. The effect was originally discovered in a flexible polyurethane foam formulated using a trimethylol propane polyol and containing a phosphate fire retardant additive. This was never marketed, but the same problem occurs with turbine lubricants used in certain marine applications and aircraft engines, which are also formulated with trimethylol propane polyols and tricresyl phosphate additives. Fortunately the toxic ester (trimethylol propane phosphate – TMPP) is not formed from other polyols such as pentaerythritol. Although the pattern of toxicity differs somewhat from that of other materials, the toxic product is formed at relatively low yields, so that the lethal toxic potency is not significantly different from other materials. Acute neurotoxic effects have not been observed with other phosphate-containing materials, and the main combustion product from phosphates is phosphoric acid, although somewhat high lethal toxicity was observed in some DIN furnace experiments involving a phosphate fire retardant used for treating cotton.[73] Given the extreme neurotoxicity of some phosphate esters it is considered that further research in this area may be indicated.

Range of lethal toxic potencies from materials and products decomposed under different combustion conditions

Having obtained rat lethal toxic potency data under both non-flaming and flaming decomposition conditions, and having established that the lethal toxic potency for materials can be calculated from chemical analysis data on effluent atmospheres with a good degree of accuracy, it is possible to establish the range of lethal toxic potencies from a wide range of materials decomposed under different combustion conditions occurring in different fire scenarios.

This is illustrated in Fig. 8.17, which shows the measured and calculated LC_{50} concentrations for materials decomposed under non-flaming oxidative thermal decomposition conditions, well-ventilated and under-ventilated combustion conditions (both pre-flashover and post-flashover (high temperature vitiated)). Also shown for comparison are the 30 min LC_{50} concentrations for individual toxic species found in fire effluents. It should be noted, as discussed in Chapter 12, that there remain differences in the ability of bench-scale methods to replicate individual fire conditions, in particular the pre- and post-flashover conditions (see Chapter 2), thus the information presented in Fig. 8.17 represents the best currently available, and not a definitive statement of the fire toxicity of each material under each fire condition.

The individual toxic species commonly found in fire effluents vary in acute toxic potency over a range of approximately five orders of magnitude from the most toxic – fresh PTFE nanoparticles (LC_{50} 0.017 g/m^3) to ethanol (765 g/m^3). Fire effluents from different materials contain mixtures of chemical species, including varying proportions of these toxic species. The lethal toxic potency (mass loss LC_{50} concentrations of fire effluents mixtures from different materials) ranges from PTFE which forms nanoparticles (LC_{50} 0.017 g/m^3) under non-flaming oxidative thermal decomposition conditions, to Scot's pine and similar cellulosic materials decomposed under well-ventilated flaming conditions at low equivalence ratios (0.5–0.8), giving an LC_{50} concentration of 119 g/m^3. In practice the lowest possible mass loss toxic potency (highest possible LC_{50} concentration) for any flammable material is limited to somewhere in the 120–150 g/m^3 range, because at these loadings carbon dioxide concentration and oxygen depletion are in the lethal range. This gives a maximum range of toxic potencies between different materials under different combustion conditions of around four orders of magnitude (a factor of 7060). However, if fluorocarbons are eliminated, the range becomes much more restricted, the maximum toxic potency being for polyamide-6 decomposed under post-flashover vitiated flaming conditions (LC_{50} 1.51 g/m^3), giving a range of approximately two orders of magnitude (factor of 79) between the most toxic and least toxic effluent atmospheres for common materials.

Another aspect evident from Fig. 8.17 is that in general the toxic potencies are lower under well-ventilated combustion conditions, and higher under non-flaming, and pre- and post-flashover under-ventilated conditions. Toxic

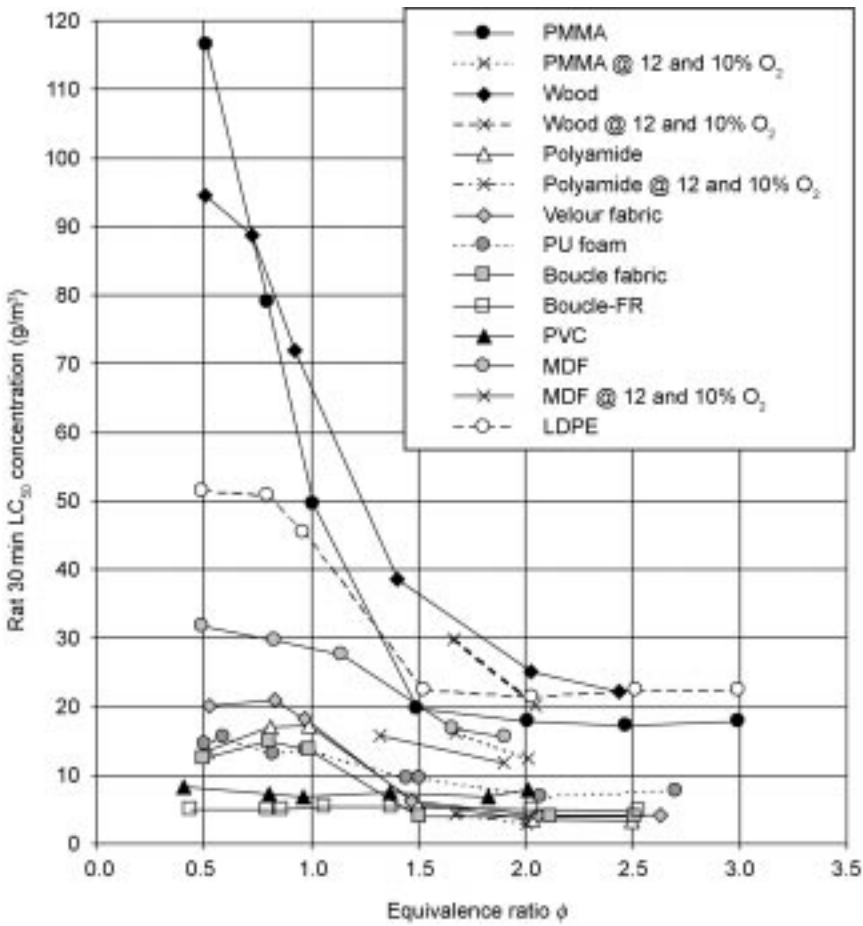
Table 8.6 Approximate LC_{50} concentrations (g/m^3) and lethal exposure doses (g/m^3 min) for common material classes under different fire conditions

Material	Non-flaming		Well-ventilated flaming		Under-ventilated flaming		Post-flashover under-ventilated flaming	
Fluoropolymers	0.17	0.51	~8	240	~8	240	5.4	162
Polyamide,	17	510	17	510	54		1.8	54
Modacrylic, polyacrylonitrile	5	150	12	240	4.4	132	1.0	60
Wool	25	750	28	840	4	120	4	120
Rigid polyurethane foam	40	1200	15	450	7	210	7	210
Flexible polyurethane foam	27	810	13	390	7	210	7	210
PVC	7	240	7	240	7	240	8	270
C,H,O polymers	17	510	70	2100	20	600	12	360
Cellulosics	24	720	119	3570	25	750	15	450

Approximate rat LC_{50} concentrations for 30 min exposure plus 14 days observation.

potencies for most materials are quite similar for pre- and post-flashover under-ventilated conditions, but can be somewhat higher under the higher temperatures in post-flashover conditions. Table 8.6 shows approximate LC_{50} concentrations and approximate lethal doses for common classes of materials under the four main fire conditions.

Flaming combustion conditions in compartment fires begin by being well ventilated and then gradually become more vitiated as the fire grows and the ventilation becomes limiting. Individual materials in fires are therefore first decomposed in well-ventilated conditions at low equivalence ratios, and the equivalence ratio increases as combustion becomes under-ventilated. The effect of this on lethal toxic potency is shown in Fig. 8.18 which shows plots of calculated LC_{50} (using the Purser N-gas model) against equivalence ratios for a



8.18 Variations in lethal toxic potency (LC_{50}) concentrations with combustion conditions in the ISO TS19700 tube.

set of materials combusted in the ISO TS19700 tube furnace. Most materials show a considerable increase in toxic product yields and overall toxic potency as the equivalence ratio increases.

8.6.6 Development of calculation methods for time to incapacitation on humans

The results of the rodent studies have been useful in establishing the small number of important toxic species produced by fire effluents from a wide range of materials, but in order to determine the toxic hazard to humans in full-scale fires it is necessary to compare the ASET with the RSET. Available safe escape time represents the time from ignition to that when conditions are such that occupants are no longer able to escape. In terms of toxic effects this is the time when occupants are incapacitated, either because the effects of smoke and irritants are sufficient to prevent effective escape, or because the exposure dose of asphyxiants is sufficient to cause loss of consciousness. The RSET includes the time required to escape, so that the effects of irritant smoke on walking speed and exit choice also influence the RSET. Details of the development of the calculation models for irritancy are discussed in Chapter 3 and for the development of calculation models for asphyxia in Chapter 4. The full set of human fire hazard calculation expressions is presented in Chapter 19. The final section of this chapter summarises the role of data from experiments on humans, other primates and rodents for the development of these models.

Behavioural and physiological effects of exposure to irritant smoke on escape capability

It is evident from fire incident investigations that the survival of human fire victims is heavily influenced by smoke exposure. During the early stages of a fire the effect may be simply behavioural, in that a building occupant may see smoke before becoming immersed in it. This affects behaviours such as whether or not to enter a smoke-logged escape route, or escape under a descending smoke layer. If a subject is immersed in smoke, the effects are both behavioural and physiological.[1] The physiological effects consist of reduced vision due to smoke obscuration and also the painful effects on vision and respiration of exposure to smoke irritants. These effects influence behaviour (decision to continue or turn back), and physical escape capability in relation to walking speed and wayfinding ability. The main source of guidance on the effects of smoke are derived from incident accounts and a small number of experiments on visibility and movement speed through smoke. These have the disadvantages that in none of them has the smoke composition been characterised, but the advantage is that they can be applied directly to the prediction of likely human performance. The only direct experiment on humans exposed to irritant smoke

involved smouldering decomposition of wood using a bee smoker.[74] Altogether these findings have been used to set acceptable generic tenability concentration limits for non-irritant and irritant smoke for fire engineering design purposes, and calculation expressions for walking speed against smoke optical density.[2,5,6]

Where consideration is given to irritant effluent mixtures from specific materials, or to effects of exposure to individual irritant chemical species in fire effluents such as acid gases, data are much more limited. It is not possible for ethical reasons to measure concentrations causing failure to escape or incapacitation in humans, or even in other primates, although some limited data are available for humans on the physiological and behavioural effects of exposure to CS riot control gases and pepper sprays,[20] which are designed to incapacitate by causing painful eye and respiratory tract irritancy, and from baboons on effects of hydrogen chloride and acrolein on escape capability, and for macaque monkeys on respiratory and operant task performance behaviour.[30,31] Other data used to set tenability limits are derived from occupational human exposures and industrial accidents, or from experiments using rodents.[75,76] Tenability limits for design purposes and methods for predicting effects on human walking speed of different irritant exposures are presented in Chapter 3. The range of uncertainty in predicting effects on humans is relatively wide for a variety of reasons as detailed in Chapter 4.

Behavioural and physiological effects of exposure to asphyxiant gases

Carbon monoxide

The effects of exposure to carbon monoxide have been extensively studied in humans over many years, through direct experimental exposures and effects of accidental incidents involving carbon monoxide gas or fire effluents mixtures containing carbon monoxide. During acute exposures to carbon monoxide there is a very good relationship between the severity of signs and symptoms and %COHb in the blood, which represent the 'dose' of carbon monoxide inhaled.[1,34,35] For this reason almost all human studies on carbon monoxide are reported in terms of %COHb, rather than simple carbon monoxide ppm $\times$ time exposure doses. Expressions have been developed for carbon monoxide uptake in humans in relation to exposure concentration, exposure time and a range of physiological variables such as activity level, V_E and body size.[77,78] With regard to signs and symptoms there are reports, mostly from accidental exposures, on the relationship between %COHb and severity of effects, but direct experiments on human capabilities in relation to %COHb are limited to relatively low (sub-incapacitating) exposure levels for safety reasons, since there is some risk of permanent brain damage at levels causing incapacitation.[79,80] Detailed experiments on neurophysiological, behavioural and cardiovascular effects of higher %COHb concentrations have been performed using macaque monkeys, and can be considered to apply directly to humans. By combining the

human and macaque data it is therefore possible to develop accurate calculation methods for uptake and effects of carbon monoxide on humans (see Chapter 4). However, there is considerable variation in susceptibility within the human population.

Hydrogen cyanide

As with carbon monoxide, the concentration of cyanide in the blood increases with time during exposure to hydrogen cyanide, but unfortunately the relationship between total blood cyanide concentration and incapacitating effects is not a simple one. Cyanide is also unstable in the blood, which causes difficulties in relating post-mortem blood cyanide concentrations to those at the time of death in cyanide poisoning fatalities. Despite these limitations, there are sufficient data to determine approximate blood levels associated with incapacitation and death. There is one account of an experimental human exposure to cyanide, and a number of studies have been made of cyanide concentrations in blood and tissues, mostly from intravenous or oral cyanide dosing. Detailed studies of the uptake of hydrogen cyanide with measurements of incapacitating physiological effects were made by Purser *et al.*, in macaques, and these have been used to develop a predicted calculation model for time to incapacitation in humans.[14,39] Owing to the smaller body size the calculation model is likely to be somewhat conservative for adult humans, but is considered to provide a good predictive model for resting infant humans and active adult humans.

Hyperventilatory and incapaciting effects of carbon dioxide

The relationship between inhaled carbon dioxide concentration and V_E has been measured directly in humans. The model used is an expression fitted to the data of Comroe *et al.*[81] Individual humans vary somewhat in their response. The incapacitating effects of high inhaled carbon dioxide concentrations have also been measured directly in humans.[82]

Low oxygen hypoxia

The calculation expression for time to incapacitation due to low oxygen hypoxia is derived directly from measurements of time of useful consciousness in humans exposed to low oxygen concentrations in decompression chambers.[43] In these experiments the oxygen concentration remains at 20.95% but the oxygen partial pressure decreases due to the decompression. This is supplemented by some data on exposures of humans to lowered oxygen concentrations at sea level barometric pressure.

Combined effect of asphyxiant gas mixtures

From the experiments on primates and rodents it has been established that carbon monoxide and hydrogen cyanide are directly additive in their asphyxiant toxic effects.[1,18] Since uptake of these gases is directly proportional to V_E, the rates of increase in exposure doses for both gases depend upon the proportional increase in V_E at different inhaled carbon dioxide concentrations. The interaction between carbon dioxide and low oxygen hypoxia is less simple, since hyperventilation is beneficial by increasing the rate of oxygen uptake. For this reason the FED of low oxygen hypoxia is treated as additive with the fractional hypoxic exposure dose from the other three gases.[1,14]

8.7 Conclusions

The threat to life from fire is most closely associated with a failure to escape. An established methodology in fire safety engineering uses the concept that the available safe escape time (ASET) must exceed the required safe escape time (RSET). The available safe escape time lasts until heat, smoke or toxic gases build up enough to prevent escape, while the required safe escape time becomes longer as smoke obscures the visibility or its irritant components impair escape. Once a fire victim becomes incapacitated and can no longer attempt escape, they will soon succumb to the lethal effects of carbon monoxide and heat, unless rescued. Thus it is essential to ensure that circumstances which lead to incapacitation are avoided. Incapacitation can result from inhalation of asphyxiants (HCN + CO) and irritant components of fire smoke (acid gases, isocyanates, aldehydes, particulates, etc.). The effects of these harmful components at different concentrations and over different exposure times have been established using a combination of results from accidental and experimental human exposures, and experimental studies in sub-human primates and rodents. From these data it has been established that incapacitating and lethal effects of fire gas exposures can largely be explained in terms of the additive effects of a small number of key irritant and asphxyiant gases. It has then been possible to develop and validate calculation models for time to incapacitation and lethality using a set of chemical composition data for the key toxic gases which can be applied to any fire effluent atmosphere for which the composition is known in terms of time–concentration curves for the key toxicants.

For bench-scale rodent toxicity tests these models show that the toxicity of fire effluents varies over two orders of magnitude as a function of material being burnt and the fire conditions (nitrogen-containing polymers such as polyacrylonitrile, and polyamide in under-ventilated fires having the highest toxic potencies, and materials such as wood, polyethylene and polypropylene in well-ventilated fires having the lowest toxic potencies). In general, oxidative pyrolysis and under-ventilated combustion produce the highest yields of toxic

products while well-ventilated flaming produces the lowest yields of toxic products. In terms of toxic potency there is one notable exception, in that the nanoparticles produced by PTFE under certain circumstances can produce effluents under non-flaming decomposition conditions with a toxicity up to 7000 times greater than wood burnt under well-ventilated conditions.

8.8 References

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9

In Vitro biological toxicity assessments for fire combustion products

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Abstract: A large range of polymers are used in building and mass transport interiors which release toxic products during combustion. *In vitro* biological toxicity assessment for fire combustion products offers a new method for the application of *in vitro* methods into a fire toxicity fields. This chapter describes the biological toxicity assessment for fire combustion products using the *in vitro* method. Several *in vitro* techniques are described for human cell exposure to fire effluents including the indirect (impinger) and direct (air/liquid interface using Harvard Navicyte chamber) exposure using passive and dynamic exposure method. A laboratory-scale vertical tube furnace arrangement is described for the generation of combustion products. A basic cytotoxicity mechanism describes the basic mechanism of substances acting at the cellular level which provides the fundamental basis for cell injury or cell death. A range of cytotoxicity assays which measure different toxic effects are described using an *in vitro* cytotoxicity assay. The end points to be measured in a toxicity assay are also described. These can be used to acquire data on thermal decomposition products and risk to humans. However, the application of *in vitro* toxicity testing has encountered a number of difficulties; several advantages and weaknesses of this method are also discussed. The *in vitro* biological toxicity assessment for fire combustion products area has become an emerging field which is challenging and promising. The need to evaluate and select materials which have fire resistant characteristics and low toxicity is of great importance. The toxicity information is an important part of fire hazard risk identification, fire prevention and protection as well as for public safety.

Key words: air/liquid interface, cytotoxicity of fire smoke, combustion products; human cell lines, *in vitro* biological toxicity, *in vitro* cytotoxicity assay, *in vitro* toxicology, *in vitro* exposure system, thermal degradation of polymers, vertical tube furnace.

9.1 Introduction

Research into combustion and fire toxicity is of great importance; however, owing to its complexity, problems are never adequately solved. The complexity in this area includes the difficulties in assessing adverse health effects and toxicity assessment because of the multiplicity of thermolysis products.[1,2] The

degree of toxicity depends on the chemical composition of the material, the fire environment and the burning stage of the fire: oxidative pre-ignition (non-flaming), well-ventilated flaming combustion or fully developed under-ventilated flaming. Added complexities include the toxicological interactions of combustion product mixtures; whether there are additive, synergistic or antagonistic interactions; and identification of the individual chemicals generated from fires and their associated toxicity.[3–5]

Currently combustion toxicity has been placed as a secondary consideration after the fire growth and decay as there is no simple tool to quantify the hazard. Traditionally, animal-based toxicology methods using rats, mice and primates have been used to assess the biological effects of combustion toxicity. Rats have been the principal test animals with an average duration of exposure of 30 min.[6] The primary end point consists of death, exposure and post-exposure observations of toxic signs, animal body weight and gross pathological examinations. Animal toxicity was reported in terms of the LC_{50}, which is expressed in terms of mass charge (mass entering the furnace/min)/l diluent air.[6] However, the use of animal experimentation raises ethical concern, as well as the issues on validity; including differences in toxic mechanism and response between animals and humans.

The introduction of *in vitro* methods to toxicology testing offers a new approach in the study of fire combustion products. *In vitro* cytotoxicity analysis has been increasingly applied to many fields and industries, such as chemicals, pharmaceutical, environmental, cosmetic products; and smoke derived from combustion against a range of human cells which replaced the need for animal-based experimentation.[3–5,7–18] The application of *in vitro* methods for fire toxicity studies combines the emerging *in vitro* toxicology fields with fire science, and a new complex research area has evolved, called '*in vitro* fire toxicity'.

In order to develop a suitable *in vitro* method for combustion toxicity studies there are several components that need validation:

- combustion equipment to model fire conditions;
- *in vitro* human cell exposure system;
- suitable end points to be measured.

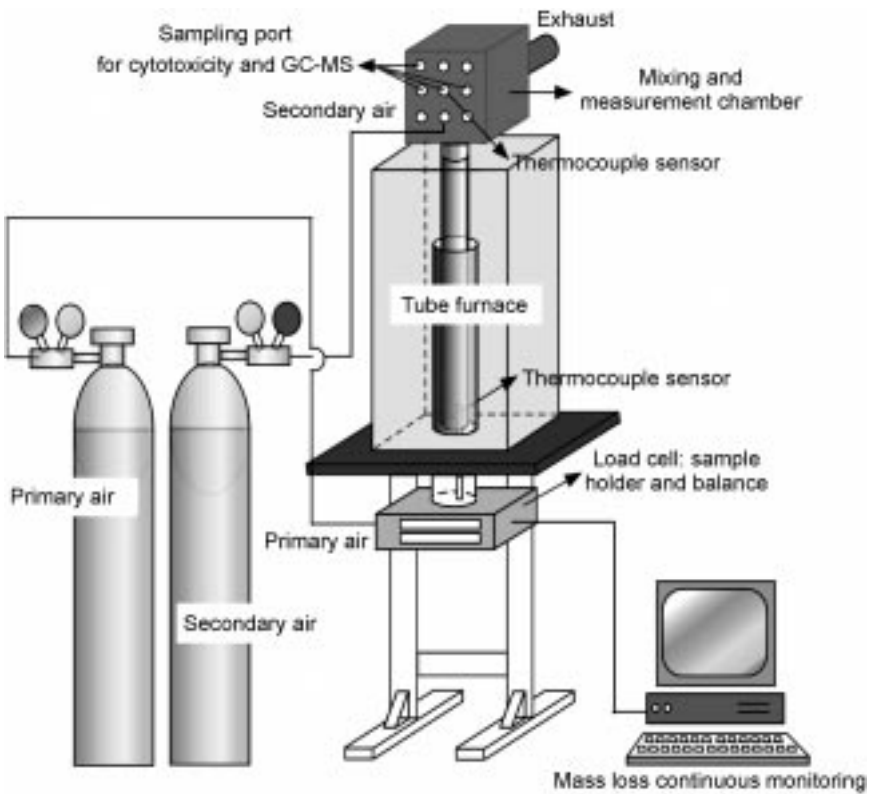
The following section will give an insight into the type of combustion furnace that can be used to model fire conditions, developments in the area of *in vitro* toxicology, a detailed description of *in vitro* human cell exposure systems and toxicity end points as an indicator for fire toxicity.

9.2 Combustion furnace

Much combustion apparatus has been developed for the generation of combustion products in a fire toxicity testing and different methodologies have been developed for the assessment of toxic potency.[5,19–23] The laboratory-scale tube

furnace can be adopted to model a wide range of fire conditions such as non-flaming and flaming regimes by using different combinations of temperature and different fuel/oxygen ratios.[22–25] Combustion products are expelled into mixing and measurement chambers which are then diluted with secondary air, followed by analytical measurements and any subsequent animal or *in vitro* exposure for toxicity assessment. Vertical orientation can be incorporated in the design to allow a simple system for mass loss measurements and enable data correlation with other fire material data such as that derived from cone calorimetry.[3–5] An example of a vertical tube furnace currently used in our research will be described below.

The vertical tube furnace was manufactured within the engineering workshop of the University of New South Wales, Sydney, Australia. The furnace (Fig. 9.1) was a modification of the current standard BS 7990 in which a vertical position was designed for mass loss measurement during combustion. The furnace consisted of a vertical furnace, a load cell and a polycarbonate chamber for mixing and measurement. A silica tube (Schott-Garsco, Germany) was placed inside the furnace. A variety of samples could be mounted vertically on the load



9.1 Vertical tube furnace arrangement for generation of combustion products.[3]

cell, and mass loss measured with a balance linked to a computer. Several ports were designed in the polycarbonate chamber for the introduction of secondary air, sampling and measurement. The secondary air stream was introduced to reduce the chamber temperature, quench any further reaction, preserve the chemical state of the decomposition products and minimise the formation of free radicals. More detail on the tube furnace arrangement can be found in previous published papers.[3,5]

9.3 *In vitro* toxicology

The term *in vitro* refers to the use of cells and tissues outside the body. *In vitro* toxicology is a field of study that applies technology using isolated organs, tissues and cell culture to study the toxic and adverse reactions of substances.[26,27] Originally, genetic toxicology was the first field in which *in vitro* test systems were used comprehensively for toxicity testing to identify the mutagenic potency of compounds such as the Ames mutagenicity assay with strains of *Salmonella typhimurium*.[28] *In vitro* cytotoxicology refers to the use of cell culture techniques in toxicology investigations.[26,27]

9.3.1 The alternative movement: from *in vivo* to *in vitro*

The focus of toxicology testing has shifted from the use of whole animal to alternative *in vitro* toxicity methods. This shift, known as the 'The alternative movement', began in 1959, with the book *The Principles of Humane Experimental Technique*, by William Russell and Rex Burch which defined the three Rs concept: replacement, reduction and refinement of animal-based methods.[29] In brief, the three Rs principle is described as: *replacement* of animal experimentation with non-animal techniques such as *in vitro* methods and computer models; *reduction* of the number of animals used via improved experimental design; *refinement* of procedures to maximise animal welfare. The 3Rs principle has been recognised as the scientific basis for humane treatment in animal experimentation and for alternative methods, and adopted for example in European Union directives.[30]

Recently, several organisations throughout the world have been established for development of alternative methods including: the Fund for Replacement of Animals in Medical Experiments (FRAME),[31] the Johns Hopkins Center for Alternatives to Animal Testing (CAAT), the Multicenter Evaluation of *in vitro* Cytotoxicity (MEIC), the Interagency Coordinating Committee on the Validation of Alternative Methods (ICCVAM),[32–34] the European Centre for the Validation of Alternative Methods (ECVAM),[35] ZEBET (Germany)[36–38] and other community societies (ESTIV) – European Society of Toxicology *In Vitro*; IVTS – *In Vitro* Toxicology Society; SIVB – Society of *In Vitro* Biology; SSCT – Scandinavian Society for Cell Toxicology). Many databases, websites and

international programmes for *in vitro* methods in toxicology such as INVITTOX, Altweb, MEIC, EDIT project (Evaluation-guided Development of new *in vitro* Tests) have been established for method development, validation and evaluation of the reliability of *in vitro* tests for predicting toxicity.[39–41]

9.3.2 Cytotoxicity mechanism

Basal cytotoxicity has been known as the foundation of all cell injury and/or cell response to toxicants. The basal cytotoxicity concept is based on the fact that chemicals are toxic to humans by interfering with cell functions common to all human cells (*cyto* = cells). The first concept of basal cytotoxicity was formulated by late Björn Ekwall in 1983. Ekwall believed that most chemicals were toxic to humans as measured by interference with cell functions common to all human cells.[40] From this concept a new classification of chemical toxicity into three categories was developed; extracellular toxicity, organ-specific toxicity and basal cytotoxicity.[26] The basic mechanism of substances acting at the cellular level provides the fundamental basis for cell injury or cell death. A chemical or other stimulus may cause cell injury by transiently (reversible) or permanently (irreversible) altering the homeostasis of the cells.

Reversible responses (also known as repair mechanisms) may represent the early stages of irreversible injury or may be sustained where the cell achieves a new steady state. Types of reversible changes resulting from cell injury, including ion deregulation and induction of immediate-early genes, may be responsible for cells re-entering the mitotic cycle (the process in cell division by which the nucleus divides), resulting in regeneration.[42]

Irreversible responses of cell injury refer to changes that lead to a new equilibrium with the environment. Types of irreversible responses include: interruption of membrane integrity; hydrolysis of phospholipids, proteins and nucleic acids; and necrosis, where organelles undergo a sequence of changes. This begins with changes in compartment volume, such as cytosols (the fluid component of cytoplasm, excluding organelles and the insoluble, usually suspended, cytoplasmic components), endoplasmic reticulum (ER) (a membrane network within the cytoplasm of cells involved in the synthesis, modification, and transport of cellular materials), and mitochondria (spherical or elongated organelles in the cytoplasm of nearly all eukaryotic cells, containing genetic material and many enzymes important for cell metabolism). It ends with the disintegration of the cell membrane, formation of dense aggregates and/or calcifications in the mitochondria, karyolysis (disintegration and dissolution of a cell nucleus when a cell dies) and apoptosis (disintegration of cells into membrane-bound particles that are then eliminated by phagocytosis). These early molecular changes may be a useful means to measure the earliest changes in toxicity from substances and as markers for cellular and molecular changes in cell toxicity.[42,43]

9.3.3 *In vitro* exposure system

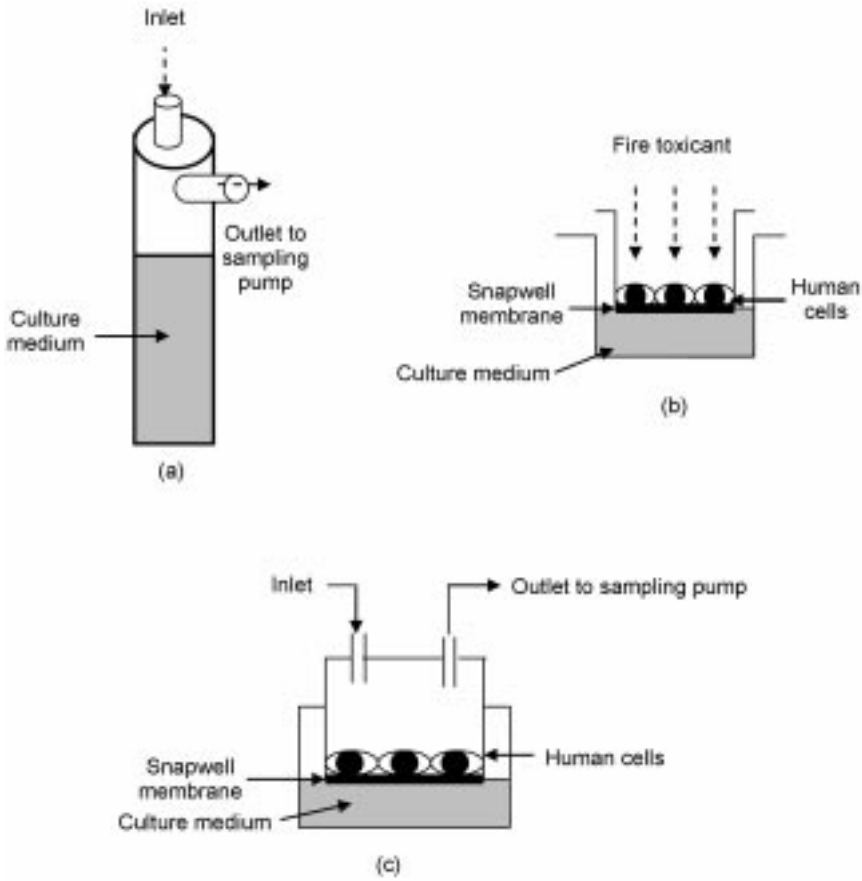
The *in vitro* exposure system plays an important role in part of fire toxicity assessment. The exposure to fire combustion products is similar to exposure to gases and particulates. Gaseous or particulate compounds have been difficult to investigate using *in vitro* studies due to inefficient methods for exposing cell cultures directly to these mixtures.[44] There are several sampling and exposure methods for *in vitro* exposure which have been investigated using the following four techniques:

- sampling the particulate phase on filters followed by the investigation of the effects of suspended or extracted particles;[45–48]
- sampling the gas phase in a culture medium, PBS (phosphate buffer solution),[47,48] and DMSO (dimethyl sulphoxide);
- exposure of adherent or suspended cells covered by medium to the gas phase;[49,50]
- direct exposure at the air/liquid interface at a specific effluent flow rate.[3,4,51,52]

The majority of *in vitro* studies for assessing the health effects relating to smoke toxicity have been derived from studies of carbon monoxide (CO),[49] nitrogen dioxide (NO_2),[50,53] volatile organic compounds,[54] combustion particles,[55] and smoke toxicity derived from cigarettes and diesel exhausts.[52,56,57] In the combustion study of thermal decomposition products, human cells can be exposed via indirect exposure using an impinger and two direct exposure methods (passive and dynamic diffusion) (Fig. 9.2). Briefly, the impinger method uses a culture medium to trap the combustion toxicants, whilst the direct exposure method involves the exposure of combustion products at the air/liquid interface). In the passive direct exposure, the combustion toxicant was introduced passively to the cells without air flow, whilst in the dynamic method a specific flow rate was applied. Comparisons between the direct and indirect methods have been made previously.[3–5]

Indirect exposure (impinger)

Conventionally, cell cultures are submersed (growing) in the culture medium, and the gaseous compounds are either bubbled into the medium or exposed in the air phase of the culture medium. The indirect exposure method uses the culture medium to trap the combustion toxicants. The method has been adopted for *in vitro* exposure to fire toxicants.[3] The combustion products were bubbled through a standard hygiene sampling impinger containing serum-free culture medium at a controlled flow rate using a personal air sampling pump (SKC, USA), usually with a 30 min exposure period. A variety of air stream flow rates can be used, ranging from 1 l/min (primary air) to 10 l/min (secondary air). The exposed culture medium was then filter sterilised and transferred into 96-well

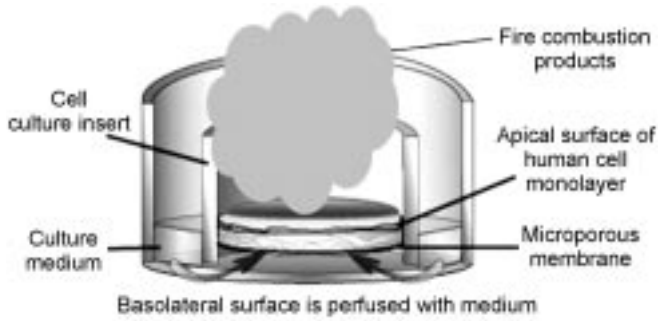


9.2 Human cell exposure systems: (a) indirect exposure (impinger); (b) passive ; and (c) dynamic direct exposure.

microplates (Greiner bio-one, GmbH), where it was serially diluted and a cell suspension was added, as described in a previous paper.[17] The microplates were then incubated for 24 h before performing the *in vitro* cytotoxicity assays. However, the major drawback with this system is that the gases are poorly absorbed by the cells or the bubbling system adversely affected the cells due to physical disturbances.[3]

Direct exposure (passive and dynamic)

The direct exposure method has been used widely to study the inhalation toxicity by which the airborne contaminants exposed are directly to toxicants. This technique is applied to overcome the major drawback of the conventional indirect exposure system using an impinger. One type of direct exposure method is called

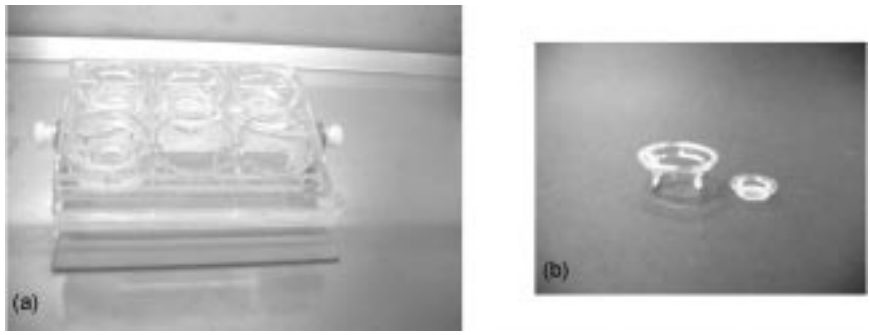


9.3 In vitro exposure at the air/liquid interface.

the air/liquid culture technique.[3–5,14–16,44,53,58–60] Several direct exposure methods using *in vitro* exposure chambers have been developed.[59–61] The Harvard Navicyte chamber can be used for exposing fire combustion products using horizontal diffusion.[60] This chamber is designed for substance transport and toxicology studies using tissues such as nasal, pulmonary, corneal or dermal cells.[60] The cells are exposed to an air/liquid interface in their normal *in vivo* environment (Fig. 9.3). The chamber creates an environment in which the apical surface of the tissue or cell monolayer is exposed to liquids, semi-solid compounds or gases, while the basolateral surface is perfused with medium.

The Harvard Navicyte chamber consists of six horizontal chambers, into which either Snapwell™ devices or tissue mounting rings may be fitted on a horizontal plane, and a heat block. Either a peristaltic or a syringe pump can be used to perfuse the lower surface of the Snapwell™ insert (a modified permeable support containing a 12 mm diameter membrane supported by a detachable ring), usually the basolateral (relating to the base and one or more sides of a part) surface. The apical (upper) surface of the diffusion chamber can be used in either an open or closed configuration; the cell surfaces are more accessible for drug transport or cytotoxicity testing of liquids and semi-solid materials in the open configuration. In the closed configuration, cells can be exposed to solutions, perfused with gas, or gas pressure can be applied. The closed system also accepts diffusion chamber electrodes for resistance measurements and electrophysiological studies. A number of studies have been conducted using a diffusion chamber for drug absorption and transport studies.[3–5,14–16,62,63]

Another type of *in vitro* exposure system is the CULTEX chamber.[61] This method allows isolated cells to be exposed to airborne inhalable compounds directly at the air/liquid interface, without dehydration.[44,53] The cells are cultivated on porous transwell membranes in a device, allowing intermittent medium supply. The system provides for the study of gases and particulates with all the requirements necessary to support the cells; medium supply, temperature and humidification can be guaranteed in the exposure system. The cells are grown on transwell membranes using the pulse submersion technique. No



9.4 Cells grown on Snapwell membrane: (a) six well plate with Snapwell membrane and (b) individual Snapwell membrane.

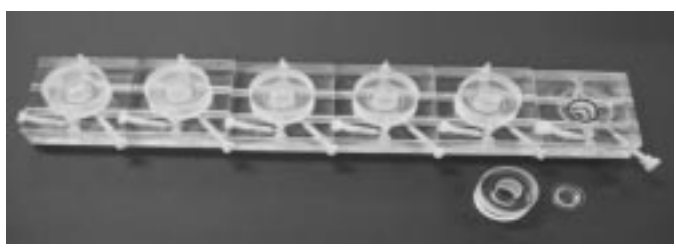
deleterious effects on cell viability resulted owing to the direct exposure to airborne pollutants.[64]

The human cells were grown on a porous membrane which prevented the culture medium from overflowing onto the apical cell surface (Fig. 9.4). This technique has now been adopted for *in vitro* cytotoxicity studies to model the exposure via inhalation route.[5,51,57] In the direct exposure method, the human cells were exposed directly to the thermal decomposition products at the air/liquid interface without medium coverage. The combustion products were introduced passively into the cells (*passive method*) or at a specific flow rate (*dynamic method*).

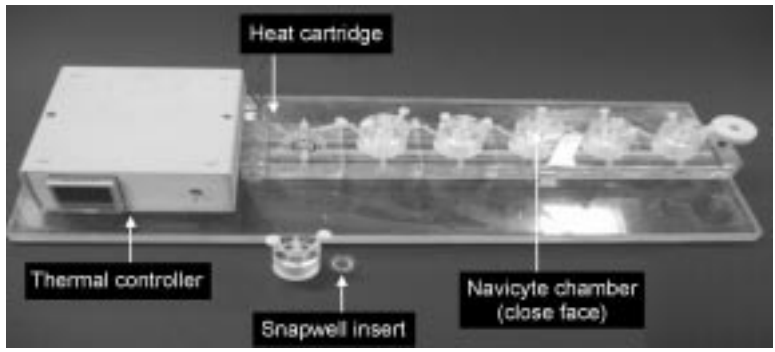
In the passive direct exposure, the Navicyte chambers (open face) as shown in Fig. 9.5 were placed in the furnace mixing and measurement chamber, and the temperature was monitored using a K-type thermocouple connected to a digital thermometer (Digitech QM1600, Australia).

In the dynamic direct exposure, combustion products were introduced to the cells by using a personal air sampling pump (SKC, USA) at a certain flow rates. The Navicyte chambers (close face) for dynamic direct exposure were fitted on the heat block equipped with a heat cartridge to maintain a temperature of 37 ºC and connected to a thermo controller (Shinho, JCS series) (Fig. 9.6).

After completion of the exposure period, the membranes were removed from the Navicyte chamber, and placed into six well plates, containing a complete



9.5 Passive direct exposure.



9.6 Dynamic direct exposure.

mixture of culture medium. The plate was then incubated for a defined post-exposure time (0 h or 24 h) before performing the *in vitro* cytotoxicity assays. Further assessment was then made to determine whether any significant reduction on cell viability due to post-exposure incubation time using the three *in vitro* assays. Currently, the air/liquid exposure has gained special interest in the area of smoke toxicity derived from cigarette smoke and several gaseous compounds.[3–5,14–16,18,19,44,52,56,64,65]

Comparison between in vitro *exposure methods*

Three *in vitro* exposure systems have been described in the previous section for the assessment of toxicological effects of thermal decomposition products from polymer combustion. These systems included: an indirect exposure method using an impinger system, which traps combustion toxicants through culture medium, and an air/liquid interface using passive and dynamic direct exposure.[3]

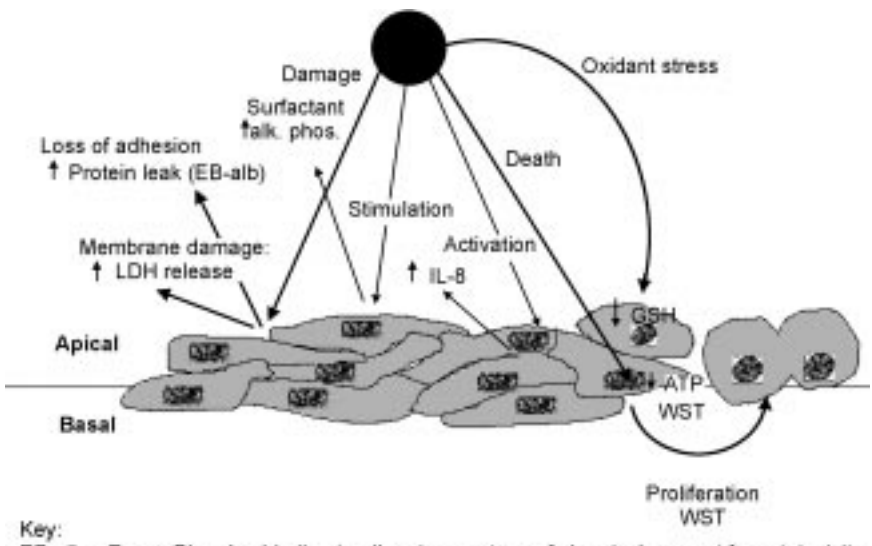
The exposure system of human cells to decomposition products using an impinger system is proved to be a simple air sampling method enabling rapid assessment using cytotoxicity analysis. However, when using the culture as a medium to extract the combustion products, the solubility of individual components of the crude combustion mixtures may have an impact on the experimental results.[5] Organic compounds, gaseous and particulate components of the thermal decomposition products which were insoluble in the culture medium, would not totally diffuse through the culture medium to come into contact with cells. The culture medium is composed of potentially reactive compounds such as antibiotics, serum, amino acids and others, which may modify the nature of the combustion products, especially free radicals.[66] Results suggested that direct exposure might provide a more reliable model of human exposure than the indirect system. In direct exposure, cultured human cells grown adherently on microporous membranes were exposed directly to the combustion products.[3] This direct contact has several advantages: (1) preventing any chemical

reactions between combustion products and the culture medium which may lead to artificial results; (2) mimicking the exposure mechanisms as they occur *in vivo*; and (3) cell nutrification on the basolateral section which was essential to preserve cell viability.[3] However, the use of air/liquid exposure does not guarantee a defined and effective gas/cell contact.[5,52]

9.3.4 *In vitro* toxicity end points

The end points to be measured in a toxicity assay are critical to acquire data on thermal decomposition products and risk to humans. There are some potential toxicity end points for *in vitro* exposure as shown in Fig. 9.7. Common cell responses that could be useful for cytotoxicity end points are: cell proliferation, GSH (reduced glutathione) release as a result of oxidant stress, LDH (lactate dehydrogenase) release from membrane damage, Alk.phos. (alkaline phosphatase), protein leak from loss of adhesion, adenosine-5′-triphosphate (ATP) content and IL-8 (interleukin 8).[58]

The major end points measured for *in vitro* cytotoxicity assays in the area of fire and smoke toxicity are the effects of toxicants on cell viability and cellular growth rates,[17,67] such as, tetrazolium salt reduction,[3,44,46,53] total cell count,[49] Neutral Red uptake (NRU),[4,46–48,54] intracellular ATP/ADP content,[4,52,53] intracellular content of reduced glutathione,[57] lactate dehydrogenase release[46] and genotoxic effects using the alkaline comet assay.[44] A current review on *in*



9.7 In vitro cytotoxicity end points within the cells.[59]

vitro exposure to combustion emissions suggests using a range of end points in assessing toxicity including cytokine production, oxidant stress and cell type-specific function.[68]

9.3.5 Cytotoxicity assay

Many cytotoxicity assays have been developed which are based on either colorimetric or bioluminescence reactions. Current development on *in vitro* toxicity assays allow measurement of a variety of different markers that can indicate the number of dead cells (cytotoxicity assay), the number of live cells (viability assay), the total number of cells, or the mechanism of cell death (apoptosis).[69] There are a variety of cytotoxicity assays that measure different end points including the NRU assay which measures cell viability; the Kenacid Blue (KB) assay for measuring protein content and proliferation, the MTT (3-4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide) and MTS (3-(4,5-dimethylthiazol-2-yl)-5-(3-carboxymethoxyphenyl)-2-(4-sulphophenyl)-2H-tetrazolium) assays which measure cellular mitochondria activity.

In the area of *in vitro* cytotoxicity, a commonly used toxicity expression is IC_{50} (50% inhibitory concentration, or a concentration that causes 50% activity inhibition of living cells) which is known to be related to LD_{50} (50% lethal dose) in conventional animal toxicity. IC_{50} values in *in vitro* toxicity are different from IC_{50} used in the combustion toxicity expression which refers to the concentration that causes incapacitation of 50% of the test animals or predicted response for humans. Cytotoxicity values (NOAEC – no observed adverse effect concentration, IC_{10} – 10% inhibitory concentration, IC_{50} – 50% inhibitory concentration, and TLC – total lethal concentration) were extrapolated graphically from the dose–response curve. NOAEC was determined at which the normalised cell viability showed no cytotoxic effect (flat regions of the curve); IC_{10} was determined at 10% of the maximum response from normalised cell viability, IC_{50} was determined at 50% of the maximum response; and TLC was determined at the maximum response from normalised cell viability, respectively. The determination of toxicity values were extrapolated using an exponential regression analysis which was based on derivative equation derived from exponential equation ($Y = ae^{-bx}$). Derivation of the exponential equation results in the following equations:

$$\ln y = \ln a - bx \tag{9.1}$$

$$x = \frac{\ln (a/y)}{b} \tag{9.2}$$

$$IC_{50} = \frac{\ln [a/(50\% \text{ of } a)]}{b} \tag{9.3}$$

where y is the intended response on normalised cell viability; a is the maximum

response of normalised cell viability; b is the curve slope; and x is the absorbance values or expressed as percentage cell viability.

The concentration to inhibit 50% of cell viability (IC_{50}) was determined based on the curve slope, b, and 50% of a. The IC_{50} was then determined mathematically using the equations above. Other toxicity values (NOAEC, IC_{10} and TLC) were determined using similar equations.

MTS assay

MTS assay measures cellular metabolism by determining the ability of viable cells to convert a soluble tetrazolium salt to a formazan product. Bioreduction of tetrazolium salts to coloured formazan products reflects the cellular (NADH- and NADPH-dependent) redox state of cells and strongly absorbs light at 490 nm. MTS possesses increased water solubility and greater stability compared with MTT assays.[70] In order to accelerate production of the formazan product and photon absorbance at 492 nm, MTS requires an intermediate electron acceptor between NADH and the tetrazolium reagent phenazine methosulphate (PMS) or phenazine ethanosulphate (PES).

The advantages of the MTS assay include[71,72] ease of use, no washing or cell harvesting required, no sample transfer, and elimination of solubilisation steps normally required for MTT assays. The assay is also non-radioactive: requires no scintillation counter or radioactive disposal, plates can be read and returned to incubator for further colour development, and it requires no volatile organic solvent (unlike MTT). The sensitivity and efficiency of MTS have been confirmed by numerous researchers.[7,8,70–75] MTS has been widely used for *in vitro* fire toxicity and air contaminants.[3–5,12–18]

NRU assay

The NRU assay is a cell viability chemosensitivity assay, based on the ability of viable cells to bind a Neutral Red dye. The neutral red (3-amino-7-dimethyl-amino-2-methylphenazine hydrochloride) is a weak cationic dye that readily penetrates cell membranes by non-ionic diffusion.[76] In intact cells, it binds and accumulates with anionic sites in the lysosome, becomes charged and does not freely pass out into the cytoplasm. Damage of the cell causes the release of Neutral Red or prevents its accumulation.[77] Alterations of the cell surface or the sensitive lysosomal membrane by the action of xenobiotics lead to lysosomal fragility, resulting in a decreased uptake and binding of the dye.[76] Damaged or dead cells lose their ability to retain the dye. The application of NRU assay for cytotoxicity testing has been demonstrated by a numerous researchers. It is considered a sensitive assay[3,4,7,67,76–90] and has been accepted as standard phototoxicity testing.[91]

9.3.6 ATP assay

The ATP assay is based on a bioluminescence method that utilises the enzyme luciferase, which catalyses the emission of light from ATP and luciferin.[92,93] This assay quantifies the ATP levels in viable cells. It was initially developed as a tumour chemosensitivity assay,[93] and then developed as a tool in molecular and cell biology.[94]

The ATP assay using CellTiter-Glo™ Luminescent Cell Viability assay is a homogeneous method to determine the number of viable cells in culture based on quantisation of the ATP present, which indicates the presence of metabolically active cells.[95] During the luciferase reaction, mono-oxygenation of luciferin is catalysed by luciferase in the presence of Mg^{2+}, ATP and molecular oxygen, and generates a 'glow' luminescent signal. The luminescence signal is then read using a luminometer. The major advantage from this method is that only a small number of cells are needed.

The application of this assay has been confirmed by a number of researchers, including cytotoxicity studies using different cell types,[3,5,96] molecular alterations within the cell and the interplay of different cell types in a number of different model systems,[93] comparisons with other cytotoxicity assays (MTT and calcein),[97] and neurocytotoxicity.[98]

9.3.7 Application of *in vitro* methods

The application of *in vitro* toxicity testing has encountered a number of difficulties. Results obtained from *in vitro* studies in general are often not directly applicable to the *in vivo* situation.[99,100] One of the most obvious differences between the situation *in vitro* and *in vivo* is the absence of processes regarding absorption, distribution, metabolism and excretion (biokinetics) that govern the exposure of the target tissue in the intact organism.[101] Indeed, the cell cultures are not able to model the biokinetics and biodynamics of the whole human body due to the lack of distribution and regulator systems (blood, hormones, nervous systems and immunity). The concentrations to which *in vitro* systems are exposed may not correspond to the actual situation at the target tissue after *in vivo* exposure.

Over the last decade, the feasibility of using mathematical models for interpretation of *in vivo* biokinetics has grown substantially.[102] Predictive studies on biological activity of compounds require the integration of data on the mechanisms of action with data on biokinetic behaviour.[34] This development has been facilitated by the increasing availability of computer-based techniques to characterise biokinetic processes[100] and the integration of data on physico-chemical properties, *in vitro*-derived toxicity data and physiologically based kinetic and dynamic models provide an important tool in hazard and risk assessment.[102]

Table 9.1 Strengths and weaknesses of *in vitro* toxicity testing[103]

Strengths/advantages	Weakness/limitations
Eliminate interspecies extrapolation	Interactions between tissues and organs cannot be tested
Controlled testing conditions	General side effects cannot be assessed (e.g. weight reduction)
Reduction of systemic effects	Systemic effects cannot be evaluated
Facilitate for the study of toxicity mechanism	Pharmacokinetic effects cannot be evaluated
Reduction of variability between experiments	Specific organ sensitivity cannot be assessed
Same doses range can be tested in a variety of test systems (cells and tissues)	
Time-dependent studies can be performed and samples taken	
Fast, cost efficient	
Very small amount of test material required	
Limited amount of toxic waste is produced	
Transgenic cells carrying human genes can be used	
Reduction of testing in animal	

Nevertheless, the *in vitro* toxicity testing offers several advantages over the conventional *in vivo* toxicity methods. Several strengths and weaknesses of *in vitro* toxicity have been recognised as presented in Table 9.1.[103] *In vitro* methods eliminate the interspecies extrapolation by using the human cells and tissues; hence reduce the animal for toxicity testing. The method is faster and cost efficient, and facilitates the study of toxicity mechanism by using a variety of toxicity end points.[18]

9.4 Future trends

The future application of *in vitro* methods for fire toxicity testing is promising. The need to evaluate and select materials which have fire resistant characteristics and low toxicity is of great importance. The toxicity information is an important part of fire hazard risk identification, fire prevention and protection as well as for public safety. Improved methods of assessment need to be developed if toxicity is to be included as part of fire hazard risk identification. Other possibilities for future applications are modelling the toxicity under different fire regimes, material selection toxicity testing, and replacing the conventional fire toxicity testing with more rapid, sensitive and specific *in vitro* test methods.

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10

A combined fire smoke and lung model test equipment

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Abstract: This chapter describes an application of the isolated and perfused lung model in combination with the steady-state tube furnace (Purser furnace, ISO 19700) This standardised furnace test method has been developed specifically to run small-scale fire smoke toxicity tests at well-defined combustion and ventilation conditions. The combination of the lung model and furnace methods provides a highly potent technique for *in vivo* investigations of smoke exposure on lung tissues. The harmful effects of fire effluents on the function of the lung have been investigated using a new technique, known as the *isolated and perfused lung model*. This has previously been used for toxicological investigations and for asthma/allergy research of substances such as terpenes and isocyanates.

Key words: smoke toxicity, particles, lung model, PVC combustion, HCI toxicity.

10.1 Introduction

A cooperative project between fire scientists at SP Fire Technology and toxicologists at Karolinska Institutet (www.ki.se) and the Department of Clinical and Experimental Medicine at Linköping University Hospital (www.hu.liu.se/ike) has resulted in the development of a method for evaluating toxic properties of fire smoke. It involves the exposure of isolated rodent lungs to fire gases and the investigation of the response of the lung and tissues. The method is completely pain-free for the animal, which is killed by an overdose of sleep-inducing drug. The heart and lungs are removed from the animal and then mounted in a container simulating diaphragm movement and 'breathing' by the lung. The internal volume of the lungs is in contact with the ambient air via a tube from the trachea, through which the lungs can be exposed to fire smoke from different materials. During the experiment, a buffered salt solution containing albumin is pumped through the blood vessels, enabling substances and metabolites to be investigated in the solution. The volume of the lungs can be measured constantly during the experiment, providing a measure of the contraction of the airways. At the end of the experiment, the lung tissue can be dissected and investigated.

10.1.1 Background

For many years, toxicity from fire smoke was considered to depend almost solely on its carbon monoxide content. Then the impact of hydrogen cyanide in the smoke was also considered important. However, fire smoke may contain many other substances that are highly toxic, including irritants, and estimation of the overall toxicity of fire smoke is quite complex if all contributing substances are included. More recently, attempts have been made to find more complete estimates of smoke toxicity,[1] including a wider range of substances in the fire smoke. A particular difficulty is to find reliable smoke toxicity data for various substances and it is hoped that the suggested methodology might be used to facilitate the search.

10.1.2 The lung model

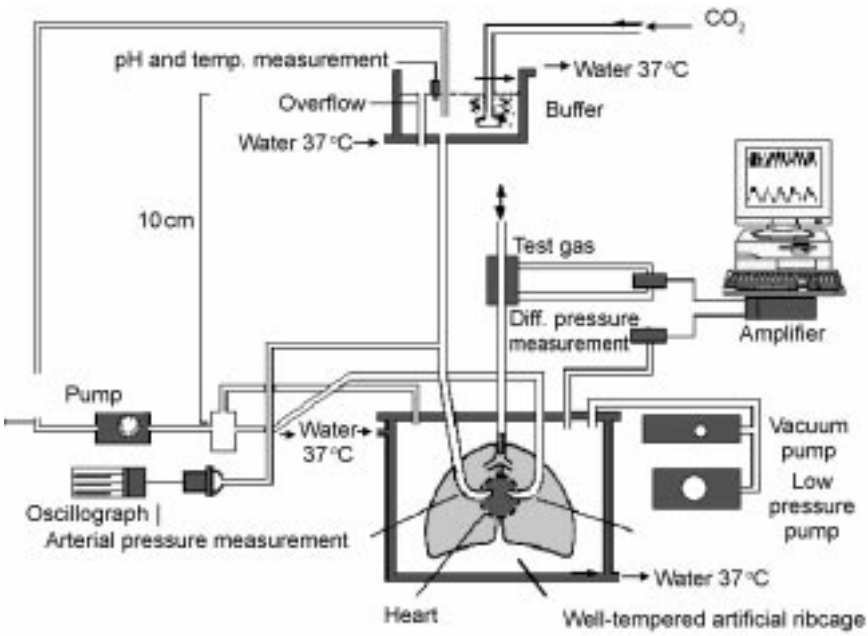
The isolated and perfused lung model is a compromise between *in vivo* and *in vitro* and has many advantages; the whole organ is intact, the cells have their 'correct' neighbours, one can study the direct effects on the lung, there are several exposure routes, e.g. inhalation, slow or rapid, (bolus) injections and constant perfusion/pressure. The isolated lung model is very useful for mechanistic studies of toxicity as different enzyme inhibitors, receptor antagonists, etc. can be added to the perfusate before the real exposure.

Figure 10.1 shows a schematic of the isolated perfused lung set-up, including the artificially pumped ribcage, heart and lung circulation system, test gas exposure system and recording device. Briefly, the heart/lungs are removed from the animal and then placed in an artificial 'ribcage', consisting of an airtight container to which a pump is connected (Fig. 10.2), which creates an alternating negative pressure in the container and thereby causes the lungs to expand or contract. The lungs, in their turn, are in contact with the ambient air via a tube in the trachea, through which they can be exposed to fire smoke from different materials.

Any type of animal lungs could be used for the model; however, most frequently a rodent lung is used. An advantage of the guinea pig lung is its resemblance in sensitivity and reaction pattern to that of the human lung.[2] However, rat lungs are also of value as they have the advantage of a better availability of toxicity data than for guinea pigs lungs, for example, from published LC_{50} values.

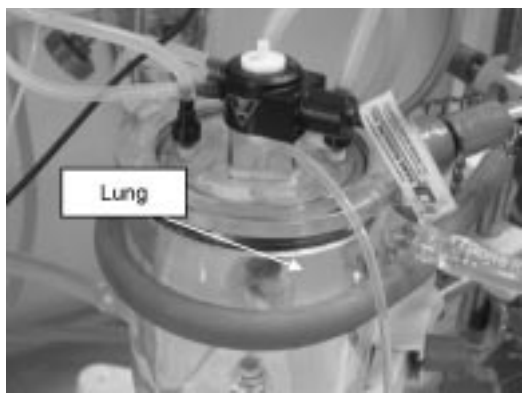
10.1.3 Experiments

The relative novelty of this technique, and its value to investigations within the fire community, indicate the need for a detailed description of the experiment before the results can be discussed. During the experiment, a buffered salt



10.1 Schematic picture of the isolated perfused lung set-up.

solution containing albumin is pumped through the pulmonary artery by single pass or recirculating perfusion under constant hydrostatic pressure, or constant flow controlled by a peristaltic pump, enabling substances and metabolites to be investigated in the perfusate solution or obtained lavage fluid (bronchoalveolar lavage (BAL) fluid). The distensibility (swelling capacity), resistance and volume of the lungs can be measured continuously during the experiment, providing a measure of the contraction of the airways. On conclusion of the



10.2 Heart/lungs in the artificial ribcage.

experiment, the lung tissue can be weighed, dissected and investigated, and lavage fluid can be analysed.

Guinea pig lung experiments

The lungs were prepared from guinea pigs of the Dunkin-Hartley strain, weighing between 325 and 450 g. The animals were anesthetised with pentobarbital (Mebumalum Vet., Nord Vacc, Sweden), 120 mg/kg injected intraperitoneally (i.p.), (i.e. injected within the peritoneal or abdominal cavity). The lungs were then surgically removed as described by Kröll *et al.*[3] and treated as described by Låstbom *et al.*[4] The lungs were perfused with Krebs-Ringer buffer pH 7.4 (composition in mM: NaCl 118.0, KCl 4.7, $CaCl_2$ 2.5, $MgSO_4$ 1.2, $NaHCO_3$ 24.9 and KH_2PO_4 1.2) containing 12.5 mM Hepes buffer, 5 mM glucose and 2% bovine serum albumin fraction V.

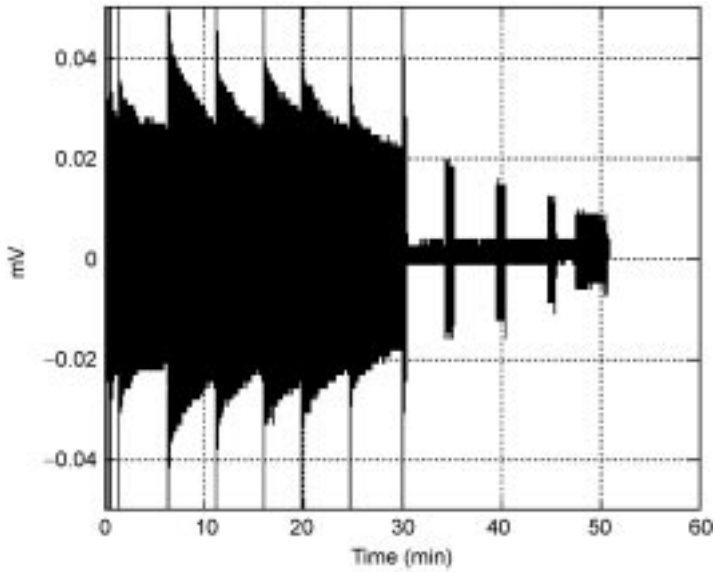
Once suspended in the thoracic chamber, the lungs were ventilated at 60 breaths/min by creating an alternating negative pressure (-0.32 to -0.58 kPa) inside the thoracic chamber using an animal respirator (model 7025, Ugo Basile, Biological Research Apparatus, Varese, Italy) and a vacuum source connected to the thoracic chamber. The tracheal air flow and pulmonary pressure were measured with a heated pneumotachograph (Hans Rudolf Inc., Kansas City, MO) and the data were recorded on a computer using the IOX 6.1a data acquisition system (EMKA, Paris). The collected data were used to calculate lung conductance (G_{aw}) and dynamic compliance (C_{dyn}). Lung conductance is a measurement of how easily the air moves in the upper airways, and lung compliance is a measurement of the elasticity of the lower part of the lung. The perfusion flow was measured manually.

The lungs were allowed to stabilise for 20 min with single-pass perfusion buffer containing albumin before the experiment was started. The model lung was exposed to normal air for 5 min and then exposed via the air passage to hydrogen chloride/nitrogen gas, PVC smoke or control air. The pneumotachograph was taken away during the exposure and put back after the exposure in order to obtain values of the conductance and compliance measurements. The reason for this was that the instrument probe consists of a fine silver mesh that most probably would have been blocked by particles or effected by the acid gases used in the experiments.

The perfusate was collected during the exposure and was subsequently analysed by gas chromatography combined with mass spectrometry (GC-MS). Immediately after the experiment the lungs were fixated with formalin and taken for histological analysis.

Rat lung experiments

Male Sprague-Dawley rats (210–320 g) were used for the studies. The animals were derived from a pathogen-free colony and housed under pathogen-free



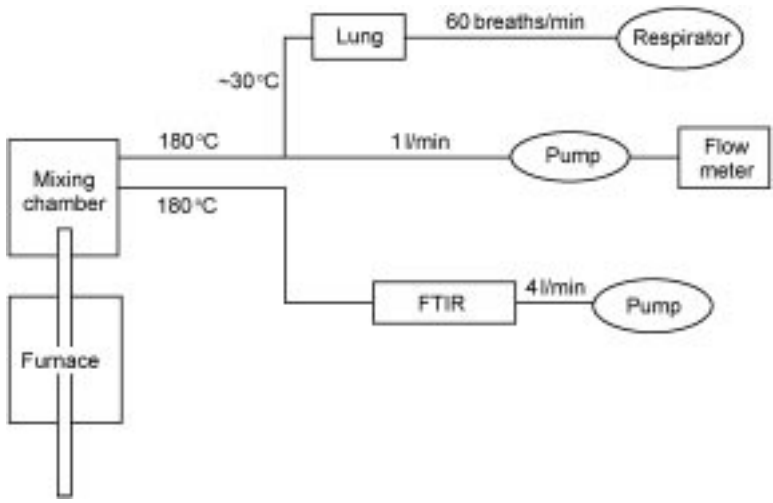
10.3 Original recording of the air flow in isolated perfused rat lungs. The recording was generated by the amplified voltage signal from the pneumotachograph and differential pressure transducer. The sudden increase in airway flow seen at regular intervals represents exerted deep breaths.

conditions. They were allowed to acclimatise for 3–5 days in isolated cages with air ventilation before the experiments. Rats were anaesthetised with pentobarbital sodium (80 mg/kg i.p.). The lungs were isolated and initially perfused with 50 ml buffer to render the lungs free of blood. The lungs were ventilated by negative pressure ventilation with 80 breaths/min and perfused with a total volume of 50 ml of recirculating buffer (pH 7.4) at constant hydrostatic pressure (10 cm H_2O).[5]

After preparation, all lungs were perfused and ventilated for 30 min, during which they were allowed to stabilise. Only lungs that showed no signs of dysfunction after this stabilisation period were used for further experimentation. Figure 10.3 shows an example of a recording of the air flow in isolated perfused rat lungs. During the first 30 min the lung is stabilised and the response recorded. During the subsequent exposure periods the lung is monitored intermittently.

Experiment set-up

The exposure gas was produced in the Purser Furnace, either by combustion of sample material or by mixing hydrogen chloride from a gas bottle with an air flow in the mixing chamber. For some experiments, the gas was extracted from the mixing chamber, in parallel to the perfused lung, to a Fourier transform



10.4 Schematic drawing of the experimental set-up.

infrared (FTIR) instrument that continuously measured the concentration of different gases, e.g. the hydrogen chloride content (see Fig. 10.4). In some other tests, a simple Draeger tube was used to obtain information on the approximate level of hydrogen chloride in the gas. In the mixing chamber, the temperature was relatively low: ~30–40 ºC, so the tubes connecting the chamber to the lung and FTIR were heated to 180 ºC in order to avoid condensation. However, a sufficient length of unheated tubing was allowed before introducing the gas into the lung in order to ensure a suitable gas temperature for the lung exposure. The animal respirator provides a small pressure variation (close to ambient pressure) over the lung which is sufficient to extract millilitre-sized gas samples from a continuous flow over the connection to the lung.

10.2 Results

10.2.1 Guinea pig lung experiments

As the probe used for measuring conductance and compliance, the pneumotachograph consists of a fine net that might be adversely affected by acid gas or particles, measurements were undertaken intermittently at 4 min intervals. Therefore, in these experiments, isolated guinea pig lungs were exposed in 2 × 4 min to either air (control), hydrogen chloride-containing gas, or fire smoke from a PVC floor covering. Average concentrations for the two exposure periods in each experiment are given in Table 10.1.

The lung physiology parameters of conductance and compliance (lung conductance is a measurement of how easily the air moves in the upper airways, and lung compliance is a measurement of the elasticity of the lower part of the

Table 10.1 Mean concentrations in mixing chamber during the two exposure periods, 0–4 min/4–8 min. Measurements by FTIR

Experiment no.	Type of experiment	HCl (ppm)	CO (ppm)	CO_2 (ppm)
L22*	HCl–air mixture	~3000	–	–
L28	PVC smoke	3110/3120	2570/1690	1.44/1.94
L29	PVC smoke	2770/2750	1760/1300	1.14/1.54
L30	PVC smoke	3470/3380	2170/1780	1.11/1.77
L31	PVC smoke	3560/3700	1240/1320	1.19/1.68
L32	PVC smoke	2850/2920	2450/1320	1.05/1.62
L33	PVC smoke	3440/3240	1760/1350	1.07/1.71
L34	Control	2/0	–	–
L35	HCl–air mixture	3680/3840	–	–
L36	HCl–air mixture	3260/3310	–	–
L37	HCl–air mixture	2730/2780	–	–

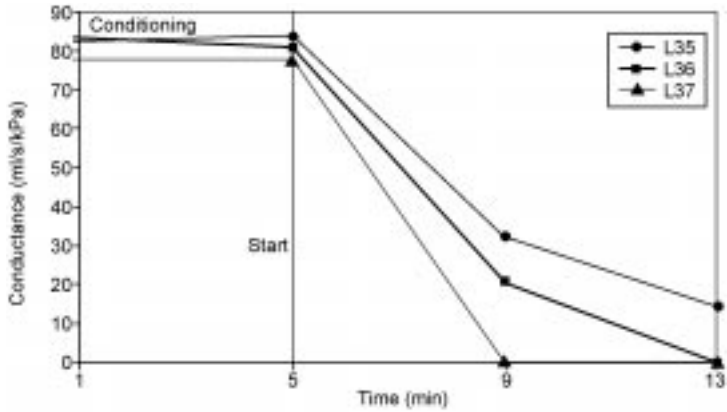
* In the L22 experiment, only a Draeger tube was used for HCl concentration measurement.

lung) decreased rapidly in the hydrogen chloride and PVC smoke-exposed lungs. In the control experiments the conductance and compliance remained stable during the 8 min of exposure.

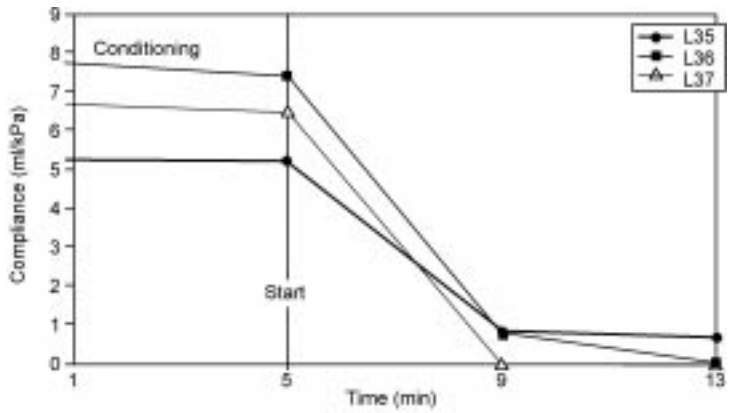
The experiment started with a 5 min continuous measurement of conductance and compliance as a sort of 'preconditioning' in order to ensure a consistent and stable baseline before the experiment started. During the preconditioning, the lung was exposed to air from the surrounding atmosphere. The probe was thereafter disconnected from the entrance to the artificial lung and sample gas was provided to the lung. After 4 min, the sample gas was removed and the probe for measuring conductance and compliance was once again attached to the system for a ~1 min continuous measurement against the surrounding air. Then another 4 min of sample gas exposure were made followed by a pneumotachograph measurement. Figures 10.5–10.10 show the experimental results. As can be seen in Figs 10.5 and 10.6, there is a variation in initial values for the lungs that might be attributed to individual differences in lung capacity and behaviour. However, it is clear that all lungs are dysfunctional after 8 min of exposure.

Guinea pig lungs that were exposed to PVC smoke with a hydrogen chloride concentration similar to the previously mentioned hydrogen chloride gas experiments showed the same type of behaviour, i.e. conductance and compliance decayed rapidly and went more or less to zero in 8 min. In experiment no. 33, the lung capacity of that particular animal was significantly lower from the start and, as a result, it also lost all function more quickly, within 4 min.

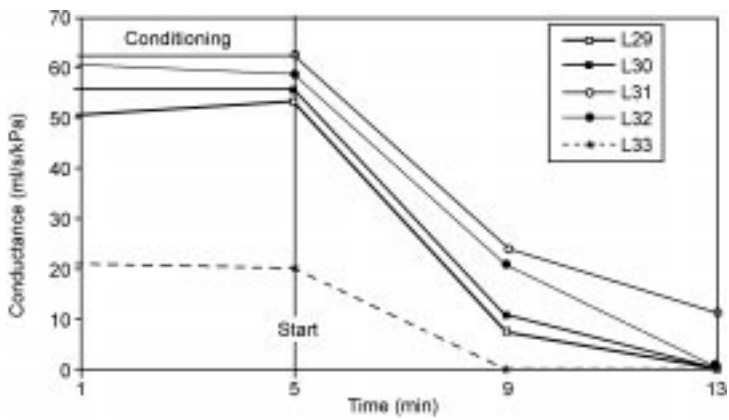
In Figs 10.9 and 10.10 the conductance and compliance are shown from a control/reference experiment during which the guinea pig lung was exposed to air. The air was provided by the exact same experimental set-up with respect to pumps and furnace as for the other experiments albeit without hydrogen chloride gas or PVC smoke.



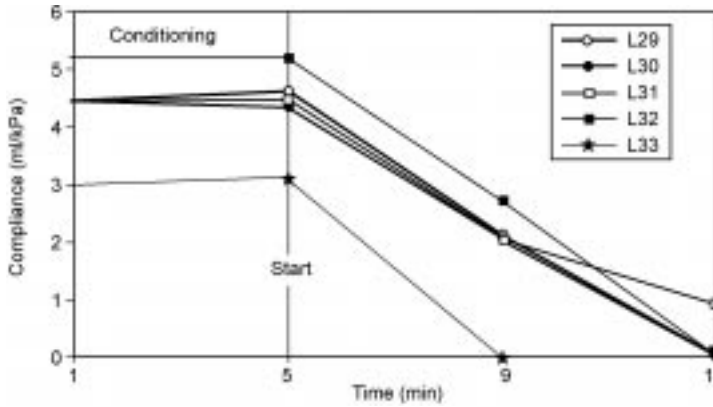
10.5 Guinea pig lung conductance during exposure to hydrogen chloride.



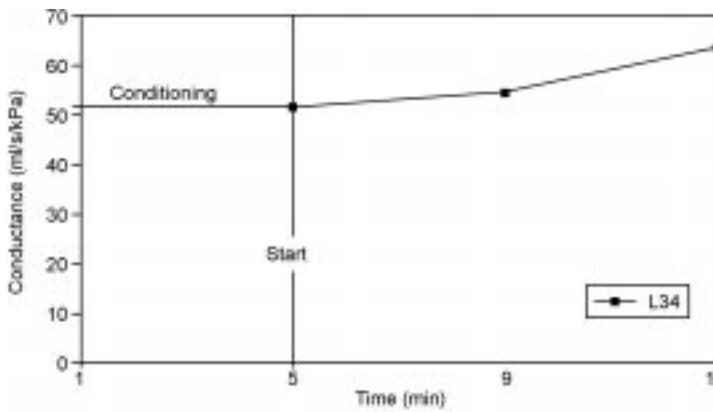
10.6 Guinea pig lung compliance during exposure to hydrogen chloride.



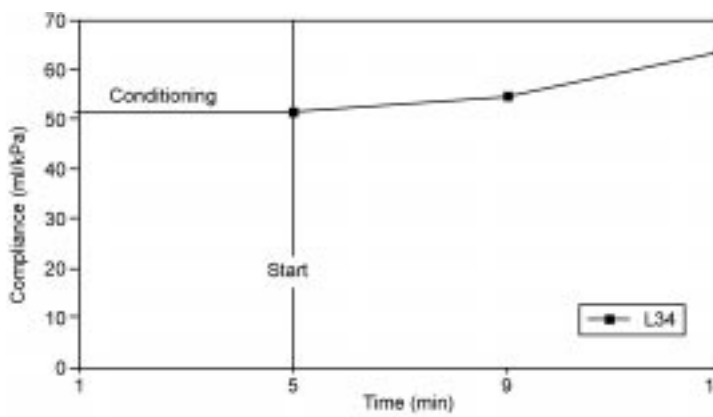
10.7 Guinea pig lung conductance during PVC smoke experiment.



10.8 Guinea pig lung compliance during PVC smoke experiment.



10.9 Guinea pig lung conductance during control (air) experiment.



10.10 Guinea pig lung compliance during control (air) experiment.

One reason for the choice of sample gas (PVC smoke and hydrogen chloride–air) was to try to differentiate the impact of the irritant hydrogen chloride from other constituents in the smoke but it was difficult to see any important differences (compare Figs 10.5–10.8). A conclusion is therefore that the exposure concentration was too high to detect any significant difference between the two types of exposure. It is also interesting to compare the results from the 8 min experiments to other reported experiments or existing toxicity limit values, such as the 1 hour hydrogen chloride LC_{50} value for rats (3124 ppm[1]). The experiments indicate that a guinea pig lung is much more sensitive than the rat even though an isolated lung system is not directly comparable to a full animal test. This difference in sensitivity has also been confirmed by the literature.[2]

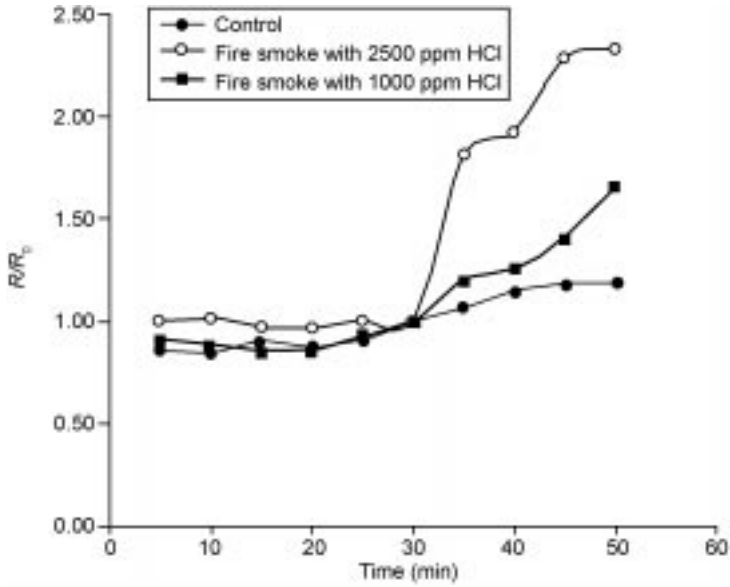
10.2.2 Rat lung experiments

As previously mentioned, the pneumotachograph consists of a fine net that might be adversely affected by acid gas or blocked by particles, so measurements took place intermittently, at 5 min intervals. Therefore, in these experiments, isolated rat lungs were exposed to either air (control) or fire smoke from a PVC floor covering at average concentrations of 1000 or 2500 ppm. The lungs were, after a 30 min stabilisation period, exposed to PVC smoke for 4 min then the sample gas was removed and the probe for measuring airway resistance was once again attached to the system for a ~1 min continuous measurement against the surrounding air. This exposure/measurement procedure was then repeated; see Table 10.2. The change in relative airway contraction over time in control (air exposed) lungs and lungs exposed to PVC smoke are given in Table 10.2 and in Fig. 10.11.

Time 35 represents the pneumotachograph measurement done 4 min after the start of smoke exposure, time 40 represents the second measurement done after an additional 4 min of smoke exposure, times 45 and 50 min represent measurements after additional two 4 min of smoke exposure, respectively.

Table 10.2 Change in relative airway contraction over time in PVC smoke exposed rat lungs

Time	Contraction											
	Control				1000 ppm HCl				2500 ppm HCl			
	Median	Max.	Min.	*n*	Median	Max.	Min.	*n*	Median	Max.	Min.	*n*
35	1.09	1.23	0.90	9	1.19	1.34	1.09	4	1.20	3.80	1.11	10
40	1.16	1.36	0.92	9	1.15	1.59	1.13	4	1.32	3.80	1.12	10
45	1.17	1.46	0.92	7	1.30	1.90	1.15	4	1.51	4.73	1.19	10
50	1.17	1.46	0.92	6	1.38	2.70	1.15	4	1.54	4.73	1.19	8



10.11 Effect of PVC smoke (hydrogen chloride 1000 and 2500 ppm), on airway resistance in the rat lung. The airway resistance at different time points (t) was measured and expressed as R_t/R_0, i.e. the resistance at a certain time point was normalised to the resistance at zero time. Values are means. (●) = controls ($n = 9$), (■) = HCl 1000 ppm ($n = 4$), (○) = HCl 2500 ppm ($n = 10$).

Values are median and maximum minimum, n = number of experiments. The Mann–Whitney test (a non-parametric significance test) was used to compare groups and the Friedman test was applied to test for consistency of trends within groups. The analysis showed that there are significant trends in all groups, including controls, of an increasing relative airway resistance over time (control, $p = 0.014$; PVC smoke 1000 ppm $p = 0.007$; PVC smoke 2500 ppm, $p = 0.0001$). Control vs. PVC smoke 1000 ppm and PVC smoke 1000 ppm vs. PVC smoke 2500 ppm showed no statistically significant differences. However, when comparing control vs. PVC smoke 2500 ppm significant differences were present at all time points analysed (time 35, $p = 0.006$; time 40, $p = 0.013$; time 45, $p = 0.018$; and time 50, $p = 0.027$).

Figure 10.11 illustrates the relative airway resistance in control and PVC smoke-exposed isolated rat lungs. The 30 min mark is the starting point for exposure and the period prior to that is the isolated lung stabilisation period (see also Fig. 10.3).

10.2.3 Analysis of the perfusate solutions

During the isolated lung experiments, the perfusion buffer passing through the heart-lung circulation was collected for subsequent analysis of combustion

Table 10.3 Results from the first series of tests by the extraction method

Test no.	Sample ID	Analysis, lighter VOC	Analysis, heavier VOC and PAH
12	Control	No VOC found	No VOC/PAH found
16	Control	No VOC found	No VOC/PAH found
17	PVC combust	Yes, benzene	Yes, C_{24}–C_{32}
25	PVC combust	Yes, benzene	Yes, C_{24}–C_{32}
23	HCl–gas	No VOC found	No VOC/PAH found
24	HCl–gas	No VOC found	No VOC/PAH found

generated compounds that might have penetrated into the circulation stream. The solutions were analysed for the presence of selected organic compounds. The substance selection was mainly based on knowledge of what type of substances might be generated during thermal degradation of PVC.

Two sets of guinea pig experiments were performed. The analysis results from the first set are shown in Table 10.3. As can be seen from the table, organic compounds were only found in the buffer solutions from the PVC floor covering tests. It is interesting to note that heavier volatile organic compounds (VOC) and polycylic aromatic hydrocarbons (PAH) were found, indicating that both benzene, which is very hydrophobic, and particulate material have passed through the blood–gas barrier to the blood side of the system.

The results of the analysis for the second series are given in Table 10.4 together with an analysis from one sample in the first series (L22). Benzene and toluene could be positively identified and quantified in all samples and styrene in one sample. The fact that organic compounds are found also in the hydrogen chloride experiments is most probably due to contamination of the sample gas in the Purser furnace and tubing system. One sample (L32) was selected for specific searching of various compounds by mass spectrometry and the results are shown in Fig. 10.12 and Table 10.5.

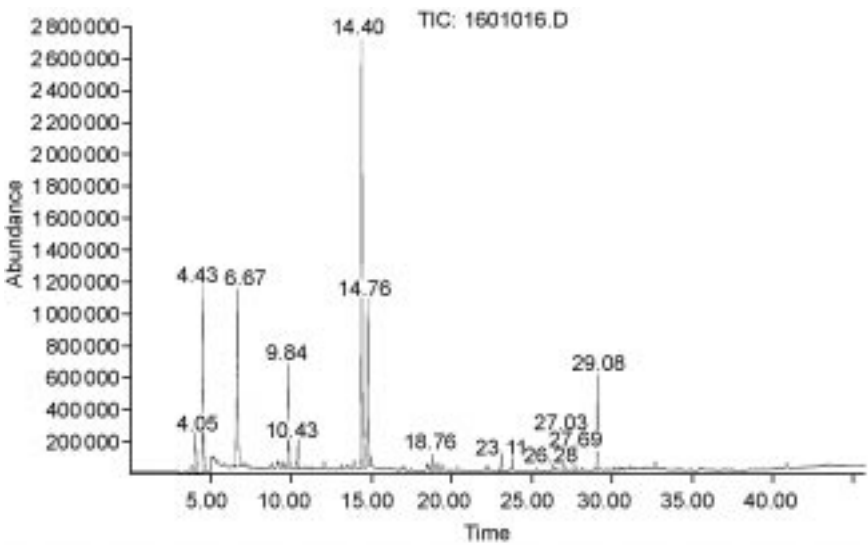
10.2.4 Lung dissection analysis

Some of the PVC exposed lungs were afterwards fixated with formaldehyde and used for histological investigation (Fig. 10.13). There were particles found in the airways, mainly in the bronchioles in the mucous layer on top of the epithelial cells. In some lungs there were particles in the alveoles and it was seen that the number of particles increased when moving from the bronchious to the alveolar section. Particles were also found inside the lung.

Particles found were both extra- and intracellular. Extracellular particles seemed to be more common and were often attached to the apical surface of the lining epithelium, embedded in the mucous layer, but without any tendency to accumulate in specific sites. The intracellular carbonaceous granules were found in intact and desquamated epithelial cells and macrophages.

Table 10.4 Compounds found in the chromatograms. X means presence in the sample

	Sample code			
	L29 PVC smoke	L22 HCl/air	L37 HCl/air	L31 PVC smoke
Test gas/compound	PVC flooring	HCl	HCl	PVC flooring
Benzene (ng/sample)	170	60	90	280
Toluene (ng/sample)	290	280	280	880
Styrene (ng/sample)	Trace	Trace	Trace	120
2-Heptanone		✘	✘	
2-Heptanol	✘	✘	✘	✘
Decene	✘			
Benzyl alcohol	✘	✘		✘
Octanol				✘
Octanoic acid	✘	✘	✘	✘
Dodecene	✘			
Benzene-bis(dimethylethyl)			✘	✘
Tetradecene	✘			
2,4-bis(1,1-Dimethylethyl)-phenol				✘
Hexadecene	✘			
Octadecene	✘			



10.12 MS chromatogram of the sample L32.

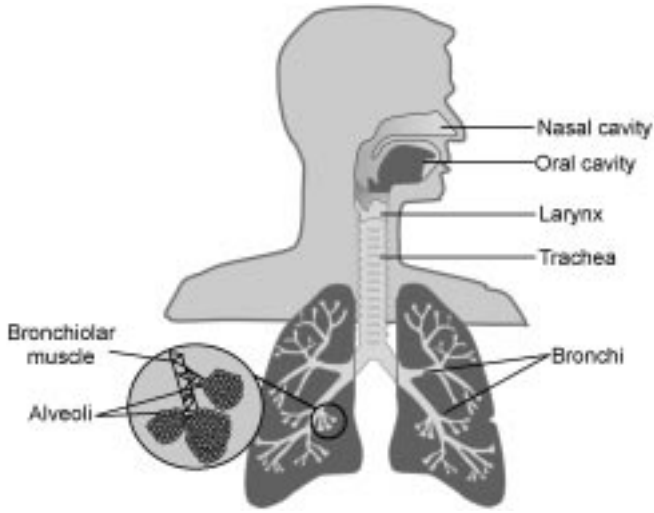
Table 10.5 Results from mass spectrometer analysis of sample 32 sorted by relative MS area

Compound	Relative amount by MS area
2-Heptanone	94
Benzene	65
Methylene chloride	56
2-Heptanol	37
1,4-bis(1,1-Dimethylethyl)-benzene	19
Isopropyl alcohol	11
Octane	7
2-Nonanone	5
Benzoic acid	5
Dodecane	5
p-Xylene	4
Decane	4
Decanal	3
Ethanol	2
2,4-Dimethyl-1-heptene	2
Styrene	2
Benzaldehyde	2
Phenol	2
Alkane	2
Alkane	2
[1,1′:3′,1″-Terphenyl]-2′-ol	2
Ethyl acetate	1
Chloroform	1
2-Pentanone	1
Methyl isobutyl ketone	1
2,3,4-Trimethyl-pentane	1
Toluene	1
Chloro-benzene	1
Ethylbenzene	1
2-Ethyl-hexanoic acid	1
Phenylethyne	Trace
Naphthalene	Trace

The majority of the particles found had a diameter of less than 1 μm but larger aggregates of particles were also found. Unfortunately, all animals showed signs of inflammation that made the search for oedema, caused only by the experimental exposure, difficult.

10.3 Discussion

A new methodology has been developed for studies of toxic effects on animal lungs (rats, guinea pigs) when exposed to irritants. The technique is also interesting for other objectives such as investigating the behaviour of particles in the lung and studying the uptake of smoke constituents in the 'blood'. The idea



10.13 Schematic view of a human lung.[6]

behind the methodology is to combine an existing method for toxicology research (perfused and isolated lung) with an ISO method for small-scale smoke toxicity studies.[1]

It is interesting to compare the fast guinea pig lung response (dysfunctional in less than 10 min) in the experiments performed with a hydrogen chloride concentration of about 3000 ppm, to recognised toxicity limit values. As can be seen, the experimental condition used in this project fits nicely into the LC_{50} 30 min mammal concentration-range in Table 10.6, although the experimental results indicate a much shorter time for potential survival than 30 min. It is clear that the isolated perfused guinea pig lung during the experiments is not protected by a hydrating and particle protecting system, such as a 'nose'. However, if a situation is considered where a person would be very stressed, e.g. in a fire

Table 10.6 Hydrogen chloride toxicity limit values

Type of limit value	Limit value (ppm)
AEGL-3[8] (lethal exposure limit)	620 (10 min) 210 (30 min) 100 (1 h)
LC_{50}, 30 min, mammal[9]	1600–6000
LC_{50}, 1-hour, rat[8]	3124
IDLH (30 min)[7]	100
ISO/TR 9122-1[1] 5 min lethal exposure limit	12 000–16 000

situation, much of the respiration could very well be through the mouth, leading to a short path of transport (and protection) before the gases would reach the lungs. As for the comparison between humans and rodents, it has been demonstrated that humans retain much more particulate material in the respiratory tract than rats both in the case of nose breathing and especially in the case of mouth breathing.[10]

It is interesting to note that a gaseous hydrogen chloride molecule will have a very high diffusion and collision rate with the mucous membranes in the upper respiratory tract, which will prevent molecules from reaching the lungs. When the hydrogen chloride molecule is travelling together with soot particles, the gas phase hydrogen chloride molecules will interact with available soot surfaces and the number of gaseous hydrogen chloride molecules will depend on the dynamics of adsorption–desorption on the particle surfaces, i.e. particles might very well act as a media for transport into the deeper regions of the respiratory system. Less of the hydrogen chloride would then be 'filtered' out in the upper respiratory tract for hydrogen chloride-containing smoke than for an hydrogen chloride gas mixture. Such behaviour is not included in the present study as the nose-filtering system is absent.

Analysis of the albumin solution used as artificial blood during the experiments shows clearly that gaseous content from the smoke will be transported into the body through the blood. Typical compounds from PVC smoke were found but also other compounds. Small amounts of combustion products were also found in the control and hydrogen chloride experiments which could be explained by soot residues in the mixing chamber and the tubes connecting the mixing chamber to the isolated lung.

The dissection performed on the lungs after the experiments showed particles on every level of the lung. The most interesting result was perhaps that particles were found that had started to be transported through the lung cells, i.e. they were found inside the lung cells.

10.4 Conclusions

In general, the isolated and perfused lung model together with the steady-state tube furnace provides an interesting methodology for investigating (in particular) the influence of irritants on lung tissues without actually running painful experiments on animals. It also provides a testing system for investigating what substances will pass over to 'the blood' side of the lungs and the impact of particles of lung tissues. The following points were found:

- Short exposures (8 min) of hydrogen chloride gas and PVC smoke at similar hydrogen chloride concentrations (~3000 ppm) caused a drastic decrease in the guinea pig lung function. The exposure time is short compared with, for example, LC_{50} data for rats but more in line with limit values given by

NIOSH (IDLH[7]), EPA (AEGL-3[8]) than those in ISO/TR 9122-1[1] (see Table 10.6).

- Rat lungs exposed to the same type of PVC smoke as the guinea pig lung showed much better endurance and it was possible to statistically verify different levels of endurance of the lung as a function of the hydrogen chloride level of the fire smoke.
- Several highly toxic substances were found in the perfusion buffer used in the experiments with PVC. Since the buffer replaces the blood flowing through the living system this is a strong indication that such substances will pass over to the blood circulation in a mammal exposed to fire smoke.
- Carbon particles from inhaled PVC smoke were recovered in the lung tissue at different levels. Long carbon chains were found in the perfusate, an indication that particles have passed over to the blood side of the lung.

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11

Sampling and measurement of toxic fire effluent

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Abstract: A key requirement for the assessment of toxic hazard in fire is a knowledge of the range, nature and concentrations of toxic/irritant species and smoke particulates present in the fire effluent. Owing to the often extremely hostile conditions present in a fire, it is necessary to adopt specialised methods for sampling and analysis if the results are to be meaningful. This chapter provides both a detailed summary of methodologies which have proved to be successful over a wide range of fire research/testing regimes, and offers guidance for setting up practical sampling and analysis systems.

Key words: fire toxicity, sampling and analysis of fire effluents.

11.1 Introduction

11.1.1 The need for sampling and analysis of fire effluent

To enable a realistic assessment of the toxicity and/or environmental impact of fire effluents and residues, it is clearly important to understand the range and concentrations of chemical species (including solid and liquid aerosols) likely to be produced in fire. In practice it is rarely, if ever, possible to obtain such data from accidental fires while they are in progress, so these data are normally obtained from physical models of fire scenarios. These physical models can range from small- to large-scale standard tests and include ad hoc experimental test fires. The choice, scope and use of such models in, for example, 'Fire Safety Engineering' are described elsewhere in this book (particularly Chapters 12 and 13) but we describe here details of currently accepted sampling and analysis methods for a wide range of important chemical species and aerosols, which can be generated in these models.

When considering human toxicity it is possible to identify two main sources of injury and death in fires from fire effluents in terms of the chemical species produced – asphyxiants (as typified by carbon monoxide, hydrogen cyanide and reduced oxygen) and irritants (as typified by inorganic halogenated species and organic oxygenated species). A range of species which have the potential to harm the environment have also been identified[1] which include dioxins, furans, perchlorinated biphenyls (PCBs), persistent organic pollutants (POPs) and

polycyclic aromatic hydrocarbons (PAH) amongst others. However, it is important to appreciate that during a fire many chemical species will have the potential to produce both a toxic hazard and a detrimental impact on the environment.

Standardised methods for dealing with these fires from an environmental impact standpoint are currently in preparation[1] and are not specifically included here – although in some cases (where indicated) the methodology will be appropriate for the analysis of environmentally harmful species.

11.1.2 The challenge to the analyst

Although detailed guidance is available,[2] the measurement of fire effluents, including solid and liquid aerosols, remains a great challenge to the analyst.[3] For example, the mobile atmosphere in the close vicinity of a full-scale test fire may typically be at temperatures of over 1000 ºC, highly turbulent, and contain a very wide range of compounds (possibly as many as a hundred or more of direct interest to the toxicologist and environmentalist) with concentrations varying over several orders of magnitude. The atmosphere will typically contain acidic/corrosive species, labile/unstable species, condensable vapours (including water) and a range of liquid and solid particles as aerosols covering a very wide range of particle-size fractions and physical properties. In addition such aerosols may also contain a wide range of adsorbed and/or absorbed chemical species that can contribute to the overall toxicity/environmental effects.

Close to the fire source, temperatures are likely to be high enough for a range of chemical reactions which will result in a time-variable content in the effluent. Chemical content of the atmosphere here is likely to be mainly governed by thermodynamic equilibrium considerations. At high temperatures reaction rates will be fast enough to allow equilibrium conditions prevail. As the distance from the fire increases, the chemical nature of the atmosphere will change due to an increase of kinetically 'frozen' chemical reactions as the gases cool. Agglomeration of aerosol particles can occur and most changes in concentrations of species will be the result of dilution rather than further chemical reaction, although some components (e.g. nitrogen oxides, aldehydes) will continue to be modified at cooler temperatures. Chemical species may also be partially absorbed and/or condensed onto cooler surfaces in both the fire enclosure and sampling equipment, rendering them unavailable for measurement, but may be re-released if the fire or heat spreads to these areas. At positions relatively distant from the fire source other phenomena may occur, such as sedimentation of particulates, which will also affect measurements.

Hence the choice of sampling position(s) is a key factor in any determination of fire effluents, and the position(s) chosen will often depend on the required end use of the data. For example fundamental combustion studies may require sampling directly from a flame, with toxicity/life threat measurements taken

further away from the fire source. Use of data for environmental impact assessment may require sampling well away, possibly several kilometres, from the fire source. Such choice of sampling position is beyond the scope of this chapter and may be found elsewhere in the book (see Chapters 12 and 13).

From an analysis standpoint, in addition to a consideration of the general nature of the fire atmosphere outlined above, the choice of analytical method must also take into account the fact that many chemical species of interest are likely to have similar chemical and physical properties, resulting in the possibility of cross-sensitivity or ambiguous data during analysis.

From a toxicity assessment standpoint, compounds of interest may be chosen considering their contribution to the toxicity of the whole fire effluent,[4] (e.g. using fractional effective dose (FED), or fractional effective concentration (FEC) models[5,6]). The main species of interest for acute effects from exposure to fire effluents are carbon dioxide (CO_2), carbon monoxide (CO), reduced oxygen (O_2), hydrogen chloride (HCl), hydrogen bromide (HBr), hydrogen cyanide (HCN), hydrogen fluoride (HF), nitric oxide (NO), nitrogen dioxide (NO_2), sulphur dioxide (SO_2), formaldehyde (HCHO) and acrolein (C_3H_4O).[7–9] However, this list is not exhaustive (e.g. recent studies[10] have shown that in specific cases, other compounds such as phenol or ammonia have to be considered). The prediction of fire toxicity is not an exact science, and large margins of error are necessary to ensure safety. As a general rule all gases present in the fire effluent with a contribution of greater than 10% to FED/FEC (see Chapters 1 and 8) should be included in the analysis.

In general, modern laboratory chemical analysis techniques for gases and vapours require a relatively 'clean', stable, cool sample, free from solid contaminants – conditions not normally associated with fire effluents. During the cleaning of a fire effluent prior to analysis, various losses and physical and chemical changes can be anticipated due to the need to cool and filter the sampled gases and to remove condensable species (e.g. water).

It is therefore necessary to take all these factors into account when sampling and analysing a fire atmosphere, and unless 'best practice' procedures, as outlined here, are carefully followed, inconsistent results are likely. However, for some species it must be accepted that accurate analysis will be very difficult, e.g. where sampling times may not be long enough for a representative sample, or where the species may be highly labile and subject to change over a short period (e.g. dioxins).

11.2 Sampling fire effluents: general principles

The requirement for any fire atmosphere sampling system is to obtain a realistic and representative sample for presentation to the analysis equipment, without unduly disturbing the operation of the fire model itself. How far this ideal is achieved depends on a number of factors – including the chemical and physical

nature of the species for analysis, the temperature, length and material used for the sampling probe and extract tubing (sampling line), sample flow rate, the type and position of particulate filters and type and position of condensate (e.g. water) traps.

Sampling can be either 'extractive' or '*in situ*'. Extractive sampling is where the samples are removed from the fire test or experiment for analysis – either immediately or at a later stage. *In situ* sampling is where the measurements of chemical species are made directly at their point of generation, e.g. the space within or immediately surrounding a flame. The choice is often limited by the methodology available for the analysis, or the type of fire being studied (e.g. bench or large scale); however, *in situ* methods (e.g. analysis by infrared spectroscopy applied directly to a flame) are usually difficult to use and are more applicable to fundamental studies (e.g. chemical reactions within flames).

The more commonly used extractive methods usually utilise a sampling probe positioned at the required sampling point, connected to an inert (often heated) sampling tube and pump to conduct samples continuously to the collection or analysis point. Particulate filters and condensate traps are also commonly used in such a sampling line. The samples may be analysed immediately or stored for analysis at a later stage. Later sections of this chapter describe the details, but as a brief summary and to indicate the range of methods available, typical extractive methods and examples of species analysed in each case include:

- direct continuous analysis from the sampling line using non-dispersive infrared spectroscopy (NDIR) for carbon monoxide, carbon dioxide; paramagnetism for oxygen; quasi-continuous analysis by Fourier transform infrared spectroscopy (FTIR) for a variety of inorganic and organic species;
- indirect analysis from the sampling line (via gas valve, gas syringe or autosampler) followed by gas chromatography (GC) or GC/mass spectrometry (GC-MS) for many inorganic and organic species;
- trapping with a solid adsorbent/absorbant, with chemical reaction, e.g. silica with a 2,4-dinitrophenyl hydrazine (DNPH) coating for aldehydes and ketones;
- trapping by solid, inert, adsorbent, e.g. 'zeolites' and activated charcoal for PAH, benzene and other volatile organic compounds (VOC) followed by GC-MS or GC/flame ionisation detector (FID);
- trapping by solution in the liquid phase e.g. sodium hydroxide (NaOH) solution for hydrogen cyanide (HCN), hydrogen fluoride (HF); water for hydrogen chloride (HCl), hydrogen bromide (HBr); hydrogen peroxide (H_2O_2) for sulphur dioxide (SO_2); and HCl + DNPH for aldehydes;
- collection in an inert bag, e.g. for analysis of oxides of nitrogen by chemiluminescence.

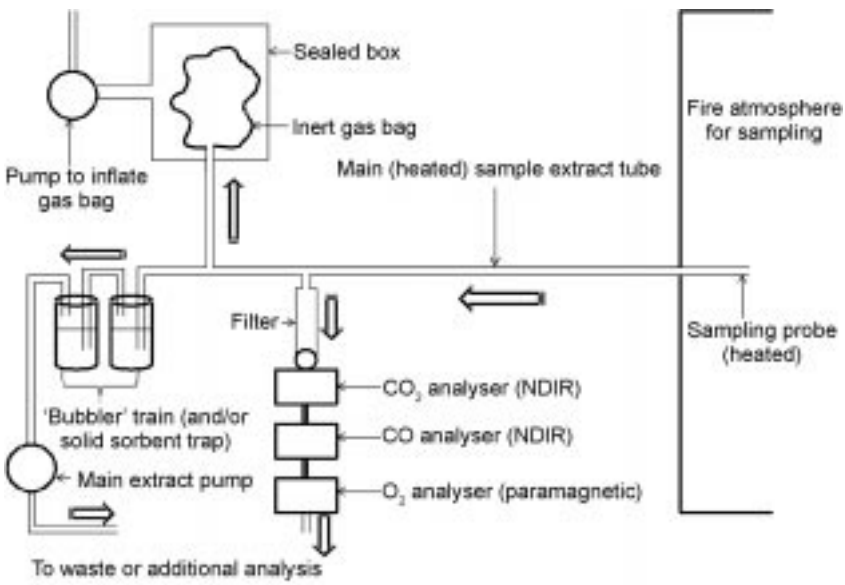
As a general rule, both the sampling probe and sampling line should:

- be inert to the species of interest and other compounds present in the effluent;
- be heated to a temperature sufficient to minimise condensation of any component of the sample;
- be as short as possible to minimise losses;
- have a high extract velocity to limit the time delay between sampling point and analysing or trapping system.

An important consideration is the compromise between sampling flow rate and sensitivity, e.g. where a relatively large sample may be required to enable small concentrations to be measured, but extraction of such a large sample might adversely affect the behaviour of the fire model itself. This may be particularly relevant for small-scale bench-top fire models. It is also often necessary to filter the sample to remove particulates and possibly condensable species, where direct input into a measuring instrument is required.

11.3 Practical arrangements for a typical sampling line for fire effluent gases and vapours

Figure 11.1 shows a schematic of a sampling train showing the key elements in a practical sampling system to enable typical 'real-time' analysis and/or storage for 'offline' analysis. A general description of the components follows the schematic.



11.1 Schematic showing the main elements of a typical sampling system to enable 'real-time' analysis and storage for 'offline' analysis.

11.3.1 Sampling probe

Samples for analysis are extracted from the fire atmosphere through a sampling probe. Depending on the physical nature of the atmosphere this may be a simple open-ended tube where the atmosphere is likely to be relatively homogeneous, or a multi-holed probe where stratification around the sampling point will require the sample to be taken across a representative section of the test atmosphere (e.g. in a duct). Further considerations are necessary when sampling for particulates, where 'iso-kinetic' sampling is required. This technique ensures that the sample extract flow velocity is equal to the main effluent flow velocity to ensure the particulate concentration is not diluted or enriched. Detailed guidance on the choice of sampling probe for various fire models has been published.[11–13]

11.3.2 Main sampling tube or line

From the sampling probe, the extracted effluent atmosphere is conducted along a heated, inert sampling tube or line. Typical materials for this are stainless-steel tubing (preferably with polytetrafluoroethylene (PTFE) internal lining, particularly where acidic species are present) with a minimum internal diameter of 4 mm. The sampling line should be heated to between 150 ºC (minimum) and 200 ºC (maximum) as measured by a thermocouple, to avoid condensation of water in the line prior to analysis. Heating of the sampling line can be carried out 'ohmically' by passing a low voltage (i.e. lower than 50 volts) electric current through the tubing with thermocouple control and a suitable electronic controller, or through manual setting. Other possibilities are the use of proprietary trace heating lines or low voltage heating tape insulated externally with glass fibre tape. It is recommended that the maximum length of sampling line is set at 4 metres, though this should be kept to a minimum. It is usually necessary to measure the sample transit time in the sampling train for a particular sampling installation, to allow for the time difference from source to sampling point to be calculated. Also, potential cooler points at connections in the sampling line and at various other points can produce condensation and modification of the effluent. Details of sampling lines suitable for various fire models are available in the literature.[12,13]

11.3.3 Sampling flow rate

A flow rate through the main sampling line of approximately 5 l/min has been found satisfactory from most medium to large-scale fire test apparatus. The sample is drawn through the line with a pump positioned at the furthest point downstream of the sampling train. The flow rate can be monitored by a suitable flow-meter positioned in the outlet pipe of this pump. With smaller test apparatus, e.g. 'bench-top', this flow rate may need to be lowered considerably to avoid disturbance or undue depletion of the sampled atmosphere. The highest

possible linear flow rate should be aimed for, as this will reduce both residence time in the line – and therefore reduce losses through adsorption/absorption on the tube walls – and also reduce the time delay between sampling and online analysis. Detailed guidance is available in the literature.[12,13]

11.3.4 Sampling arrangements where 'real-time' continuous analysis of gases and vapours is possible

Carbon dioxide, carbon monoxide and oxygen can be routinely sampled on a continuous basis in real time using proprietary 'stand-alone' instruments (carbon dioxide and carbon monoxide by non-dispersive infrared, and oxygen by paramagnetism). These analysers are usually fitted with internal sampling pumps, allowing direct connection via a 'tee' piece into the main sampling line. Further, as these analysers are 'non-destructive' to the sample, it is possible to connect them in series from one 'tee' piece; the outlet of the first passing to the inlet of the second, etc. Although these analysers are also commonly fitted with an internal particulate filter this is usually inadequate for most fire effluent sampling applications. It is therefore essential to provide particulate and moisture filters, usually immediately after the 'tee' piece from the main sampling line and before the analysers. These can be conveniently prepared by packing two flexible transparent tubes (each typically 300 mm long and 25 mm internal diameter) with glass wool (to remove particulates) and small (5–10 mm) chunks of anhydrous calcium chloride (to remove moisture). Connection to the heated 'tee' piece should be made with heat-resisting tubing (e.g. silicone rubber). It is also possible to remove water (and other condensable species) by passing the sampling line through a coolant at a temperature below the dew point of the effluent, using a suitable housing to allow periodic draining of the condensate.

It should be noted that the relatively new analytical technique of FTIR for fire gas analysis is gaining in popularity as a means of obtaining an almost continuous analysis of fire effluents for many important toxic components which are also IR active. Such analysers normally require specialised filtering and sample flow and pressure conditions[12,13] but can be effectively added to the 'continuous real-time' sampling line arrangements described here.

It is important to appreciate that when carrying out analysis with non-destructive methods, the final outlet should be positioned so that it cannot produce a toxic hazard to personnel.

11.3.5 Sampling arrangements where storage of samples for later analysis is necessary

Many species of interest to the fire toxicologist are difficult to measure continuously in real time, and for these species, collection and storage of the

samples for later analysis are necessary. This can be achieved in a number of ways depending on the species of interest (see Table 11.1 and Appendix A). For example the effluents may be collected in an inert gas sampling bag; trapped in liquid solution 'bubblers'; or trapped using liquid or solid sorbents. Unfortunately with these methods, it is often difficult to obtain sufficient samples to adequately follow the concentration–time profile in the fire for the species of interest. The analytical data will apply to relatively long time periods during the progress of the fire providing only an integrated sample. This problem may be solved by the use of online FTIR which has the potential to provide rapid analysis and the technique is likely to become increasingly used in the future.[12,13] Other solutions to providing rapid single samples over short time periods have included the use of evacuated glass vessels, which can be arranged to extract an effluent sample by sucking in the effluent using the vacuum. The vessels can be arranged to extract at frequent intervals to cover the fire profile adequately and stored for later comprehensive analysis (e.g. by combined GC-MS[14,15]). Detailed information regarding trapping by solid and liquid sorbents with appropriate analytical methods is also available.[2,16,17]

Table 11.1 Trapping and analysis summary for liquid systems

Analysed gas	Analyte(s) in liquid phase	Analytical technique	Trapping solution
HCl, HBr	Cl^-, Br^-	HPIC	0.1 M KOH or NaOH or H_2O_2/water or eluant
HCN	CN^-		0.1 M KOH or NaOH
HF	F^-		1.0 M NaOH or KOH
Formic acid	$HCOOH/HCOO^-$		0.1 M KOH or NaOH eluant
Ammonia NH_3	NH_4^+		0.024 M HCl or 0.003–0.009 M CH_3SO_3H
SO_2	SO_4^{2-}, SO_3^{2-}		Add 10 ml H_2O_2 30% (V/V) per litre of water (prepare the solution immediately prior to use)
H_2S	HS^-/S^{2-}		0.1 M NaOH or eluant
Formaldehyde Acrolein	HCHO CH_2CHCHO	HPLC	HCl 2M saturated with DNPH (decant the solution before use to eliminate the excess of DNPH) Cartridges of silica impregnated with DNPH can be used to trap aldehydes in gas phase.
Phenol	C_6H_5OH		Methanol/water (60/40)
		GC-MS	Methanol/water (60/40)

HPIC, high performance ion chromatography; HPLC, high performance liquid chromagtography; GC-MS, gas chromatography combined with mass spectrometry.

Figure 11.1 shows a 'tee' piece connected to the main sampling line with an inert bag attached. The bag is housed in a sealed outer box connected to a vacuum pump. Prior to sampling, the bag is completely evacuated. Samples are taken by connecting the vacuum pump to the sealed box which fills the bag with fire effluent without the effluent coming into contact with pump components, which might modify the sample. The bag fill rate (controlled by the vacuum pump rate) is chosen for the particular sampling rate required. For example in a bench-scale test with a steady-state period over which the sampling is required, the sampling rate would be adjusted to fill the bag over this period. However, when frequent sampling is required (e.g. to follow a fire time profile) more rapid sampling will be necessary. Following the collection of the samples they can be stored (see Section 11.3.7) before analysis. Analysis is usually achieved by introducing the sample directly into the measuring instrument (e.g. oxides of nitrogen by chemiluminescence). Use of proprietary colour-change measurement systems (with appropriate reference to their scope and limitations) to quantify specific species can also be conveniently used on the contents of bag samples.

Figure 11.1 also shows a 'bubbler train system' (or alternatively or additionally a sorbent trapping system) attached to the main sampling line. With the bubbler system, samples are drawn through the liquid contained in each vessel, which are positioned one after the other in series. In some cases it may be necessary to connect the bubbler train to a separate tee piece in the main sampling line with a separate pump, to allow a lower flow rate through the bubblers consistent with achieving maximum trapping efficiency. The second bubbler in the train is regarded as a 'carry-over' trap from the first which provides the main trap. In practice both vessels' contents are usually combined for analysis or the second bubbler checked for 'carry-over'. The absorbing solution is chosen to ensure efficient trapping of the species of interest and as these are often acidic species a common trapping medium is dilute alkali (e.g. sodium hydroxide).

11.3.6 Basic principles of solid/liquid sorbents for trapping fire effluents

Solid-phase systems (adsorption)

Solid-phase systems can use chemical or physical adsorption. In chemical adsorption, the species of interest react chemically with a solid substrate to form a solid-phase compound. The method is usually highly selective. An example is DNPH–silica cartridges, able to react with aldehydes and ketones to produce a derivative suitable for later analysis.

In physical adsorption, dipole–dipole interaction between polar species, or van der Waals forces (weak attractions arising when any molecular species are in close contact) trap the species. This method is less selective, and uses such sorbents as activated charcoal. Nevertheless, some adsorbers such as zeolites

(i.e. microporous alumino-silicate materials) are specific to a given size of molecule trapped in their pores.

The use of solid adsorbers is achieved over two stages. Firstly, the fire effluent is sampled at a given flow rate and passed through a tube packed with the adsorbing medium. Secondly the species of interest is desorbed prior to analysis. This stage can be achieved by solvent extraction specific to the species of interest (e.g. acetonitrile, carbon disulphide) or by a physical method, e.g. by heating – 'thermal swing adsorption' (TSA) or under pressure – 'pressure swing adsorption' (PSA).

Liquid-phase systems (absorption)

Here, a liquid-phase medium uses the absorption/solvent properties of liquids to trap the species of interest. These species are kept in the liquid phase either by dissolution or ionisation. Gases such as hydrogen chloride and hydrogen bromide are trapped by water, sulphur dioxide requires a solution based on hydrogen peroxide in water, while sodium hydroxide solution is suitable for hydrogen cyanide, hydrogen fluoride or nitrogen dioxide. Aldehydes are absorbed in an acid saturated in DNPH.

The analytical techniques used after trapping (see Section 11.5 for details) include chromatographic methods (GC, high performance ion chromatography (HPIC) and high performance liquid chromatography (HPLC)), and traditional methods (titrimetry, electrochemistry, spectrophotometry). Table 11.1 shows the analysed gas or vapour, the analyte (i.e. moiety actually analysed) and the trapping solutions and analytical method used in each case.

11.3.7 Sample storage

Consideration must also be given to the storage of samples which are not analysed in real time directly from the sampling line. This will arise where samples such as those from a bubbler train, solid sorbant sampling tube, or inert gas bag are to be analysed at some period of time after collection. To reduce losses it is important to store such samples for the minimum possible time and under refrigerated conditions where possible. In some cases the adsorbing and/or absorbing medium, where used, can react with the required species over time and produce a lowering of the measured concentration. Where doubt exists, this can be checked with a separate study.

11.4 Analysis of gaseous fire effluents: general principles

Clearly the ideal analytical result would be a continuous measurement of each species of interest with time, over the period of generation of the fire

atmosphere. In practice, because of the restraints summarised in Section 11.1, this ideal is rarely achievable. The options for analysis depend on the species to be measured and the available instrumentation, and the latter may not necessarily be the ideal owing to, for example, economic restraints and available operator skills. It is also important to consider the end use of analytical data when deciding on the methodology to employ for specific species. For example, it may not be appropriate to choose highly sophisticated, expensive-to-operate and sensitive equipment to obtain very accurate and precise analytical data for trace compounds, when the accuracy, precision and scope of the end use application is far less. For example, the toxic effects of fire effluents on humans vary from person to person, and are based on estimates from sub-lethal human exposures or animal exposure experiments. Often relatively simple techniques may suffice, providing the limitations of the method are understood and allowed for.

11.5 Analysis of fire effluents: summary of principal methods available

11.5.1 Infrared spectroscopy

Infrared (IR) light radiation has a range of frequencies just below those of visible light in the spectrum. It has the property of interacting with molecules which have a dipole moment, i.e. positively and negatively charged regions which, in the presence of electromagnetic radiation can be induced to absorb specific energies corresponding to vibrational transitions of the molecule, giving rise to absorption of the IR radiation. The frequency of this field variation is largely dependent on the functional groups in the molecule and the molecule will absorb IR radiation at frequencies corresponding to the vibration of bonds. Many inorganic and organic irritants as well as carbon dioxide and carbon monoxide in fire effluents are IR active. A particular IR active molecule will typically absorb radiation over a number of bands of frequencies forming the basis of species identification and quantification. The absorption spectrum is classically displayed as a series of absorbance peaks on a chart as the frequency or wavelength is 'scanned' by a source and dispersing prism or grating. However, such classical IR analysis has very limited application to fire gases due to the relatively long periods needed for a single sample to be analysed and variants such as FTIR (Section 11.5.3) and NDIR (Section 11.5.2) are used.

11.5.2 Non-dispersive infrared spectroscopy (NDIR)

By careful choice of IR absorption bands (i.e. a frequency band which is relatively unique to a particular species) it is possible to use that frequency to quantify a specific compound continuously and this is the basis of NDIR

instruments. Typical applications for NDIR are for carbon dioxide and carbon monoxide analysis.

The advantages of NDIR are:

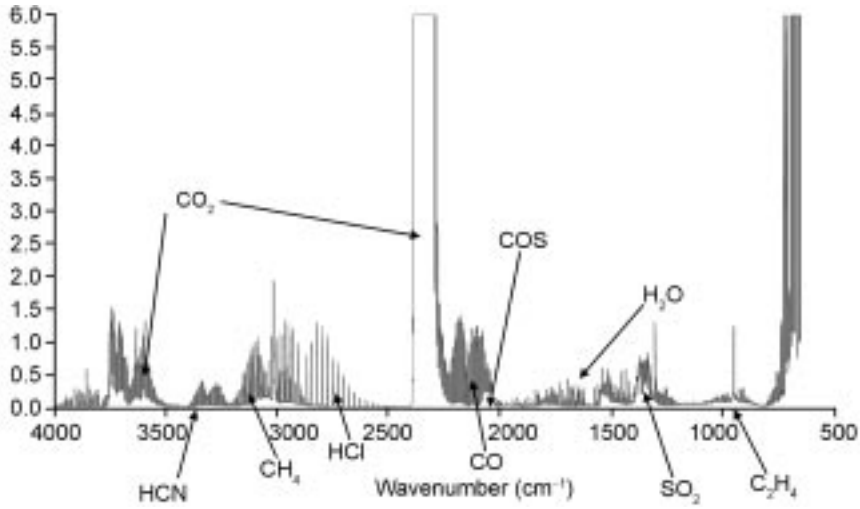
- generally robust, portable, self-contained equipment, relatively simple to operate and maintain;
- can be directly coupled to the sampling line from the effluent generating equipment;
- gives a continuous readout of concentration with time;
- non-destructive, i.e. after measurement gases can be used for further analysis;
- easy to calibrate with standard proprietary gas mixtures;
- easy to change range to cover all typical concentrations in fire atmospheres;
- simple to couple to data-logging equipment;
- fairly specific.

The disadvantages of NDIR are:

- only suitable for a very limited range of species (albeit very important ones in fire toxicity), e.g. carbon dioxide, carbon monoxide;
- requires extensive aerosol filtering and removal of condensable liquids before introducing the sample to the instrument, although sample losses are likely to be relatively low;
- high interference with water.

11.5.3 Fourier transform infrared (FTIR) spectroscopy

With FTIR the sample is continuously irradiated by two beams of IR light which pass through the sample via different paths. When the beams then combine, the resulting 'interferogram' can be mathematically resolved (Fourier transform) to determine the infrared absorption as a function of frequency and used to identify and quantify different species. The value of FTIR over classical IR spectroscopy is that samples can be analysed for many components in one sample and a complete spectrum can be obtained over a relatively short time period (a few seconds). Modern software can identify and quantify many IR active species from a single sample scan and this results in the possibility of quasi-continuous concentration–time plots when the FTIR is connected directly to the sampling line. Sensitivity is dependent on the optical path length through the analysed gas passing through the gas cell, and the type of detector. Typically in the assessment of the toxicity of a fire effluent a folded path length cell of perhaps 4 m is fitted inside the 10 cm path length of the spectrometer. The 'deuterated triglycine sulphate' (DTGS) detector operates at ambient temperature, whereas the 'mercury–cadmium–telluride' (MCT) detector operates at low (liquid-nitrogen cooled) temperature, but has a sensitivity ten times higher than the DTGS detector.



11.2 Example of a typical FTIR spectrum of fire effluents.

Fire effluent gas and vapour analysis using FTIR is now routinely used in the field of fire safety, often following the original guidance from a European Union funded research programme 'Smoke Analysis by Fourier Transform Infrared spectroscopy' (SAFIR).[12] The SAFIR guidance has also been extended and applied to an International Standard, ISO 19702, for the use of FTIR in fire gas analysis.[13]

In summary, this technique involves sampling gas through a single measurement cell and recording the spectral response, generally within the frequency (or for more convenient units which are still proportional to energy 'wavenumber' the number of oscillation per centimetre) range from 650 to 4000 cm^{-1}. As for the classical infrared method described in Section 11.5.1, the absorbing frequencies and the intensity of absorption at those frequencies allow identification and quantification (through suitable calibration) respectively.

The FTIR technique is capable of measuring concentrations below 1 ppm and allows dynamic online measurement of these concentrations, typically every 5 seconds. These data are particularly valuable for use in mathematical models which calculate toxicity of fire effluents as a function of time.

The advantages of FTIR are:

- potential to identify and quantify a wide range of fire effluent species in one sample;
- can be directly coupled to the sampling line from the effluent source;
- rapid scanning and data reduction can provide a quasi-continuous analysis of species;
- data can be re-processed at any time after collection to improve data analysis.

The disadvantages of FTIR are:

- expensive, generally bulky equipment requiring skilled operations and interpretation;
- intensive maintenance required to retain optimum performance;
- extensive filtration required prior to entry into the instrument resulting in potential sample loss.

Figure 11.2 shows a typical FTIR spectrum with absorbance peaks due to various species of interest in combustion toxicity.

11.5.4 Paramagnetism (for oxygen)

Paramagnetism is a property of relatively few materials (and distinct from ferromagnetism resulting in permanent magnetic materials, or diamagnetism, possessed by all materials) which are weakly attracted to an applied magnetic field. Chemical species with unpaired electrons in their electronic structure, such as oxygen (which has two) exhibits paramagnetism in the presence of an external magnetic field. Oxygen's paramagnetism is exploited in many commonly found continuous oxygen analysers.

The advantages of paramagnetism are:

- generally robust, portable, self-contained equipment, relatively simple to operate and maintain;
- can be directly coupled to the sampling line from the effluent source;
- gives a continuous readout of oxygen concentration with time;
- easy to calibrate with air and standard proprietary oxygen mixtures;
- easy to change range to cover all typical concentrations in fire studies;
- simple to couple to data-logging equipment;
- highly specific for oxygen (nitric oxide and nitrogen dioxide interfere, but are not present in sufficient qualities (typically 0.1%) to cause interference in fire effluents).

The disadvantages of paramagnetism are:

- only suitable for oxygen;
- requires extensive aerosol filtering and removal of condensable liquids before introducing the sample to the instrument, although sample losses are likely to be relatively low;
- some interferences can occur in presence of high quantities of other paramagnetic species (e.g. NO_x).

11.5.5 Chemiluminescence (for oxides of nitrogen)

Chemiluminescence refers to any chemical reaction which produces light. By measuring the light intensity it is possible to quantify the species involved in the reaction. A classic example is the reaction of nitric oxide with ozone to produce

nitrogen dioxide. The NO_2 formed in this way is in an electronically excited state (NO_2*) and decays from this state with the release of light across the visible and IR spectrum. These reactions are summarised below:

$$NO + O_3 \rightarrow NO_2^* + O_2$$

$$NO_2^* \rightarrow NO_2 + h\nu \text{ (light)}$$

The relatively weak light is amplified in a photomultiplier tube before measuring. The intensity of the light is proportional to the concentration of NO in the sample. Fire effluent may contain NO_2 as well as NO, although this NO_2 does not display chemiluminescent reactions. However, by conversion of the fire effluent NO_2 (through controlled heating) to NO, this can then undergo the ozone reaction above to form the activated form of NO_2*. The concentration of activated NO_2* derived from the original fire effluent NO_2 can therefore be obtained. A high temperature stainless steel furnace (up to 800 ºC) or a moderate temperature molybdenum catalytic furnace (about 380 ºC) produces the conversion of NO_2 into NO. Self-contained analysers are available which can give a direct readout of NO and NO_2 concentrations from a discrete sample. Some are equipped with an acid gas scrubber, to remove interfering species such as hydrogen cyanide.

The advantages of chemiluminescence are:

- relatively specific for oxides of nitrogen;
- possible to differentiate between NO and NO_2 concentrations (i.e. providing a value for 'NO_x');
- relatively easy to operate and calibrate using standard proprietary gas mixtures.

The disadvantages of chemiluminescence are:

- bulky equipment requiring intensive, skilled operation with expensive maintenance to preserve optimum operating characteristics;
- can be cross-sensitive to other nitrogenated species, especially when a converter is used.

11.5.6 Chromatography

General principles

Chromatography refers to the separation of a mixture of compounds into its individual components, by passing the mixture over a substrate, which selectively retards progress of the individual components along the substrate until separation is complete. The earliest examples separated plant pigments, giving rise to visible bands of colour of each component, hence the name 'chromatography'. This basic principle has, however, evolved into a wide range

of highly refined, often automated, component-separating instruments for both liquid and gas/vapour mixtures.

A chromatograph can be used as a 'stand-alone' instrument or in conjunction with other instruments, which can take advantage of the separating powers of the chromatograph. These include the mass spectrometer (MS), resulting in a very powerful tool for separating, identifying and quantifying the individual components of extremely complex mixtures.

It may appear that these techniques are ideally suited to the measurement of compounds typically encountered in the fire atmosphere and indeed many studies have utilised these instruments. However, there are several factors which militate against its routine use in this field. The instruments are relatively expensive, often require skilled operators and have fairly complex maintenance requirements to maintain acceptable operating characteristics. However, these factors have been addressed in modern instruments and their use is likely to increase in this field.

Some important specific types of chromatography are briefly described below.

Gas liquid chromatography

Separation of a mixture of gases and vapours or volatile liquids into their individual components is achieved by passing the mixture through a column packed with a finely powdered solid coated in a high boiling point liquid. Volatile liquid mixtures to be separated can be injected (typically a few μl) into a heated port, or gas or vapour mixtures of a few ml through a heated port or 'gas valve' connected to the entrance to the column. The gas/vapour mixture is swept through the column by an inert carrier gas, e.g. helium, nitrogen or argon, and gradual separation of the mixture occurs as each component is selectively retarded in its progress by its specific interaction with the stationary liquid phase. The packed column is often enclosed in an oven which can be temperature ramped to ensure the mixture components emerge over an acceptable time period. A common variant of the packed column utilises a fine tube many metres in length with an absorbent internal surface coated with a high-boiling point liquid as the substrate. This is known as a capillary column.

Individual mixture components emerging ('eluants') from the column are passed to a detector of which there are several types:

- The flame ionisation detector (GC-FID) is sensitive to organic compounds. The flammable eluants are passed through a small hydrogen flame containing electrodes and as the eluant burns, the electrodes detect increased electrical conduction through the flame and this is electronically processed to produce a signal proportional to the concentration of eluant. This type of detector combines high sensitivity, operates over a wide range of concentration and has a very stable baseline.

- The thermal conductivity detector (GC-TC, the so-called 'katharometer') has moderate sensitivity to almost all volatile compounds. The eluants are passed across an electrically heated wire which experiences a temperature change and therefore an electrical resistance change which is used as the basis of detection. The detector exhibits a low sensitivity for a very wide range of species.
- The electron capture detector (GC-EC) is sensitive to halogenated and nitro compounds and uses a radioactive source to provide a stream of electrons which are attenuated according to the nature of the detected species. The detector exhibits a high sensitivity for a small range of species.
- The flame photometric detector (FPD) uses a similar flame to the FID but detection is by absorption of light.

The gas chromatograph is also commonly linked directly to a mass spectrometer where rapid compound identification of each eluant is possible. There are very many variables in gas chromatography which can be changed to suit the separation required and modern instruments are largely automated in operation with powerful software control and data processing and presentation.

The advantages of gas chromatography are:

- potential for extremely detailed separation and detection of many fire effluent components from one sample;
- can be directly coupled to the effluent source.

The disadvantages of gas chromatography are:

- expensive, generally bulky equipment requiring skilled operators;
- intensive maintenance required to retain optimum performance;
- individual samples require a relatively long time for analysis (typically 30 min per sample).

Liquid chromatography

Similar principles apply as with gas chromatography, although in this case the mixture to be separated remains as a solution and is passed through the column using a high-pressure pump. Liquid chromatography may be termed 'high performance liquid chromatography' or 'high pressure liquid chromatography', both designated 'HPLC'.

A range of detectors is available but commonly a spectrophotometric method is used, where the eluants are identified through their varying ability to absorb light (often visible to ultraviolet). An important variation of HPLC is 'high performance ion chromatography' (HPIC) which detects eluants by measuring their conductivity in solution (conductometric detector) or their electrical activity (amperometric detector), the latter being used for cyanides.

As with gas chromatography, modern instruments may be highly automated both for the chromatographic process and data collection and presentation.

The advantage of liquid chromatography is:

- direct analysis of several liquid-trapped species from one sample.

The disadvantages of liquid chromatography are:

- expensive generally bulky equipment requiring skilled operators;
- intensive and expensive maintenance required to retain optimum performance;
- difficult to separate some components in fire effluents.

11.5.7 Mass spectrometry (MS)

A mass spectrometer is normally used to identify individual chemical species – either introduced directly as a solid, liquid or gas/vapour, or (very commonly) from a gas or liquid chromatography column.[18] Typically the (single) compound enters a high vacuum enclosure where it is bombarded by a stream of electrons at a fixed controlled energy level. This has the effect of breaking the compound molecules into charged fragments (ions) which are then passed to a detection stage. (There are several alternative ways of generating these ions, a significant alternative being 'chemical ionisation' which relies on electron bombardment in association with chemical reactions to generate the ions.)

There are two main detector types:

- 'Magnetic sector' – where the charged fragments are passed between the poles of a powerful electromagnet whose field strength is scanned, bringing successive fragments to a focus on a sensitive charged-particle detector.
- 'Quadrupole' – where the separation is achieved by passing the ions through electric and radiofrequency fields.

There are several other detector types, notably the 'time of flight' which separates the ions on the basis of their transit time in an accelerating field.

The fragmentation pattern under the standardised conditions of the spectrometer ion source is characteristic of the original compound and identification (often automatically) is assisted by comprehensive 'libraries' of spectra.

The advantages of MS are:

- relatively unambiguous identification of a very wide range of typical fire effluents;
- can be coupled directly to a chromatograph (e.g. GC-MS), producing possibly the ultimate separating and identification procedure for fire gas analysis.

The disadvantages of MS are:

- expensive, generally bulky equipment requiring skilled operators;
- intensive and expensive maintenance required to retain optimum performance;

- unsuitable for online analysis, though samples taken in sorption tubes can be preserved for subsequent analysis.

11.5.8 Colorimetry

For analysis of species in solution, a common method is colorimetry (or spectrophotometry). The species of interest undergoes a chemical reaction with a specific reagent to produce a coloured product which can then be measured using a colorimeter or spectrophotometer. These instruments use filters or a monochromator (respectively) to pass light of suitable wavelength(s) through the sample where it is partially absorbed by the coloured product, the degree of absorption being proportional to the concentration of the original species. The apparatus is normally calibrated by measuring absorbance with various standard solutions of the coloured derivative of the required species. As an illustration of these methods, analysis of two common fire effluents, hydrogen cyanide and hydrogen fluoride is summarised in Table 11.2.

11.5.9 Ion-specific electrodes (ISE)

Many important fire effluents produce ions in solution. Samples trapped by a suitable absorbing liquid can be analysed by measuring the voltage between two electrodes (one is a reference electrode at an accurately known potential) inserted into the solution. Selectivity is achieved by choice of measuring electrode – various designs and constitutions of electrode have been developed which, together with a fixed electrode potential, have proved relatively selective for particular ions. The potential generated is compared with the reference

Table 11.2 Specific spectrocolorimetric methods for HCN and HF

Analysed gas	Analyte(s) in liquid phase	Analytical technique	Advantages and disadvantages
HCN	CN^-	Picric acid colorimetry. In presence of cyanides, picric acid (2,4,6-trinitrophenol) produces a red colour linked to cyanide concentration.	Fast and low cost Few interferents Low limit of detection
HF	F^-	2-(p-sulphophenylazo)-1,8-dihydroxynaphthalene-3,6-disulphonic acid (SPADNS) inverse colorimetry. In presence of zirconium ions, SPADNS produces a red colour destroyed by presence of fluoride ions.	Fast and low cost Few interferents High limit of detection

electrode and measured with a sensitive voltmeter. Quantification is achieved by calibrating the measuring electrode voltage with standard solutions of the required ion.

The advantages of ISE are:

- cheap and simple to operate by relatively unskilled operators;
- simple apparatus suitable for 'field' work.

The disadvantages of ISE are:

- often cross-sensitive to several ion types including the required ion;
- requires frequent calibration and checks on the efficiency of the electrodes;
- many ISEs are easily 'poisoned' by other species present in fire effluents.

Potentiometry

A method particularly suited to chloride and bromide ions (e.g. derived from hydrogen chloride and hydrogen bromide respectively) is silver nitrate potentiometry. For this technique, a silver electrode measures the variation of electrical potential in the tested solution during the addition of silver ions. The sudden potential variations obtained correspond to the presence of chloride or bromide ions, and the amount of silver ions added is related to the concentration of the chloride or bromide ions. This technique has been successfully used in the past, but is cross-sensitive to many other compounds. When both chloride and bromide ions are present, interpretation of results is often complex.

The advantages of potentiometry are:

- relatively simple apparatus, easy to maintain;
- can be installed close to sampling point.

The disadvantages of potentiometry are:

- often cross-sensitive to species other than that required;
- requires frequent (time consuming) calibration;
- high limit of detection.

11.5.10 Colour-change detector tubes

These are proprietary methods which draw the fire effluent sample through a transparent glass tube packed with chemical reagents. These act specifically on the required species to form a coloured derivative. The rate and volume of sample flow are carefully controlled (a hand bellows or separate pumping system is used), resulting in a length of coloured derivative in the tube, which is proportional to the concentration of the required species. The tube is often calibrated directly in concentration units.

The advantages of colour-change detector tubes are:

- very compact, portable equipment requiring minimal skills to achieve an acceptable 'readout';
- suitable for situations where a permanent sampling line is not possible or desirable;
- easy to maintain; tubes are pre-calibrated and ready for instant use.

The disadvantages of colour-change detector tubes are:

- can be cross-sensitive to species other than the one required, particularly where the same chemical groupings are present – however, this aspect is recognised by manufacturers and guidance given on dealing with it;
- may take a relatively long time (in fire terms) to take a measurement directly from the effluent generating equipment – more suitable for 'offline' measurements of stored samples.

11.5.11 Direct gas-phase techniques

Direct MS analysis of fire effluents has been successfully used although the technique is limited to mixtures of few components – rarely encountered in fire effluent studies. The technique is mainly suitable for combustion research. Raman IR spectroscopy has also been studied with limited success. This form of IR spectroscopy enables normally unpolarised – and therefore normally IR inactive – species such as hydrogen, nitrogen or oxygen to exhibit an IR spectrum, however, it is much less sensitive, and FTIR remains the preferred IR technique.

11.5.12 Electrochemical cells

Commercial electrochemical cells, designed for automotive and flue gas emissions monitoring provide a rapid and reliable means of quantifying carbon monoxide, carbon dioxide, nitric oxide, and nitrogen dioxide from ppm levels to 0.1%. They rely on simple electrochemical cells and selective filters to minimise interference. They have relatively quick response times (~20 seconds), but a limited operational life of 2–3 years.

Oxygen electrochemical sensors are of the self-powered, diffusion-limited, metal–air battery type, comprising an anode, electrolyte and an air cathode. The rate at which oxygen can enter the cell is controlled by the size of the capillary hole at the top of the sensor. When oxygen reaches the working electrode, it is immediately reduced to hydroxyl ions:

$$O_2 + 2H_2O + 4e^- \rightarrow 4OH^-$$

These hydroxyl ions migrate through the electrolyte to the lead anode where they are involved in the oxidation of the metal to its corresponding oxide:

$$2Pb + 4OH^- \rightarrow 2PbO + 2H_2O + 4e^-$$

As the two processes above take place, a current is generated which can be measured externally by passing it through a known resistance and measuring the potential drop across it. Since the current produced is proportional to the rate at which these reactions occur, its measurement allows accurate determination of the oxygen concentration.

As the electrochemical reaction results in the oxidation of the lead anode these sensors have a limited life. Once all the available lead has been oxidised they no longer work. Typically oxygen sensors have 1–2 year lifetimes; however, this can be lengthened by increasing the size of the anode or restricting the amount of oxygen that gets to the anode.

Toxic gas sensors (such as those for carbon monoxide, nitric oxide and nitrogen dioxide) are micro-fuel cells, designed to be maintenance-free and stable. They have a direct response to volume concentration of gas rather than partial pressure. The simplest form of electrochemical toxic sensor comprises two electrodes, sensing and counter, separated by a thin layer of electrolyte. Again this has a small capillary to allow gas entry to the sensing electrode. Any simple resistor circuit that allows the voltage drop resulting from any current flow to be measured will give an output proportional to concentration. Since the rate of gas entry into the sensor is controlled by the capillary diffusion barrier, the current generated is proportional to the concentration of gas present outside the sensor and gives a direct measure of the toxic gas present.

The reactions that take place at the electrodes in a carbon monoxide sensor are:

$$\text{Sensing: } CO + H_2O \rightarrow CO_2 + 2H^+ + 2e^-$$
$$\text{Counter: } \tfrac{1}{2}O_2 + 2H^+ + 2e^- \rightarrow H_2O$$
$$\text{Overall: } CO + \tfrac{1}{2}O_2 \rightarrow CO_2$$

Similar reactions take place for all other toxic gases that are capable of being electrochemically oxidised or reduced.

From the reaction at the counter electrode, it is evident that oxygen is required for the current generation process to take place. This is usually provided in the sample stream by air diffusing to the front of the sensor, or by diffusion through the sides of the sensor (a few thousand ppm is normally sufficient). However, continuous exposure to an anaerobic sample gas may result in signal drift, despite the oxygen access paths, so this type of sensor cannot be located in an anaerobic gas mixture, such as a smoke-logged corridor.

Carbon monoxide sensors show a significant response to hydrogen which can make the accurate measurement of carbon monoxide difficult when hydrogen is present. Using a sensor with an auxiliary electrode, all of the carbon monoxide and some of the hydrogen reacts on the sensing electrode leaving only hydrogen to react with the auxiliary electrode. Once the ratio of the responses on each electrode is known, a hydrogen-compensated signal can be obtained by subtracting the auxiliary signal from the sensing electrode signal.

The advantages are:

- low cost;
- simple operation, reliable;
- high tolerance to hostile environments, acid gases, etc.

The disadvantages are:

- some possibility of interference (e.g. hydrogen for carbon monoxide cells);
- limited lifetime.

11.5.13 Techniques not suitable for fire effluents

Some analytical techniques, for example those used in fixed combustion installations (e.g. flue gas analysers), are often inappropriate for fire effluents. Detectors operating on solid-state semiconductor principles or surface electrical effects may be cross-sensitive to many interfering species (although methods for dealing with these have been developed). Also, the UV-fluorescence method for sulphur dioxide, and non-dispersive IR techniques for species such as hydrogen chloride or sulphur dioxide have similar limitations when applied to fire effluents.

11.6 Sampling and analysis of aerosols

The techniques required for the sampling and analysis of aerosols in fire effluents, are different in some respects from those used for gases and vapours. Solid and liquid aerosols in fire effluents are characterised by four main properties:

- concentration;
- particle size distribution;
- chemical nature (which may depend on particle size);
- morphology (i.e. form and structure – which may depend on the chemical nature of the aerosol).

The sampling process for aerosols must attempt to preserve all these properties, and extensive details are available.[19–21] However, in general terms, the sampling probe used has to be designed to operate at a velocity set to provide isokinetic sampling (i.e. the velocity of sampling is equal to the velocity of the sampled effluent flow, thus avoiding any change in concentration or particle characteristics through use of the probe).[22]

The material and temperature of the probe and sampling lines are also important, as with the sampling of gases and vapours. It is also important to appreciate that pressure can have a marked effect on liquid aerosols compared with solid aerosols. This makes the sampling, analysis and interpretation of

liquid aerosol properties relatively difficult and results must be treated with caution.

After sampling, the physical and chemical nature of the aerosols must be preserved as much as possible prior to analysis. This can be achieved by immediate dilution after sampling. When concentrated, solid aerosol particulates and liquid droplets tend to agglomerate into larger particles/droplets with time. This effect can be substantially limited by dilution. However, the sampling flow rate and post-sampling dilution techniques are still influenced by the analytical technique used.

For micronic aerosols (i.e. with particle sizes upwards of 1 μm), the main use of the analysis data is the estimation of direct health risk. The smallest particles in this range can penetrate the human respiratory tract as far as the alveoli and are termed the 'alveolar fraction'. The penetration of these particles is mainly a function of the mass median aerodynamic diameter (MMAD); i.e. 50% of the mass of the particles will be below the geometric mean aerodynamic diameter of the particles and 50% above it. Measurements of MMAD can be achieved using cascade impactors.

There is currently much debate and extensive research on nanometric aerosols, which consist of particles with at least one dimension less than 100 nm.[23] For these extremely small particles, the separation and measurement of particle size distribution is complex but can be achieved by various techniques. With these aerosols, the aerodynamic diameter is not the controlling factor affecting the depth of penetration into the respiratory tract. Care has to be taken when comparing results based on different separation and measurement techniques, for example when comparing electric mobility diameter with aerodynamic diameter.

A variety of measurement techniques can be used to measure aerosol characteristics. These techniques are based on the use of optical benches (light transmission, light scattering), or on a separation technique (i.e. based on aerosol diameter or mobility diameter) coupled with a quantification device (i.e. measuring mass or number). The most common techniques used for measuring aerosols generated in fires are presented in Table 11.3. Appendix B gives further information on techniques successfully used for aerosol measurement in fire effluents. The different techniques that can be used, together with their justification, are discussed in detail in the literature.[19] There is currently one International Standard being developed which deals with the measurement of aerosols in fire effluents (ISO Committee TC92 SC3 WG2 'Generation and analysis of fire effluents'; see Chapter 17).

The effects of aerosol particles on fire effluent 'toxicity' are strongly related to their size distribution (among other characteristics) by mass. Because of this, it is considered more important to know their size distribution rather than the total quantity of particles. For toxicity assessment, the most suitable techniques consist of particle separation based on MMAD coupled with measurement of mass, e.g. cascade impactors.

Table 11.3 Main techniques for measurement of aerosols in fire

Name	Principle of measurement	Information provided	Range (μm)	Uses in fire hazard assessment
Light extinction	Attenuation of a light beam is linked to soot concentration	Extinction coefficient, soot concentration and soot yield	0.1–1	Visual observation
Light scattering	Scattering of a light beam across smoke is measured at fixed angles	Extinction coefficient, particle size distribution	>1	
Direct gravimetric method	Soot is deposited on a filter at a fixed mass flow and filter is weighed after collection	Soot main concentration and soot yield	Total	Carbon balance
Cascade impactor	Soot is classified by aerosol aerodynamic diameter and measured by gravimetric method	Mass distribution (aerodynamic diameter)	0.3–30[a] 0.02–30[b]	Effect on lung function
Electrical low pressure cascade impactor (ELPI)	Same as cascade impactor, but quantification is made continuously by electrostatic measurement	Time-dependent number distribution (aerodynamic diameter)	0.02–30	Changes during transport, e.g. agglomeration
Scanning mobility particle sizer (SMPS)	Aerosol is separated in a diffusion mobility analyser (DMA) followed by measurement of electric mobility diameter by condensation nucleus counter (CNC)	Number distribution (electric mobility diameter)	0.01–1	
Aerodynamic particle sizer (APS)	Aerosol is accelerated and a double laser beam measures velocity. Acceleration is a function of the aerodynamic diameter of the aerosol	Granulometric distribution (aerodynamic diameter)	0.5–20	

[a] Standard cascade impactors
[b] Low pressure cascade impactors (DLPI)

It must be appreciated, however, that the physical and chemical properties of solid and liquid aerosols, and in particular the size of the particles, are very variable and strongly dependant on particle 'history'. Hence, the characteristics of aerosols will change, from their generation and residence time in a flame or site of smouldering combustion, through to cooling and agglomerating as the particles move away from their source, and finally to settling out of the gas phase when temperature, convection currents, and the size of the particles allow. Although laboratory studies to evaluate and quantify these processes are currently in progress, they are not yet considered fully representative of the real fire situation.

There is also a problem of analyte gases being absorbed or adsorbed onto solid or liquid aerosol particles. If these are then removed by filtration some of the analyte will be lost. In addition, further analyte maybe picked up on the filters. Hydrogen chloride is known to attach itself to soot particles, which would reduce the amount reaching the analyser, but increase the amount reaching deep into the lung, through the more direct route taken by larger particles.

11.7 Lower limits of detection, quantification, accuracy and precision

Data on the potential toxicity and environmental impact of fire effluents may be required from a variety of sources by the toxicologist or environmentalist and for a variety of end uses. For example, data can be obtained from bench-scale toxicity testing (see Chapter 12). Here, the primary requirement is to decompose materials and products under conditions which replicate 'real' fires: the yield of a variety of chemical species from the test specimen is measured and can be used in FED calculations for human tenability. Another example is where data are obtained from larger or full-scale fire tests (either standard or experimental tests). In these tests, concentrations of species are measured at a selected location with results used for estimation of toxic hazard in a specific scenario, as discussed in Chapter 13. Also, some effort is currently underway to provide guidance for sampling and analysis from accidental or arson-initiated fires (ISO Committee TC92 SC3 WG2 'Generation and analysis of fire effluents').

In setting up sampling and analysis procedures, it is important to ensure that the techniques and methodologies employed reflect the required limits of concentration, quantification, accuracy and precision of the end use of the results. Thus, there is probably little value in employing a range of highly sophisticated (and possibly expensive) instrumentation to determine the concentrations of a large number of species to a high degree of accuracy and precision, when the data will be used for estimations of hazard using far less sophisticated calculations with relatively wide 'error bands'. It is suggested here therefore, that for toxicity studies in general, chemical species in fire effluent which are expected to contribute at least 10% of the FED should be measured, while lower concentrations are considered when appropriate.

Therefore, for any particular sampling and analysis regime, it is clearly important to state the limits of detection (LoD) and limits of quantification (LoQ) for specific compounds, which will be influenced by the variables outlined in Sections 11.1 and 11.2. This will ensure that the final use of the data (e.g. life threat in fire or environmental impact assessment) is sufficiently realistic. It is also necessary to choose a methodology which has been proven to be repeatable and reproducible and not overly sophisticated and/or expensive for the particular end use required.

For the purposes of this discussion three main parameters have been identified which will define the quality of the methods chosen for analysis of the fire effluent. These are:

- range;
- fidelity (repeatability and reproducibility);
- trueness (accuracy).

Range is defined as the values between which a quantitative analysis is feasible and can be achieved in practice. It is mainly characterised by the limits of detection and quantification for the particular species with the chosen method.

Fidelity is concerned mainly with repeatability and reproducibility. Repeatability can be defined as the degree of agreement between results obtained for successive particular measurements (e.g. using a published standard method) in one laboratory, by one operator and using one piece of equipment. Reproducibility can be defined as the degree of agreement between results obtained for successive particular measurements (e.g. using a published standard method) between various laboratories.

For both repeatability and reproducibility, it is also essential to separate the processes involved in the chemical analysis, the sampling and the processes involved in the fire effluent generator (e.g. a bench-scale test). This separation of fidelity terms is sometimes problematic and extensive statistical analysis has to be performed. Many studies have been performed to increase the accuracy of methods in terms of fidelity. ISO 19702[13] and Fardell *et al.*[14] give information of such repeatability and reproducibility measurement in various conditions and with various test methods. Guillaume *et al.*[24] present an example of a complete method validation.

Trueness is defined as the difference between the real value and the true value, where the latter is never really known. Trueness, although a key parameter, is difficult to measure in fire effluent analysis. In different studies,[13] research on the trueness of a particular method is performed by checking on carbon balance during a fire test or by using reference materials of known thermal decomposition characteristics. Nevertheless, this method of determination of trueness is limited to reference materials and cannot readily be extended to real complex fire effluents.

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Appendix A Summary of sampling and analytical methods for fire gases and vapours

Analysed gas	Method name	Extractive sampling method	Sampling/analysis method (summarised)	Data provided	Approximate concentration range covered	Limitations/ interferences
Oxygen (O_2)	Paramagnetic	Direct or indirect in gas phase	'Dioxygen' reacts in magnetic field because of its diamagnetic momentum. Produces pressure variations in a cell that are linked to O_2 concentration	Continuous concentration on dry gas	0–21% LD > 0.01%	Interference from nitric oxides at high concentrations Response time
	Electrochemical cell	Direct or indirect in gas phase	Metal-air battery type	Continuous concentration on non-condensing gas	0–21% LD > 0.05%	
Carbon oxides (mainly acute narcotic/asphyxiant toxicants)						
Carbon dioxide (CO_2)	NDIR	Direct or indirect in gas phase	Infrared absorption of CO_2 over a wide band is compared to reference gas	Continuous, concentration on dry gas	Few ppm to more than 10%	Interference from water
	FTIR	Direct or indirect in gas phase	Infrared absorption of CO_2 is compared to a reference spectrum obtained on an interferometer	Almost continuous concentration on dry or wet gas	Few ppm to few per cent	Interfering species (N_2O, H_2O)
Carbon monoxide (CO)	NDIR	Direct or indirect in gas phase	Infrared absorption of CO over a wide band is compared to reference gas	Continuous concentration on dry gas	Few ppm to more than 10%	Interference from water
	FTIR	Direct or indirect in gas phase	Infrared absorption of CO is compared to a reference spectrum obtained on an interferometer	Almost continuous concentration on dry or wet gas	Few ppm to a few percent	Interfering species (N_2O, H_2O, carbonyl sulphide (COS))
	Electrochemical cell	Direct or indirect in gas phase	Electrochemical fuel cell	Continuous concentration on non-condensing gas	Few ppm to 10%	Interference from hydrogen (can be compensated for)

Nitrogenous gases (mainly acute irritants/toxicants)

Nitric oxide (NO)	NDIR	Direct or indirect in gas phase	Infrared absorption of NO over a wide band is compared to reference gas with 'beam correlation' technique	Continuous concentration on dry gas	Few ppm to several hundreds of ppm	Interfering species
	FTIR	Direct or indirect in gas phase	Infrared absorption of NO is compared to a reference spectrum obtained on an interferometer	Almost continuous concentration on dry or wet gas	Few ppm to few thousands of ppm	Interfering species (C_2H_4)
	Chemi-luminescence	Direct or indirect in gas phase	NO reacts with O_3 forming 'excited' NO_2 which releases light. Quantity of light produced in a mixing chamber is then linked to NO concentration	Continuous or discrete concentration on wet gas	Tens of ppb to thousands of ppm	Interfering species, especially nitrogenous compounds such as NO_x, HCN
	Electrochemical cell	Direct or indirect in gas phase	Electrochemical fuel cell	Continuous concentration on non-condensing gas	Few ppm to 1%	NO_2, HCl
Nitrogen dioxide (NO_2)	HPIC	Indirect in liquid phase	NO_2 is trapped as nitrite and nitrate ions in 0.1 M NaOH and measured by HPIC	Total released concentration or total yield	Detection limit < 0.1 mg/l, depending on sampling time and dilution volume	Few co-eluants
	FTIR	Extractive, direct or indirect in gas phase	Infrared absorption of NO_2 is compared to a reference spectrum obtained on an interferometer	Almost continuous concentration on dry or wet gas	Few ppm to few thousands ppm	Interfering species (SO_2)
	Electrochemical cell	Direct or indirect in gas phase	Electrochemical fuel cell	Continuous concentration on non-condensing gas	0–200 ppm	H_2S, SO_2
	Chemi-luminescence	Extractive, direct or indirect in gas phase	NO_2 is converted into NO by a catalytic converter, and then measured as NO (see above)	Continuous or discrete concentration on wet gas	Tens of ppb to thousands of ppm	Interfering species, especially nitrogenous compounds such as NO_x, HCN. Conversion efficiency

Appendix A *continued*

Analysed gas	Method name	Extractive sampling method	Sampling/analysis method (summarised)	Data provided	Approximate concentration range covered	Limitations/ interferences
Hydrogen cyanide (HCN)	FTIR	Direct or indirect in gas phase	Infrared absorption of HCN is compared to a reference spectrum obtained on an interferometer	Almost continuous concentration on dry or wet gas	Few ppm to a few thousands ppm	Interfering species (C_2H_2)
	Colorimetry Spectro-photometry	Indirect in liquid phase	HCN is trapped as CN^- in 0.1 M NaOH and measured by various colorimetric methods: (picric acid, dimedon or chloramin-T)	Total released concentration or total yield	Detection limit <0.1 mg/l, depending on sampling time and dilution volume	Interfering species
	HPIC	Indirect in liquid phase	HCN is trapped as CN^- in 0.1 M NaOH and measured by HPIC in amperometric detection mode	Total released concentration or total yield	Detection limit < 0.1 mg/l, depending on sampling time and dilution volume	Extensive usage has shown accelerate ageing and degradation of HPIC columns
Ammonia (NH_3)	FTIR	Direct or indirect in gas phase	Infrared absorption of NH_3 is compared to a reference spectrum obtained on an interferometer	Almost continuous concentration on dry or wet gas	Few ppm to a few thousands ppm	Interfering species (C_2H_4) Sensitivity to water (highly hygroscopic)
	HPIC	Indirect in liquid phase	NH_3 is trapped as NH_4^+ in H_2O and measured by HPIC	Total released concentration or total yield	Detection limit <0.1 mg/l, depending on sampling time and dilution volume	Sensitivity to water
Sulphur compounds (mainly acute irritants/toxicants)						
Sulphur dioxide (SO_2)	FTIR	Direct or indirect in gas phase	Infrared absorption of SO_2 is compared to a reference spectra obtained on an interferometer	Almost continuous concentration on dry or wet gas	Few ppm to a few thousands ppm	Interfering species (H_2O, C_2H_2, HCN, CH_4)

	HPIC	Indirect in liquid phase	SO_2 is trapped as SO_4^{2-} in H_2O_2 and measured by HPIC	Total released concentration or total yield	Detection limit <0.1 mg/l, depending on sampling time and dilution volume	Few co-eluants Partial oxidation can result in formation of SO_3^- ions
Hydrogen sulphide (H_2S)	HPIC	Indirect in liquid phase	H_2S is trapped as HS^- and S^{2-} in NaOH and measured by HPIC	Total released concentration or total yield	Detection limit < 0.1 mg/l, depending on sampling time and dilution volume	Co-eluants
	GC-MS--GC-FPD	Indirect in gas or solid phase	H_2S is trapped in adsorber or in a gas bag and injected directly in GC for analysis Suitable detection methods are FPD and MS	Total released concentration or total yield	<1 ppm to saturation of adsorber	Quantitative analysis difficult
Carbon disulphide (CS_2)	GC-MS--GC-FPD	Indirect in gas or solid phase	CS_2 is trapped in adsorber or in a gas bag and injected directly in GC for analyse. Suitable detection methods are FPD and MS	Total released concentration or total yield	< 1 ppm to saturation of adsorber	Quantitative analysis difficult
Halogenated acids (mainly acute irritants/toxicants)						
Hydrogen fluoride (HF)	FTIR	Direct or indirect in gas phase	Infrared absorption of HF is compared to a reference spectrum obtained on an interferometer	Almost continuous concentration on dry or wet gas	>10 ppm to several hundreds of ppm	Interferences (H_2O) Adsorption losses by pipes and filters
	HPIC	Indirect in liquid phase	HF is trapped as F^- in 1 M NaOH measured by HPIC	Total released concentration or total yield	<0.2 mg/l to 15 mg/l	Sensitive to matrix effect and difficult to separate
	ISE	Indirect in liquid phase (direct for research)	HF is trapped as F^- in 1 M NaOH and measured in a Total ionic strength adjustment buffer (TISAB) by ISE	Total released concentration or total yield (continuous in research studies)	< 0.1 mg/l to 10 mg/l	Interfering species (OH^- ions)

Appendix A *continued*

Analysed gas	Method name	Extractive sampling method	Sampling/analysis method (summarised)	Data provided	Approximate concentration range covered	Limitations/ interferences
	Spectro-colorimetry	Indirect in liquid phase	HF is trapped as F^- in 1 M NaOH and measured by SPADNS inverse colorimetry in presence of zirconium ions	Total released concentration or total yield	About 1 mg/l to 20 mg/l	High limit of detection
Hydrogen bromide (HBr)	FTIR	Direct or indirect in gas phase	Infrared absorption of HBr is compared to a reference spectrum obtained on an interferometer	Almost continuous concentration on dry or wet gas	Few ppm to a few hundreds ppm	Interferences Adsorption and losses on pipes and filters – highly hygroscopic
	HPIC	Indirect in liquid phase	HBr is trapped as Br^- in water and measured by HPIC	Total released concentration or total yield	$<$ 0.1 mg/l to 15 mg/l	Often poor separation from co-eluants
	Titrimetry	Indirect in liquid phase	HBr is trapped as Br^- in water and measured by titration with silver nitrate solution	Total released concentration or total yield	10 mg/l to several hundreds of mg/L	High limit of detection Interference from HCl
	ISE	Indirect in liquid phase	HBr is trapped as Br^- in water measured by ISE	Total released concentration or total yield	$<$ 0.1 mg/l to tenths mg/l	Interferences (CN^-, Cl^-) Matrix effect
Hydrogen chloride (HCl)	FTIR	Direct or indirect in gas phase	Infrared absorption of HCl is compared to a reference spectrum obtained on an interferometer	Almost continuous concentration on dry or wet gas	Few ppm to hundreds ppm	Interferences (CH_4, C–C, C–H) Adsorption and losses on pipes and filters – highly hygroscopic
	HPIC	Indirect in liquid phase	HCl is trapped as Cl^- in water and measured by HPIC	Total released concentration or total yield	$<$ 0.1 mg/l to 15 mg/l	Often poor separation from co-eluants

	Titrimetry	Indirect in liquid phase	HCl is trapped as Cl^- in water and measured by titration with silver nitrate solution	Total released concentration or total yield	10s of mg/l to hundreds of mg/l	High limit of detection Interferences with HBr
	ISE	Indirect in liquid phase	HCl is trapped as Cl^- in water and measured by ISE	Total released concentration or total yield	$<$ 0.1 mg/l to tenths mg/l	Interferences Matrix effect
Aldehydes (mainly acute irritant toxicants)[a]						
Formaldehyde (methanal) (HCHO)	FTIR	Direct or indirect in gas phase	Infrared absorption of formaldehyde is compared to a reference spectrum obtained on an interferometer	Almost continuous concentration on dry or wet gas	Few ppm to tens of ppm	Interferences (HCl, CH_4, C–C, C–H) Adsorption and losses on pipes and filters
	HPLC	Indirect in solid phase	Formaldehyde is trapped as hydrazone in silica coated with DNPH. DNP–formaldehyde is extracted by acetonitrile and measured by HPLC	Total released concentration or total yield	$<$ 0.01 mg/l to tens of mg/l	Chloride and chlorinated compounds
	HPLC	Indirect in liquid phase	Formaldehyde is trapped as hydrazone in HCl 2 M saturated with DNPH solution and DNP–formaldehyde is measured by HPLC	Total released concentration or total yield	$<$ 0.01 mg/l to tens of mg/l	DNP–formaldehyde is in solid and liquid form and has to be extracted using chloroform liquid-liquid extraction
Acrolein (2-propenal) (CH_2CHCHO)	HPLC	Indirect in solid phase	Same as formaldehyde	Total released concentration or total yield	$<$ 0.01 mg/l to tens of mg/l	Same as formaldehyde
	HPLC	Indirect in liquid phase	Same as formaldehyde	Total released concentration or total yield	$<$ 0.01 mg/l to tens of mg/l	Same as formaldehyde

Appendix A *continued*

Analysed gas	Method name	Extractive sampling method	Sampling/analysis method (summarised)	Data provided	Approximate concentration range covered	Limitations/ interferences
Fuels or unburned gases (mainly combustible species without acute toxic effect in fire effluents)[b]						
Hydrogen (H_2)	GC-thermal conductivity (TC)	Indirect in solid phase	H_2 is trapped in a zeolite and thermally desorbed in a GC equipped with catharometer (hot wire) detector	Total released concentration or total yield	–	Mainly qualitative analysis Difficult to separate H_2 properly Trapping difficult
Methane (CH_4) Acetylene (C_2H_2) Ethylene (C_2H_4) Ethane (C_2H_6)	FTIR	Extractive or *in situ*, direct or indirect in gas phase	Infrared absorption of hydrocarbons is compared to reference spectra obtained on an interferometer	Almost continuous concentration on dry or wet gas	Few ppm to a few hundreds of ppm	Interferences with: HCl, HCHO (CH_4) HCN (C_2H_2) NH_3 (C_2H_4)
Propane (C_3H_8) Other hydrocarbons	GC-FID – GC-MS	Indirect in gas or solid phase	Hydrocarbons are trapped in adsorber and desorbed with CS_2 or collected in gas bag and injected in gas-phase for GC analysis	Total released concentration or total yield	–	Mainly qualitative analysis. Quantitative analysis difficult.
Total hydrocarbons Volatile organic compounds	FID	Direct or indirect in gas phase	On-line FID 'counts' carbon atoms ionised in a flame. Catalytic furnace can allow to separation of C_1 hydrocarbons from others	Continuous concentration on dry gas, expressed as methane equivalent	Few ppm to a few hundreds ppm	Interferences Upper limit of carbon atoms is a function of temperature Interpretation can vary
Other organic compounds						
Acrylonitrile (CH_2CHCN)	GC-MS	Indirect in gas or solid phase	Acrylonitrile is trapped in adsorber and desorbed with CS_2 or collected in gas bag and injected in gas phase for GC-MS analysis	Total released concentration or total yield	Few ppm to a few hundreds ppm	Matrix effects Adsorber saturation Quantitative analysis difficult

Formic acid ($HCOOH$)	HPIC – HPLC	Indirect in liquid phase	Formic acid is trapped as $HCOO^-$ ions in NaOH or KOH and measured by HPIC or HPLC	Total released concentration or total yield	< 0.1 mg/l to tens of mg/l	Separation, co-eluants
Phenol (C_6H_5OH) Benzene (C_6H_6) Toluene ($C_6H_5CH_3$)	HPLC	Indirect in liquid phase	Species are trapped in 70% methanol solution and analysed by HPLC	Total released concentration or total yield	< 0.01 mg/l to tens of mg/l	Separation, co-eluants
Styrene (phenylethene) ($C_6H_5CHCH_2$)	GC-MS – GC-FID	Indirect in solid phase	Species are adsorbed on activated charcoal, then thermally desorbed and analysed by GC-MS	Total released concentration or total yield	Few ppm to few hundreds of ppm	Quantitative analysis difficult
Other families (mainly environmental toxicants)						
Metals	ICP – AAS ILC	Indirect in liquid phase	Species are trapped in an acid solution and measured as metallic ions with various techniques including inductively coupled plasma spectrometry (ICP), atomic adsorption spectroscopy (AAS) and HPIC	Total released concentration or total yield	< 0.01 mg/l to tens of mg/l	Reactions can in fire effluents can produce metallic compounds not amenable to this kind of analysis
Dioxins and furans Polyaromatic hydrocarbons (PAH)	GC-MS	Indirect in solid phase	Species are adsorbed on activated charcoal, then thermally desorbed and analysed by GC-MS	Total released concentration or total yield	–	Concentrations often so low that it is difficult to measure properly because of limits of detection

[a] Other aldehydes and ketones can be trapped in DNPH solution or silica greffed with DNPH and measured by HPLC at the same time. These includes acetaldehyde, methacrolein and other species form both these families. Separation by HPLC is relatively easy in MeOH solution with detection by UV spectrometry.
[b] This technique is mainly of interest to research into thermal decomposition products of polymers before ignition.

Appendix B Table of analytical methods for aerosols

Principle	Method	Information provided	Usage	Range (μm)	Resolution	Max. conc.	Ease of usage[a]	Ease of interpretation
Light extinction	*In situ*, non-intrusive, time-dependent	Extinction coefficient, soot concentration and soot yield	Modelling Regulation	0.1–1	NA	Not limited	+++	+++
Light scattering	*In situ*, non-intrusive, time-dependent	Extinction coefficient, particles size distribution	Modelling Research	>1	NA	Limited by signal	++	++
Microphotography/ ombroscopy	*In situ*, non-intrusive, time-dependent	Soot concentration and size distribution	Few usages	>5	–	Low concentrations	++	+
Holography	*In situ*, non-intrusive, time-dependent	Soot concentration and size distribution	Few usages	>10	–	Low concentrations	++	+
Photon correlation spectrometry	*In situ*, non-intrusive, time-dependent	Soot concentration and size distribution	Research	0.01–1	–	Low concentrations	+	+
Doppler method	*In situ*, non-intrusive, time-dependent	Soot concentration and size distribution	Research	>1	–	Low concentrations	+	+
Direct gravimetric method	Extractive method, integrated	Soot main concentration and soot yield	Comparisons, modelling	Total	NA	Limited by device	+++	+++

Cascade impactor	Extractive method, integrated	Mass distribution (aerodynamic diameter)	Toxic effect	0.3–30[b] 0.02–30[c]	+	0.1–1 g	++	++
Electrical low pressure cascade impactor (ELPI)	Extractive method, time-dependent	Number distribution (aerodynamic diameter)	Effluent characterisation	0.02–30	+	0.1–1 g	+	++
Tapered element oscillating microbalance (TEOM)	Extractive method, time-dependent	Soot yield at a given cut-off size	Toxic effect Regulation	0.5–100	NA	–	+++	+
Crystal vibration frequency	Extractive method, time-dependent	Soot yield at a given cut-off size	Toxic effect Regulation	0.5–100	NA	–	+++	+
Scanning mobility particle sizer (SMPS)	Extractive method, time-dependent	Number distribution (electric mobility diameter)	Research Nanoaerosols	0.01–1	+++	–	+++	++
Engine exhaust particle sizer (EEPS-FMPS)	Extractive method, time-dependent	Granulometric distribution (electric mobility diameter)	Research Nanoaerosols	0.005–0.56	++	–	++	+
Aerodynamic particle sizer (APS)	Extractive method, time-dependent	Number distribution (aerodynamic diameter)	Comparisons Research	0.5–20	++	< 1000 part/cm^3	+++	++

NA Not applicable.
+++ Very high resolution, usage or interpretation very simple.
++ High resolution, usage/interpretation subject to caution.
+ Medium resolution, usage/interpretation needs important expertise.
– Bad resolution.

[a] Flexibility, usage on different fire models
[b] Standard cascade impactors
[c] Low pressure cascade impactors (DLPI)

12

Bench-scale generation of fire effluents

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Abstract: Fire toxicity is highly dependent on fire conditions, and these conditions are difficult to replicate on a bench-scale. This has held back the scientific study of fire toxicity. Three types of test are considered, open, closed and flow through. Where the data can be related to a defined set of fire conditions, these have been compared to full-scale test data. This shows that only the ISO 19700 Steady State Tube Furnace and the ASTM E2058 Fire Propagation Apparatus faithfully reproduce the high toxicant yields associated with under-ventilated flaming.

Key words: bench-scale, ISO 19700, E2058, NF X 70-100, carbon monoxide, toxicity.

12.1 Introduction

Assessment of fire hazard requires information on the harmful potential of fire effluents generated by burning materials, usually using a bench-scale test apparatus and procedure. Gases, vapours, aerosols, soot particles and heat are generated during flaming combustion and non-flaming pyrolysis of materials and products during a fire. The yield and nature of the fire effluents are a function of the fuels involved and the prevailing thermal and oxidative conditions of that fire stage. These conditions affect the burning rate and the degree of oxidation of the effluent. The yields of combustion products in a bench-scale method also depend on apparatus conditions, such as the fuel/air equivalence ratio, whether the decomposition is flaming or non-flaming, the persistence of flaming of the sample, the temperature of the specimen and the effluents produced, the stability of the decomposition conditions, and the interactions of the apparatus with the decomposition process, the effluents and the flames. The combustion conditions replicated by the physical fire model have a significant influence on the production of toxic gases. In particular, the production of carbon dioxide (CO_2), carbon monoxide (CO) and minor organic species; nitrogen-containing combustion products such as hydrogen cyanide (HCN), nitric oxide (NO) and nitrogen dioxide (NO_2); aldehydes including formaldehyde and acrolein; and sulphur-containing combustion products such as sulphur dioxide (SO_2) are all highly dependent on these conditions. The combustion conditions have a lesser influence on the production of hydrogen

halides, such as hydrogen chloride (HCl) and hydrogen bromide (HBr). The thermal conditions include external applied heat flux and the distribution between radiative and convective heat transfer, as well as the heat flux from any flaming combustion.

Fire toxicity is a function of material and of the fire condition. This chapter describes various bench-scale methods for generation of fire effluents which are used to quantify toxicity (using live animal exposure) or toxic product yields (using chemical analysis). The sensitivity of fire toxicity and toxic product yields to fire conditions underlines the importance of correctly replicating the fire condition. After an introductory section in which the general requirements of a bench-scale toxicity test are outlined, four general methods are considered.

- *Open tests* which only replicate the least toxic, well-ventilated fire condition.
- *Closed chamber tests* which do not allow correlation to individual fire stages.
- *Non-steady flow-through tests* which vary in their complexity and ability to replicate individual fire stages.
- *Steady-state tube furnace methods* which can readily be correlated to individual fire stages, and have shown good agreement with large-scale toxic product yields.

12.2 Bench-scale generation of fire effluents: general requirements

In all fire smoke toxicity tests, specimens are decomposed by exposure to heat, resulting in 'forced combustion' driven by an applied heat flux from a flame, radiant panel, etc. Some tests use a pilot flame or spark igniter to facilitate ignition, while others rely on self-ignition of the sample. When flaming combustion occurs, this will increase the radiant heat flux back to the sample, increasing the rate of pyrolysis, and hence fuel gasification, typically between 2 and 10 times. This will have two significant effects on the fire effluent. Initially, the existence of flames will help to drive the combustion process to completion, by increasing the concentration of the highly reactive radicals, as well as increasing the temperature, resulting in large increases in reaction rates. This will tend to reduce the toxicity of the fire effluent (favouring carbon dioxide over carbon monoxide and organic molecules) provided there is sufficient oxygen. As the reaction proceeds, the higher heat flux will pyrolyse more material at a greater rate, increasing the amount of material in the vapour phase, increasing the rate of fuel oxidation and heat release while reducing the concentration of oxygen. The higher fuel/air ratio will result in an increase in the toxicity of the fire effluent. These effects are so large that, rather than cancelling each other out they follow each other sequentially and can result in very large differences in the toxic product yield between different fire stages or different toxicity tests. Clearly, the presence or absence of flaming combustion is critical

to the interpretation of the results from combustion toxicity assessments. Under certain conditions, some specimens will pyrolyse without flaming while others will undergo spontaneous ignition. The scatter of results will be very large if flaming combustion is inconsistent. Once flaming is established, combustion will drive itself to completion (and hence the toxicity will be reduced), provided there is sufficient oxygen, and the flame is not quenched. If the flame is cooled rapidly, e.g. by excessive ventilation or a cool surface, the yield of toxic products will increase. Similarly if the applied heat flux is too low to sustain flaming combustion, the rate of decomposition will fall. Most materials have a critical heat flux for ignition/extinction which will be inversely dependent on the oxygen concentration. As the oxygen concentration falls, greater heat fluxes are needed to sustain flaming combustion. Ultimately the value of the bench-scale toxicity assessment is dependent on its ability to predict large-scale burning behaviour, since this is when fire toxicity represents the greatest threat to human life and therefore validation must involve comparison with developed flaming from large-scale test data.

Some criteria for the assessment of physical fire models have been published in ISO 16312-1.[1] The goal of a bench-scale apparatus is to recreate the thermal and reactive chemical environments of the full-scale fires to which the hazard assessment relates. These vary with the fire scenario and with the stage of the fire; some apparatuses are not able to differentiate individual stages of a fire, while others are only capable of replicating certain stages. The validity of the representation depends on the degree to which the combustion conditions in the bench-scale apparatus mirror those in the fire stage being replicated, and on the degree to which the yields of the important combustion products obtained from burning at full scale are replicated by the yields from burning specimens in the bench-scale model.[1] The species of interest are toxic gases, soot particulates and aerosols, and the toxic gases absorbed onto them.

Fire safety engineering requires data on the toxic product yields of commercial products or their components as a function of fire condition. The yields of combustion products depend on the conditions set up in the apparatus such as the fuel/air ratio; whether it is flaming or non-flaming; the stability of the flame; the temperature of the specimen and the effluent produced; the stability of the decomposition conditions; and the interaction of the apparatus with the flames and the effluent.

Ideally, all bench-scale fire effluent toxicity test methods should be capable of reproducing the conditions in each of the stages of actual fires, including incipient, growing and fully developed fires. Specimens burned under constant, predetermined conditions of thermal attack and oxygen availability (ventilation) would allow yields to be characterised, and clearly relate to the different fire conditions. The apparatus should not have a significant influence on the results. For example, flame quenching on cool surfaces or direct contact with heating elements should not change the composition of the fire effluent. Ideally, ageing

effects on the effluent should mimic those in a real fire (see Chapter 7). These factors depend on the design of the combustion zone and effluent plume treatment.

To be of value, the method should produce direct measurements of the yields of toxic gases and smoke. These may be expressed as mass of toxicant per mass of specimen (the mass charge basis preferred by fire safety engineers) or a mass of toxicant per unit mass loss of specimen (the mass loss basis which is useful for comparing flammable materials containing significant qualities of non-combustible filler or reinforcement). If the yields cannot be directly measured, it may be possible to calculate them from measurements of the concentration of gases and smoke, provided the masses involved in each stage are known. The gases include those expected to contribute to the toxic potency of fire effluent which typically include oxygen, carbon dioxide, carbon monoxide, hydrogen cyanide, hydrogen chloride, hydrogen bromide, hydrogen fluoride, nitric oxide, nitrogen dioxide, sulphur dioxide, acrolein and formaldehyde (discussed in Chapter 1).

Toxic product yields depend on the material composition[2] and the fire conditions.[3] The most significant differences arise between flaming and non-flaming combustions. For flaming combustion the most significant factor is the fuel/air ratio, although the oxygen concentration and the compartment temperature can also affect the yields. As an enclosure fire develops, the temperature increases and oxygen concentration decreases. This has been set out as series of characteristic fire types (Chapter 2), usually ranging from oxidative pyrolysis to well-ventilated flaming, which, without intervention, generally leads to small or large (post-flashover) under-ventilated flaming. Carbon monoxide is often considered to cause the greatest number of fire deaths, and the evolution of carbon monoxide is highly dependent on conditions, the most significant of which are difficult to create on a small scale.

Fire gases result from the pyrolysis, oxidative pyrolysis and flaming combustion of organic materials, and can comprise a complex mixture of many different compounds. The temperature and oxygen concentration vary significantly during a fire and between different fires and, as a consequence, the gases produced in different stages of a fire, vary significantly.

The fire stages characterised in ISO 19706 and described in Chapter 2 identify steps in the transition from non-flaming combustion to fully developed flaming, usually under-ventilated, which has the greatest toxicological significance. For a bench-scale method to differentiate between the fire stages of a fire, it must allow quantification of the equivalence ratio and/or the combustion efficiency so that the individual fire stages can be identified, and the product yields correlated to each stage.

In particular, combustion efficiency should be measured continuously during a test, since a change in its value indicates a change in the combustion conditions; unfortunately it is often reported as a global value, averaged over the full

burning time. From a toxicological perspective this can be misleading, since most of the impact will result from the period(s) when the combustion efficiency is low. Different measures of fire condition (heat release, oxygen consumption or carbon dioxide formation) can give different values of combustion efficiency, even when using standard methods such as those prescribed in ISO 19703.[4] The combustion efficiency is affected if the flames impact on quenching surfaces within the test apparatus.

12.2.1 Thermal environment of the test specimen

In order to assess the validity of a particular bench-scale fire model, it is necessary to consider the parameters affecting the burning behaviour at each fire stage, and the yields of toxic products which are replicated by the model. The three-dimensional temperature profile around a product undergoing combustion determines both the burning rate and the yields of the combustion products. The nature of this profile varies with the fire type. The challenge any bench-scale apparatus has to meet is to be capable of replicating each of the conditions below.

Self-sustaining, smouldering combustion

This type of combustion, occurring only in porous materials where surface reaction of the solid occurs with air that is diffusing into the pores (e.g. cellulosic material, such as wood char, cotton or polyurethane foam insulation), and is characterised by the direction in which the combustion front moves relative to the air flow and the peak fuel temperature. It can occur at a steady rate, sometimes for several hours, often unnoticed, with build up of toxic products and lethal consequences for any occupants. The peak temperatures occur where the oxygen is reacting most rapidly, generally below the external surface of the product. Thus, there is a 'thermal wave' that passes through the material. Because the oxygen concentration goes to zero at the reaction site (due to an excess of fuel) and because the combustion gases have a long residence time in a reducing atmosphere, much of the carbonaceous gases are not fully oxidised to carbon dioxide. This type of combustion is characterised by (a) the thermal wave direction relative to the direction from which the air is arriving and (b) a peak fuel temperature. Since the smouldering process is relatively slow, there is little heating of the fire room.

Pyrolysis

Thermal breakdown of a product can be forced by an external heat source, ceasing when the source is removed from the fuel. Conductive heating, such as from contact with an overheated electrical component, can result in the release

of gaseous by-products with little or no oxygen participation (non-oxidative). When the breakdown occurs on a surface exposed to both heat and oxygen (such as flame radiation impinging on an outer surface of a non-burning object), a different set of gases and aerosols generally results. In both cases, the fuel temperature is at a maximum near the surface facing the heat source and falls progressively away from it. Pyrolysis due to conductive or convective heating is characterised by the surface temperature and its decrease with distance from the surface. Degradation due to radiative heating is generally characterised by the radiative heat flux to the surface, although this results in a qualitatively similar thermal profile to the other modes of heating. Non-oxidative pyrolysis is generally endothermic, and even oxidative pyrolysis generates little heat. Thus, there is little heating of the fire room. As in the smouldering case, the pyrolysis products are likely to be more noxious and irritating than the products of complete combustion, under well-ventilated conditions.

Flaming

Flaming can be described as radiation-enhanced surface pyrolysis of the fuel followed by rapid vapour phase free radical oxidation of the fuel gases. The surface temperatures may be higher than for pyrolysis, especially for charring materials. The temperature profile within the fuel will be qualitatively similar to pyrolysis: high on the exposed surface, decreasing with depth. The rate of heat release from flaming combustion is generally far higher than for smouldering or pyrolysis, so in real-scale fires the heating of the room and fire spread are correspondingly larger and faster. The hot environment becomes a second source of thermal radiation (in addition to the flames), which further enhances the burning rate. Thus, the various stages of flaming combustion are characterised by a total radiant flux that includes both immediate and room-scale contributions. The radiation to the fuel surface is proportional to the fourth power of the temperature of the flame, its optical thickness, and the fraction of the field of view of the flame by the fuel. Small flames are often optically thin and thus impose lower levels of radiation than do larger flames from the same fuel; sooty flames are optically thicker than low-soot flames. Early in a fire, when the room is still relatively cool, external radiation from the hot upper layer is small; as flashover is approached, that radiation dominates.

Oxygen depletion

The rate of burning, the combustion efficiency and the yields of specific combustion products depend heavily on the percentage of oxygen in the surrounding atmosphere and the rate at which the depleted oxygen is replenished. The heat from the fire acts to maintain its oxygen supply as far as possible, entraining air from the surroundings by thermal buoyancy and turbulent flame motion. As the

fire grows, the oxygen supply will ultimately be restricted by the presence of obstacles or limited openings in the fire compartment, or even by the flames themselves.

Changing fire stages

As the combustion proceeds through different fire stages, there are likely to be dramatic changes in the nature and yields of the products of incomplete combustion. Thus, for the measured yields to be meaningful, it is important that effluent samples are correlated with only a single stage of a fire, especially where several fire stages are replicated in a single experiment. This requires a clearly defined transition through the fire stages, and from the combustion zone to the analysers. Further information is presented in a more detailed account of current protocols in toxicity testing.[5]

Yields from multi-layered products

Some finished products used in buildings and transport applications consist of more than one layer: for example, surface covering materials melamine–formaldehyde (Formica) worktops and upholstered furniture. During the very early stages of a flaming fire (approximately the first minute or so), it may be that only the upper surface is exposed to the heat and ignited, while the layer below is protected. During this period, only the upper surface layer will generate fire effluent. As the fire develops, it will spread laterally, across the surface, and penetrate into the surface. Before the fire has grown to a size capable of presenting a hazard to occupants (usually after 2–3 min or so), it will have spread both across the surface of the burning object and into its depth, so that for a two-layered object, some areas of the fire involve the upper surface while others involve the deeper layers (Fig. 12.1). Similarly for char-forming materials such as wood, the very early stages of the fire involve mostly virgin wood, while subsequent stages involve some areas of virgin wood at the same time as other areas of char-enriched material.

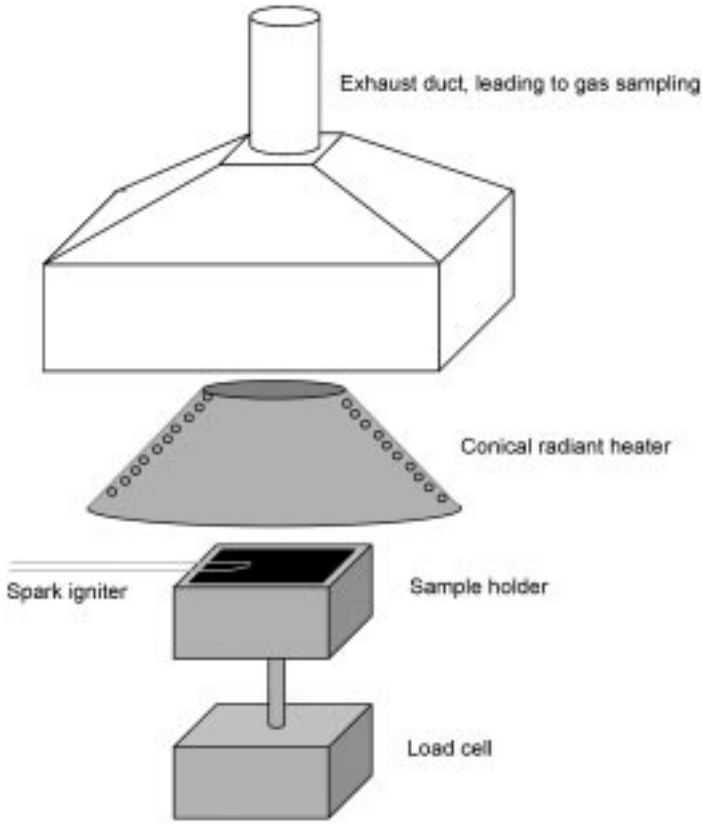
12.1 Combustion of two-layered product after first minute or so of fire.

12.3 Classification of test methods

Most bench-scale methods used for toxicity testing are designed to reproduce a single fire stage or combustion condition, where real-scale fires simultaneously involve different fire stages in different places, which are changing with time. These methods can be grouped as those with constant combustion conditions, often achieving a prolonged steady-state period, and those with non-constant combustion conditions. Those with constant combustion conditions are best suited to producing data suitable for comparison and modelling, but only the German tube furnace method, DIN 53436, and its derivatives, such as the ISO steady-state tube furnace method, ISO 19700, achieve this. Most other bench-scale methods have non-constant combustion conditions, such as those in closed or semi-closed chambers exposed to a constant source of heat, including the NBS smoke chamber (ISO 5659), and the toxicity tests derived from it, and stationary tube furnace tests, such as the NF X 70-100. Intermediate between these two extremes are those that can produce partially constant combustion conditions such as the Cone Calorimeter ISO 5660-1, and the Fire Propagation Apparatus ASTM E 2058. Alternatively, the methods can be grouped according to their physical arrangement; the method preferred here, which separates open tests, such as the cone calorimeter, from closed tests, such as those based on the smoke chamber, and flow-through tests, such as the stationary and steady state tube furnaces, the controlled atmosphere cone calorimeter and the fire propagation apparatus.

12.3.1 Open tests: the cone calorimeter[6,7]

The fire zone of the standard cone calorimeter[8] apparatus is well ventilated and therefore wholly unsuitable for assessment of fire toxicity for anything but the least toxic well-ventilated flaming fire stage. The fire model is based on the radiant ignitability test, BS 476 part 13[9] (and now ISO 5657[10]) but has been modified to measure heat release, either directly using thermopiles, or using oxygen depletion. The cone calorimeter (Fig. 12.2) was developed specifically to determine the rate of heat release and effective heat of combustion of building materials. It was subsequently modified to determine smoke generation (ISO 5660-2) and later applied to furniture. The cone calorimeter is probably the most widely used apparatus for measurement of flammability properties, and most reports of new fire retardant materials have their flammability characterised by cone calorimetry. A horizontal specimen, 100 mm square and up to 50 mm thick is exposed to a conical radiator pre-set to between 10 to 100 kW m^{-2} (typically 35 or 50 kW m^{-2}) mounted beneath an instrumented hood and duct. A spark ignition is used and the specimen is mounted on a load cell. The fire model of the cone calorimeter always appears to be well ventilated and to meet with ISO stage 1b for non-flaming tests and to stage 2 for flaming tests. The carbon monoxide yields in the cone calorimeter have been found to correlate with an



12.2 Diagram of cone calorimeter.

equivalence ratio of 0.7 for a range of cable materials.[11] The relatively high dilution of fire gases in, and stainless steel construction of, the hood and duct may lead to difficulties in detecting some effluent components. Fire gases pass through the conical heater, in direct contact with its hottest surfaces which may modify their composition.

Oxygen depletion calorimetry relies on the air flow through the system to be precisely known. It is necessary, therefore, either to remove the carbon dioxide, with a relatively expensive scrubber system, or to quantify the carbon dioxide and carbon monoxide and subtract their volumes from the gas flow.[7] As a result, most instruments record carbon monoxide and dioxide evolution, and present the data as concentrations and yields. This has led to fire retardant materials' developers reporting carbon monoxide yields of their new formulations, with the suggestion that a lower carbon monoxide yield corresponds to lower fire toxicity. However, since the ventilation is not controlled, this only indicates the degree of gas phase flame inhibition (useful for distinguishing between gas and condensed phase action of fire retardants), but not fire toxicity, which is minimal

for most materials under the well-ventilated conditions found in the cone calorimeter.[8] In effect, the cone calorimeter measures the gas yields at such an early stage of flaming that the fire would be too small to produce enough toxicants to cause harm. However, the apparatus has been modified in an attempt to replicate oxygen-depleted conditions, as discussed in Section 12.4.1.

12.3.2 Closed chamber tests

These methods attempt to address the transition through the fire stages by enclosing the sample in a fixed volume of air, heating it, with or without ignition, and monitoring the formation of toxic gases, as the oxygen concentration falls, and the fire condition changes from well ventilated to under-ventilated. The methods can be subdivided into two broad categories – those where decomposition or combustion occurs in the main chamber, and those where it occurs in a side chamber, with some examples between the two. The NBS smoke chamber, ISO 5659, designed to quantify smoke obscuration, has been modified as a toxicity test, by the mass transport industries. In the aircraft,[12] maritime[13] and railway tests,[14] the decomposition system is mounted within the chamber. In the radiant cup furnace (Pott's pot)[15] they are an appendage to the main chamber; in the radiant furnace test, ASTM E 1678,[16] it is connected to the cabinet by a short duct, where the geometry of the attachment to the main chamber controls the degree of ventilation, hence the rate of burning, and the toxicity.

In theory, for a closed chamber apparatus, the instantaneous global equivalence ratio may be determined from the sample mass loss rate (or the cumulative concentrations of carbonaceous by-products) and the oxygen concentration in the chamber. However, a local decrease in oxygen concentration in the vicinity of the sample, coupled with inadequate mixing of the chamber gases during the test, will result in an inhomogeneous atmosphere. Conversely, forced convection, for example from a fan, will radically alter the burning behaviour. Thus, determination of the instantaneous equivalence ratio is not possible, and only a global equivalence ratio may be determined, covering several fire stages. During the test, the decreasing oxygen availability will decrease the combustion efficiency, changing the nature and concentration of the fire effluents. Thus, the production of toxic gases will be weighted toward the end of the test, and the length of the procedure and ability to maintain flaming combustion will affect the toxic product yields. This change in decomposition conditions during the test makes it difficult to determine yields for a specified fire condition, particularly if the specimen mass is not monitored. The long residence time of the combustion products during a test can lead to significant deposition of combustion products on the chamber walls.

A direct consequence of the closed cabinet is that the fire effluent accumulates within the cabinet, the fire gas concentrations therefore increase as the specimen burns and the gases will change with oxygen depletion. For laminated

or layered specimens, the effluent will also change as flame burns through different layers.

As the specimen decomposes, the hot effluent rises to the upper part of the chamber where it may accumulate as a hot, upper layer, meet the cool upper surface and drop several centimetres, or cool enough to circulate around the chamber due to natural convection. Thus the measured product concentration will depend critically on where the gas samples are taken from and whether they grab only the plume, only that which has escaped from the plume, or an unknown mixture of both. The smoke density values will be unaffected provided a vertical light path is used. Although mixing fans are used in some smoke density tests, they are rarely used in toxicity tests because of their effect on the flaming combustion. Both the aircraft and maritime tests require the smoke to be sampled at specified times (although burning may have proceeded at different rates) from gas sampling probes in the geometric centre of the cabinet.

If the effluent is stratified the gas sample is obviously unrepresentative, but if it is uniformly distributed, then the gas flowing into the fire zone will be oxygen depleted and fire gases recycled through the fire zone. These latter effects will be greater with thicker specimens which would be expected to generate more smoke, due to under-ventilation.

In summary, the methods suffer from four major disadvantages:

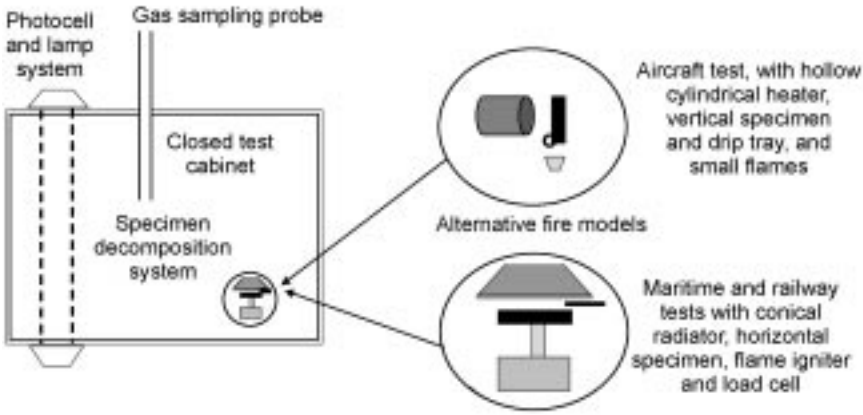
- The ventilation condition in which the products are generated is unknown, because an unknown fraction of the available oxygen will be accessible to the fire plume.
- Sampling of the fire effluent will change its composition – if the fire gases are sampled in real time, it may be possible to isolate individual fire stages, but then the effluent may change during analysis, or may not be returned to the chamber after analysis.
- The distribution of the fire effluent within the chamber will depend on the specific conditions, such as heat release, thermal properties of walls, etc., and therefore sampling from a fixed point will range from missing the main effluent plume altogether to sampling from its centre, without dilution.
- Large areas of the chamber wall will promote deposition and disproportionate losses of certain analytes, such as hydrogen chloride or hydrogen bromide.

Toxicity tests based on the smoke chamber

A number of industry-specific toxicity tests have been developed based on the smoke chamber.

The smoke chamber ISO 5659-2[17]

The smoke chamber (Fig. 12.3) is a well-established piece of equipment, designed to monitor the smoke evolution from burning materials, in order to



12.3 Diagram of fire smoke toxicity test based on NBS smoke chamber.

quantify visual obscuration during a fire. It serves this purpose well. Visual obscuration is measured using a lamp and photodetector at the bottom and top of the chamber, respectively.

Decomposition takes place inside the closed cabinet of volume 0.51 m^3. In all of these tests, the specimens, 75 mm square and up to 25 mm thick, are exposed to radiant heat with and without a pilot flame(s); ISO 5659-2 specifically states that the results are valid only for the specimen thickness tested. Air flow through the fire zone and the effluent is circulated by natural convection within the closed cabinet. Flaming tests result in some oxygen depletion which can vary with the thermal stability and thickness of the specimen and also decreases with increasing test duration. The flaming fire stage is difficult to assess because the fire stage changes by an unknown amount during the test. When a sample is decomposed or burnt, a smoke layer containing the fire effluent forms across the top of the chamber. Depending on the temperature of the effluent and of the chamber walls, this plume may sink or remain buoyant at the top. Since smoke is measured from top to bottom, plume sinking has no effect on the result. However, its widespread availability and use have led to its adoption for a number of industry-specific toxicity tests.

In contrast to measurement of visual obscuration where the smoke is unaffected by the analysis, and is independent of the plume height, using the smoke chamber for toxic gas generation immediately presents two problems.

- Since the gases in the chamber are not mixed, the sampling position will critically affect the results.
- Sampling sufficient gases from a chamber of fixed volume will change their composition. If the analyte is returned to the chamber, it will usually have been filtered, removing both the particulates and the gases absorbed onto them, and acid gases may have deposited onto the sampling line.

In addition, there has been extensive discussion but little agreement as to when gas samples should be taken from the chamber. While some protocols (such as EN TS 45545) stipulate sampling after fixed time intervals, others (such as ISO DIS 21489) require an initial test to be run to determine the maximum smoke density (Dmax) and samples to be taken at Dmax. However, the major problem is the uncertainty surrounding the oxygen concentration near the fire plume, and hence the relationship of the toxic product yields to a particular fire stage.

Therefore, at best the smoke chamber tests give a complete product yield of burning from well-ventilated through to somewhat under-ventilated conditions, but without giving any indication of how the yield varies with fire stage. Other potential sources of error occur as the fire effluent is heated and excess pressure is released, or stickier components within the effluent, such as hydrogen chloride are deposited onto the walls of the cabinet.

Industry-specific tests

The aircraft test[12] (prEN 2824, 5 and 6) uses the vertical radiator and test specimen of ASTM E 662[18] and is specified for components for passenger aircraft cabins (Fig. 12.3). Airbus ABD 3 and Boeing BSS 7239[12] use the same apparatus but specify different gas analysis methods. In the aircraft test, flaming conditions are generated by a series of small flames along the base of the vertical specimen, but in other tests it occurs when specimens are ignited by the pilot flame or self-ignite. Specimens which drip in the aircraft test may give erroneous results if the molten fuel misses the drip tray, falls to the floor of the cabinet and does not burn.

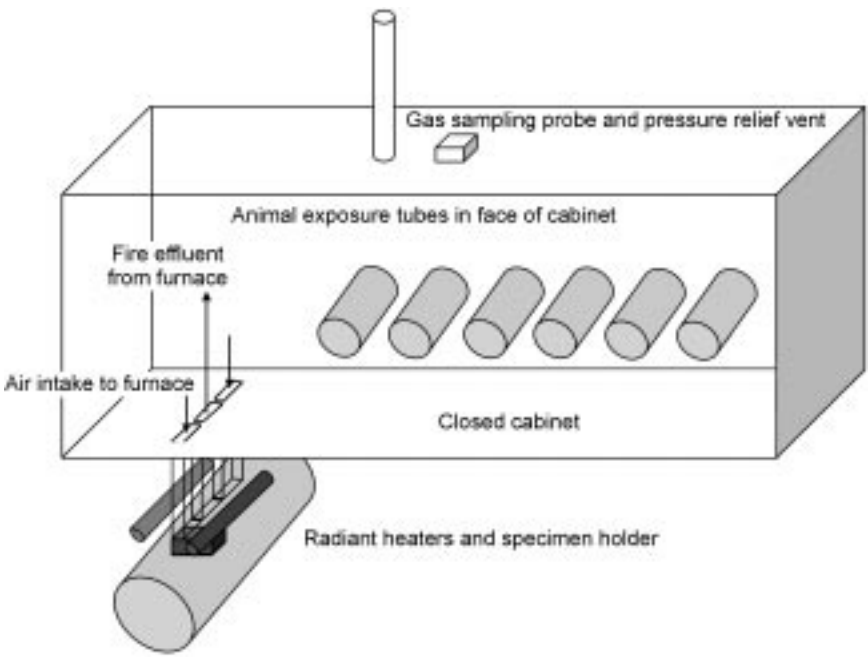
The maritime industry (IMO) test[13] uses the smoke chamber, cone heater and load cell of ISO 5659-2 to specify materials and products for large passenger ships and high speed surface craft, although a modified standard using FTIR gas analysis is currently under consideration (ISO DIS 21489). A reduced version of this test is used in the UK for railway vehicles[19] as BS 6853, B2. The draft European specification[14] (EN TS 45545-2) uses the IMO toxicity test at 50 kW/m^2 without the pilot igniter and with FTIR analysis to determine the toxicity of railway vehicle components.

In each case, individual tests use different protocols for grab sampling after certain intervals. The aircraft test[12] compares gas concentrations after 90 and 240 seconds (aircraft theoretical escape and flashover times respectively) with reference data. The IMO test[13] compares gas concentrations using different reference values determined during the 3 min around the time to maximum smoke density, without stating the rationale for doing so. The BS railway test[19] calculates an index using reference data related to immediate danger to life and health (IDLH) values for a 30 min exposure. EN TS 45545-2 proposes to sample the gases at the peak of smoke obscuration.

The advantages of these tests are that they use a widely available, standard smoke test apparatus, with the addition of simple gas sampling probes in the centre of the cabinet and relatively simple gas analysis systems to determine specified gases.

NIST Radiant Furnace method (ASTM E1678)[16]

This test method (Fig. 12.4) was developed to determine toxic potency data for materials and products used in the building and furnishing industries. Horizontal test specimens, up to 76 mm × 127 mm and up to 50 mm thick are exposed to a radiant heat flux of 50 kW m^{-2} for 15 min with a spark igniter in a small chamber connected by three parallel, vertical ducts to the upper, closed chamber of 200 litres. The central slot acts as a chimney, while the outer slots replenish the air to the fire. Thus the degree of ventilation to the fire will be a function of the convective heat release. The hotter the air from the burning sample, the greater the circulation of fresh air in the remainder of the box, and the lower the toxicity of the fire effluent, especially the asphyxiants carbon monoxide and hydrogen cyanide. However, the greater air circulation is also likely to drive the fire effluent towards the end of the animal chamber, exposing more animals to a more dilute effluent. The design of the apparatus is such that materials could be optimised to perform well in the test although their fire toxicity, for example in a



12.4 Diagram of ASTM E 1678 toxicity test.

large-scale test, was unaffected. Nose-only exposure animal ports are fitted to the upper chamber. Natural convection causes the effluent to move through the upper, closed cabinet where it accumulates and is mixed by natural convection. The specimen decomposition stage lasts for 15 min after which the exposures continue for a further 15 min, i.e. 30 min total.

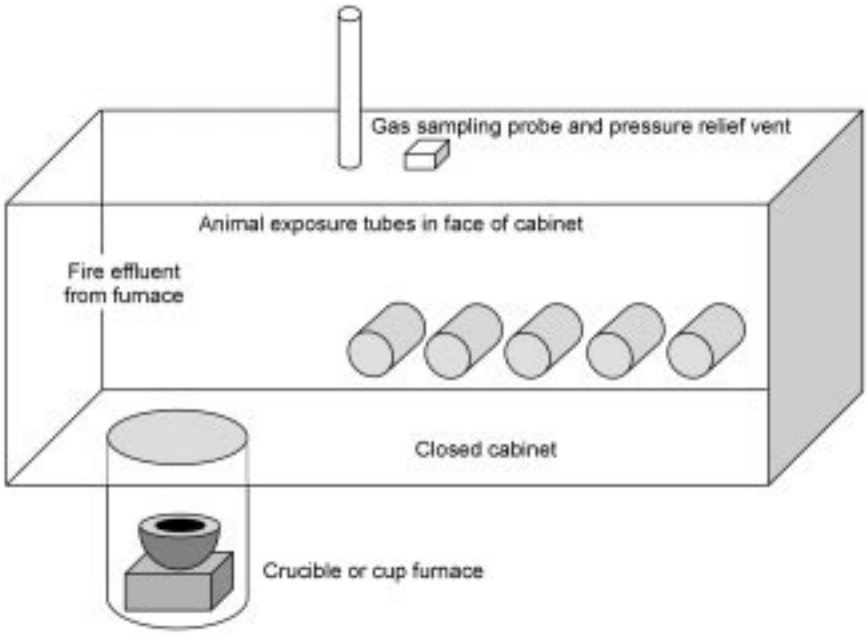
Again, since the total amount of air is limited, and the oxygen concentration is reduced during the test, it is not possible to relate the results to a particular fire stage. As the test relies on animal exposure it is necessary to adjust the test specimen area to give a fractional effective dose (FED) value of 0.5 to 1.5. In a remarkable admission of failure to replicate different fire stages, the ASTM standard addresses the underestimation of carbon monoxide yield for developed fires by a statement that for under-ventilated fires a carbon monoxide yield of 0.20 g/g should replace the experimental result.[20] No compensation is made for other species whose yield increases with vitiation, such as hydrogen cyanide, or for materials which have been shown to give higher or lower carbon monoxide yields in under-ventilated conditions (see Chapter 14). Rather tellingly, one of the test's developers reports that

> the actual use of this test has been minimal. The reason is that it was mostly developed for precautionary reasons: If products should come onto the marketplace which produce toxic effects significantly in excess to what could be expected from their basic HRR [heat release rate] (or mass loss) traits, then such a test could be used to quantify such effects.[21]

NBS cup furnace method[15]

This method (colloquially known as Pott's pot) was the precursor of ASTM E 1678 and uses the same apparatus except that the effluent is generated by thermally decomposing the specimens (approximately 10 g) in a heated crucible positioned below the upper cabinet (Fig. 12.5). This test is essentially an animal exposure test with some chemical analysis. The results are given as LC_{50} and IC_{50} values and include the animal response to the effluent, the effects assessed by post-mortem and blood analysis.

In general, the discussion of ASTM E 1678 will also apply to the NIST cup test for most aspects except for the fire model in which small pieces of the specimen are heated from all sides, so it is generally unsuitable for layered or surface fire retarded materials. It has been reported that temperatures within the crucible can vary from top to bottom and that fire effluent may be recycled within the crucible. The test achieved notoriety when polytetrafluoroethylene (PTFE) was tested. It was found that a few milligrams of PTFE were sufficient to kill 50% of the exposed rodents. However, the initial pyrolysis was complete after a few seconds, but the furnace remained heated for several minutes. When a lid was placed over the furnace after all the PTFE had been pyrolysed, the toxicity fell by several orders of magnitude. It was concluded that the



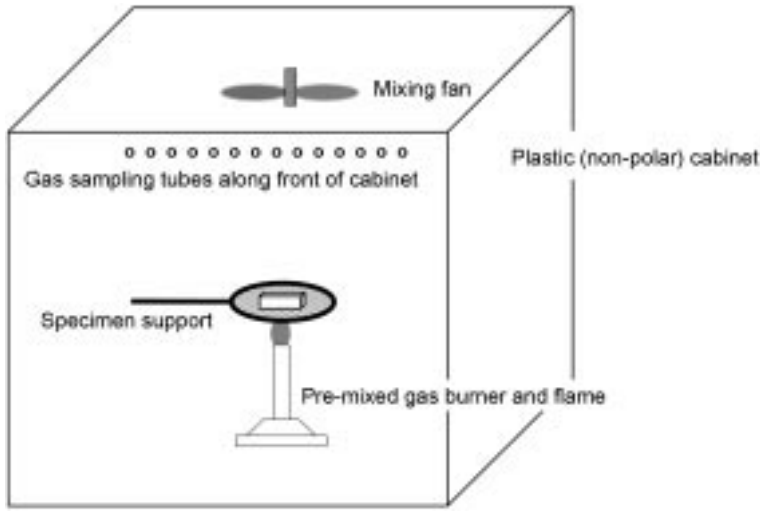
12.5 NBS cup furnace ('Pott's pot').

recirculation of the PTFE pyrolysate through the furnace resulted in the formation of lethal particulates containing end-chain peroxy radicals.[22] This underlines the importance of particulates in fire toxicity studies, and illustrates the type of experimental artefacts that can result from inappropriately generated fire effluents. These toxic effects are discussed in more detail in Chapter 8.

DEF STAN 02-713[23]

This method, originally designated NES 713, determines the toxicity index of the products of combustion from small samples of materials (Fig. 12.6). It forms part of a series of tests intended to shortlist materials for more detailed investigation for use in warships and is used by UK Ministry of Defence.

The specimen, typically 1 g, is held on wire gauze immediately above a premixed gas/air flame. Gases accumulate within a closed cabinet (>0.7 m^3), mixed using a fan and the gas concentrations are determined, from which the contribution of carbon dioxide, carbon monoxide and NO_x from the burner flame are subtracted. The test determines the following gases: carbon monoxide, carbon dioxide, NO_x, hydrogen chloride, hydrogen bromide, hydrogen fluoride, hydrogen cyanide, formaldehyde, acrylonitrile, phenol and phosgene, using chemical reagent tubes. Test results are presented as an index which is the sum of the ratios of the gas concentrations to specified concentrations, nominally for



12.6 Diagram of DEF-STAN 02 – 713 (NES 713) test apparatus.

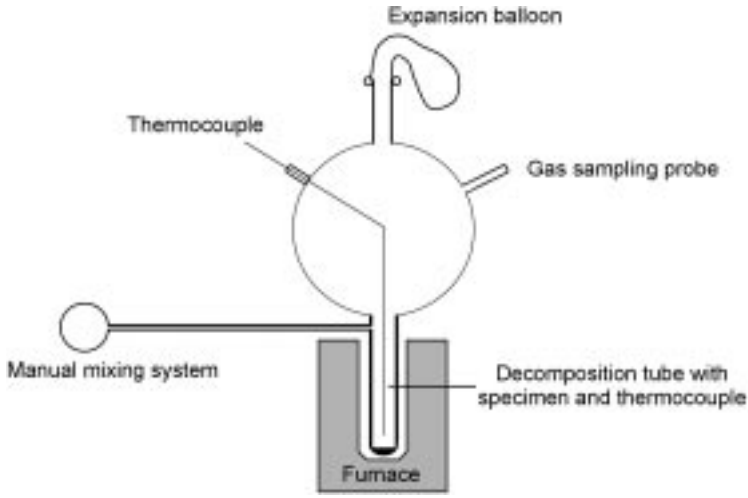
30 min lethal exposure, and normalised to 100 g of test material or to 1 m of cable when burned in a 1 m cube. The fire zone is not representative of a particular ISO fire stage although the premixed methane gas/air flame surrounds the specimen and might be considered to represent a well-ventilated, hot fire.

This test uses a very simple apparatus and gas analysis system. The high temperature, premixed gas flame tends to produce simple gas mixtures, which may not be representative of the likely fire scenario. Thus it cannot be considered as a suitable test for determining fire effluent toxicity. In addition, the specified chemical reagent tubes used for gas analysis may lead to errors because of possible interferences, or lack of sensitivity. The inappropriateness of this fire model is often used to justify the need for proper guidance on the fitness for purpose of fire toxicity tests.

The Israeli Standard Method[24] *SI-755*

This test (Fig. 12.7) is used to classify building materials. It is unusual as the specimen is thermally decomposed inside the lower, tubular extension of a closed spherical vessel fitted with a balloon to allow for expansion. The vessel is inserted into an oven heated to either 250 or 550 ºC which were selected to be below and above the auto-ignition temperatures of many materials. The vessel contains excess air and there is no ignition system. The effluent is mixed manually with a rubber bulb, and gases are sampled at different times to determine the maximum concentrations of specified gases.

The maximum concentrations of carbon monoxide, hydrogen cyanide, NO_x, hydrogen chloride, sulphur dioxide and formaldehyde are determined by

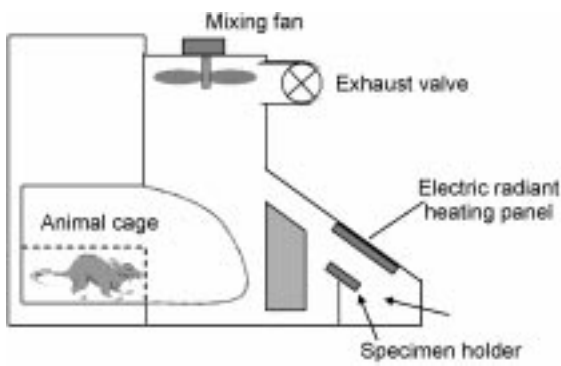


12.7 Diagram of SI-755, test method for the classification of the behaviour of building materials during fire.

chemical analysis. The gas concentrations are used to calculate a simple toxicity index based on the critical concentrations for escape from a fire in a room with a 3 metre high ceiling.

Gost 12.1012 Toxic potency of effluents[25]

This test is a standard method for determining fire effluents in the former USSR (Fig. 12.8). Essentially, an inclined specimen ($40 \times 40\,mm^2$ and up to 8 mm thick) is exposed to radiant heat (pre-set to produce 25–96 $kW\,m^{-2}$) and the effluent flows into a chamber (approximately 0.5 m^3) where it is mixed with a fan. Tests can be carried out in non-flaming and flaming modes of operation. The chamber contains cages of rodents which are exposed to the



12.8 The Russian toxicity test (GOST 12.1012.USSR).

effluent for 15 min. The method can also be used to determine the optical density of smoke.

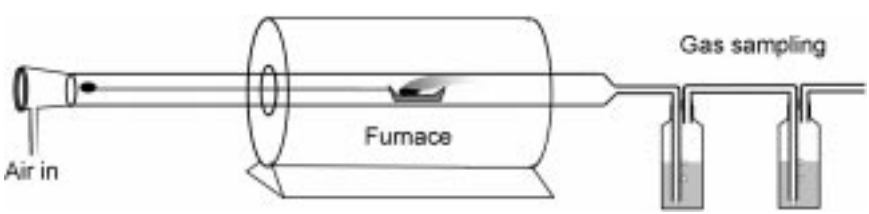
12.4 Flow-through methods

In these methods the specimen is thermally decomposed, with or without flaming, in a furnace over a metered volume of flowing air, which drives the effluent to the sampling system or gas measurement devices. Mass loss is obtained by weighing the sample before and after test (horizontal tube furnaces), or during the test (vertical tube furnaces), or estimated from measurement of the principal carbonaceous by-products (mainly carbon dioxide and carbon monoxide) and knowledge of the chemical composition of the sample. Determination of the equivalence ratio is not possible unless the rate of pyrolysis is known, for example from online analysis or by the establishment of a steady state. Since different products burn at different rates and have different stoichiometric oxygen requirements, using the same air flow will lead to equivalence ratios that vary from product to product.

12.4.1 Non-steady state flow-through methods

Simple tube furnace flow-through test

The NF X 70-100 method[26] (Fig. 12.9) was developed in France to estimate the toxicity of materials and products used in railway vehicles. This is a small-scale static tube furnace test, in which 1 g (or 0.1 g for low density materials) of specimen in a quartz crucible, is inserted into the middle of the furnace tube and thermally decomposed in flowing air at 2 l min^{-1}. Furnace temperatures of 400, 600 and 800 ºC are used. Typically, at a temperature of 400 ºC they may pyrolyse without ignition; at 600 ºC, the rate of burning may be fairly steady, and possibly well ventilated; at 800 ºC, the fire condition may be closer to under-ventilated as the rate of pyrolysis exceeds the air supply rate corresponding to stoichiometric combustion. Thus the three temperature conditions could be assumed to represent oxidative pyrolysis, well-ventilated and under-ventilated conditions respectively. The effluent is driven through gas detection systems, bubblers or into gas bags for subsequent analysis.



12.9 Schematic of NF X 70-100 test.

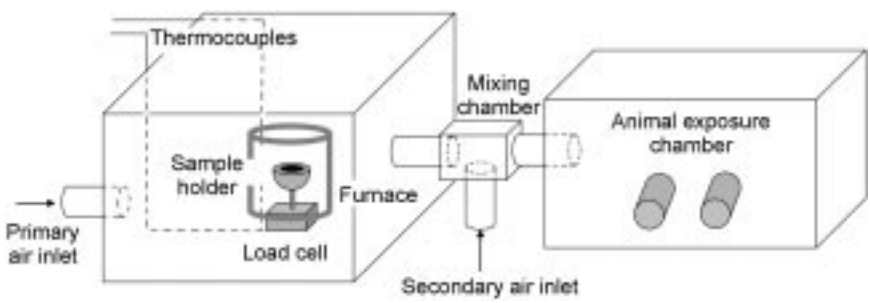
This method is easy to use, uses simple equipment with specified operating conditions of temperature and air flow. The greatest sensitivity in the test, leading to problems of repeatability and reproducibility, occurs when the sample is on the border of ignition and in some cases flaming combustion occurs, while in other cases it does not. As part of EN TS 45545, this method is increasingly used for fire toxicity testing of materials used for railway vehicles. The lack of requirement for flaming to be observed leaves the assignation of fire stages to be assumed. A practical problem is that a number of replicate test runs often are needed to obtain sufficient sample volume for complete gas analysis.

The UPITT[27] *method*

This test (Fig. 12.10) generates toxic potency data and was developed to meet the New York State requirement for materials used in buildings. Test specimens (approximately 5 g) are cut into pieces, placed on a tray, and heated from ambient temperature at a fixed rate, which may or may not cause ignition. Air flows through the furnace, and the effluent is diluted before passing through an animal (mouse) exposure chamber. The material can pass through several ISO fire stages including 1b, 2 and 3a, but these cannot be distinguished. The results reflect a preset fire path which will partly depend on the thermal stability of the test material.

The respiratory rates and times of death within the exposure period and the subsequent 10 min are recorded. Post-mortem data are also recorded. The method also determines the specimen mass loss, gas concentrations and yields. The test results may be expressed as average LC_{50} and IC_{50} values with the mass loss for lethality and incapacitation.

The method is relatively simple. The use of animal exposures are claimed to identify unusual toxicity. The variable and ill-defined (in terms of ISO fire stages) test conditions make it difficult to apply to real situations. The mixing conditions within the system may result in non-representative sampling while the relatively large mixing and exposure chambers may lead to condensation of vapours.



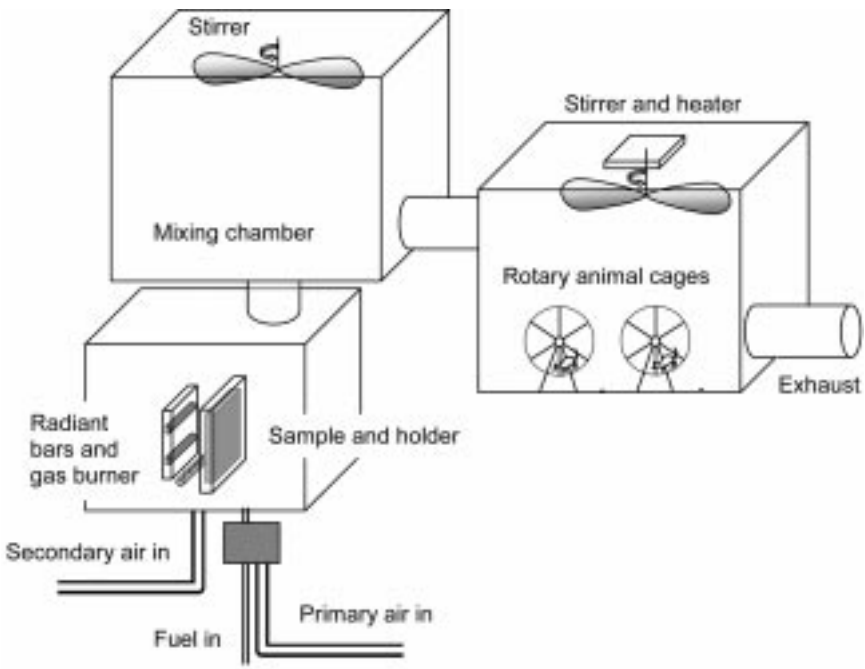
12.10 Diagram of UPITT apparatus.

JIS A 1321[28]

This Japanese test (Fig. 12.11) is intended to generate toxic potency data for building and furnishing materials. The test specimen is a vertical plaque, 220 mm square ($180 \times 180\,mm^2$ exposed surface) and not more than 15 mm thick. The specimen is exposed to the gas burner for 3 min and then to additional radiant heat for a maximum of 15 min. The primary air flow to the burner is $3\,l\,min^{-1}$ and the secondary flow into the furnace is $25\,l\,min^{-1}$. The effluent passes through a fan driven mixing chamber and $10\,l\,min^{-1}$ are withdrawn before the effluent passes into an animal exposure chamber containing rotary mouse cages.

The apparatus and method appear to indicate that the test generates the ISO stage 3a, vitiated flaming. The method also determines the times to incapacitation of the mice and blood samples may be analysed.

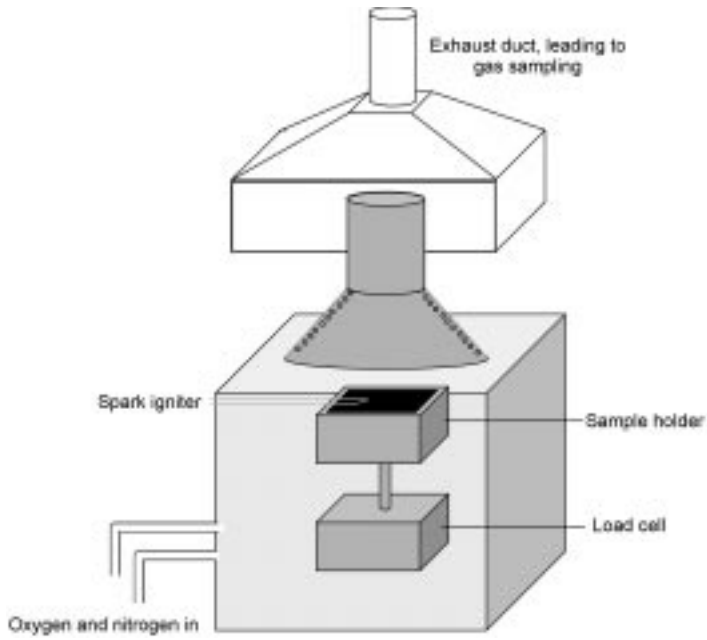
The test conditions are well defined and controlled. The vertical test specimen may cause errors with materials which drip, especially if the liquid fails to burn at the base of the furnace. The test provides a direct measure of the incapacitation effects of the effluent and will identify unusual toxicity. However, it is limited to a single fire stage, and errors due to the deposition of effluent may result because the effluent mixing fan may enhance deposition onto the large surfaces of the mixing and exposure chambers.



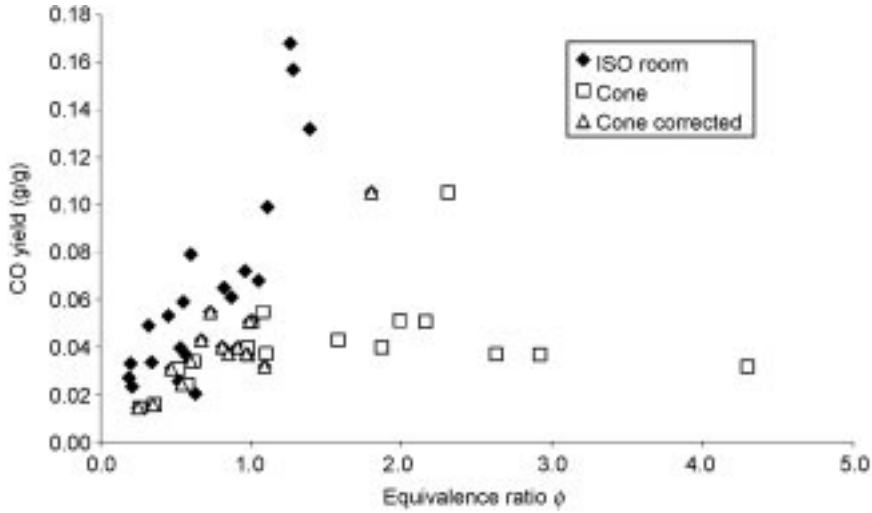
12.11 Diagram of Japanese fire effluent toxicity test apparatus.

The controlled atmosphere cone calorimeter

The non-standard modification of the cone calorimeter apparatus, the controlled atmosphere cone calorimeter,[29] encloses the fire model in a heat-resistant glass chamber (of dimensions 400 (h) × 300 (w) × 300 (d) mm^3) so that the air flow into the chamber may be controlled (see Fig. 12.12). It is included here as it has also been used to determine the composition of fire effluents, although the various designs do not follow a particular standard. However, standardisation of the vitiated cone calorimeter is currently under preliminary discussion within ISO TC92. This uses an enclosure around the specimen and radiator, and a controlled input flow of nitrogen and air, but has met with limited success. In some tests the effluent may continue to burn as it emerges from the chamber giving ultimately well-ventilated flaming. In others, under reduced oxygen concentrations, the fuel lifts from the surface, and ignition does not occur.[30] Hietaniemi[31] used the controlled atmosphere cone calorimeter (also known as the vitiated cone calorimeter or controlled ventilation cone calorimeter), but argues correctly that an instantaneous 'effective' global equivalence ratio ϕ_{eff}, should be used, rather than an averaged local equivalence ratio, based on the oxygen supply to the chamber, because, he reports 'in some of our experiments, especially in those performed with the polymer samples, substantial burning occurred outside the test chamber. In such cases the amount of oxygen available to combustion exceeds the amount that was fed to the test chamber.' He corrects



12.12 Controlled atmosphere cone calorimeter.



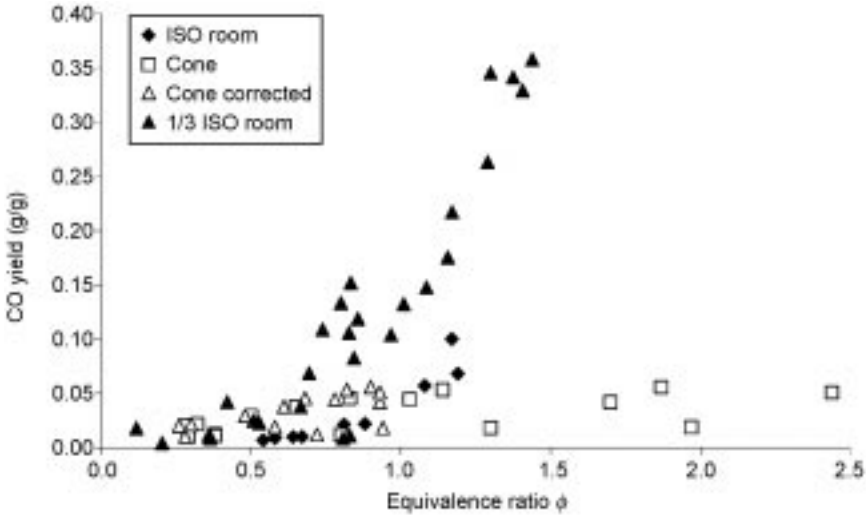
12.13 Carbon monoxide yield from polypropylene determined in the controlled atmosphere cone calorimeter, using the average and 'effective' values of the equivalence ratio, compared with values in the large-scale ISO 9705 room.

data reported from the same project and the same experiments as reported by Andersson,[32] reducing the equivalence ratio range of the apparatus to below 1, but in doing so brings the data back into line with the well-ventilated stages of large-scale fire test data.

Figure 12.13 shows the effect of this correction on data reported from the Toxfire project.[31–34] A phi meter[35] was used to establish the fire condition inside a lightweight concrete room with dimensions in accordance with the ISO 9705 room test. (A phi meter determines the equivalence ratio of the fire by adding oxygen to the fire effluent, passing the mixture over a catalyst at 900 ºC then measuring the resulting oxygen concentration.) Up to an equivalence ratio of 1, the corrected cone calorimeter data follow the same trend, but there is only a single data point at a higher equivalence ratio.

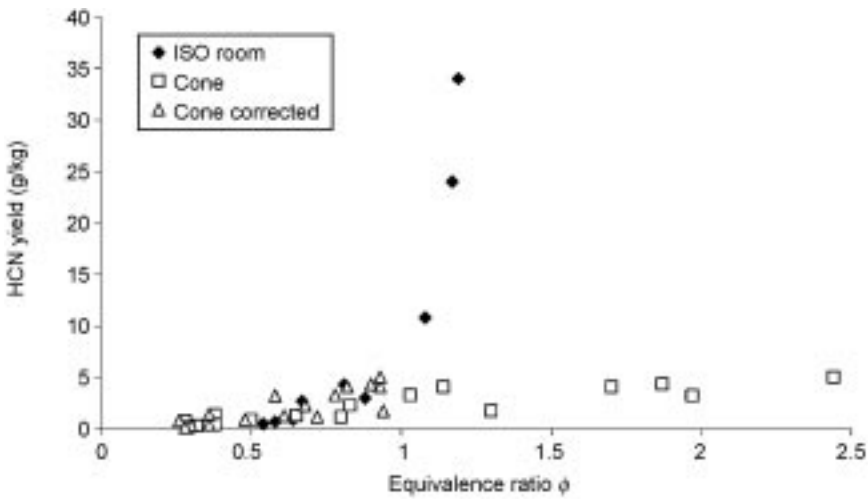
Figure 12.14 shows the difference between the controlled atmosphere cone calorimeter and the large scale for polyamide-6.6 under a range of ventilation conditions. It is notable that the controlled atmosphere cone calorimeter results, based on the averaged local equivalence ratio, reported by Andersson *et al.*[32] show higher carbon monoxide yields in well-ventilated conditions and, crucially, lower carbon monoxide yields in under-ventilated conditions. Again, the data have been corrected by Hietaniemi[31] by calculation of the effective equivalence ratio ϕ_{eff} (not the average equivalence ratio) in the controlled atmosphere cone calorimeter, which aligns the yields to the well-ventilated stages of the large-scale data.

Figure 12.15 shows the failure of the controlled atmosphere cone calorimeter to replicate the conditions of under-ventilated combustion even more dramatic-



12.14 Polyamide-6.6 carbon monixide yield for large-scale (ISO room and 1/3 scale ISO room) and controlled atmosphere cone calorimeter.

ally. The ~50-fold increase in hydrogen cyanide yield as the fire condition changes from well ventilated to under-ventilated is not seen using the controlled atmosphere cone calorimeter. The correction to ϕ_{eff} merely compresses the data to below an equivalence ratio of 1.0.

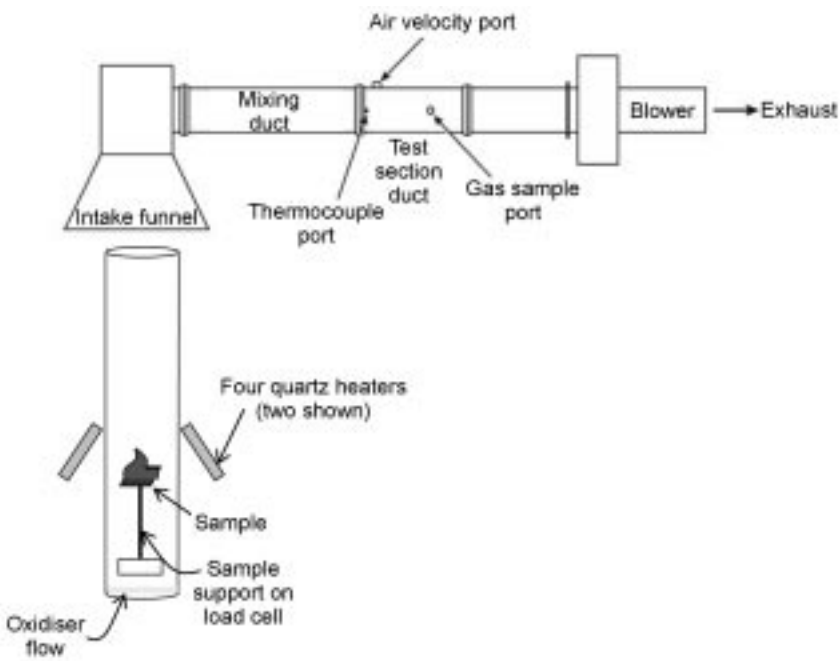


12.15 Polyamide-6.6 hydrogen cyanide yield for large-scale ISO room and controlled atmosphere cone calorimeter.

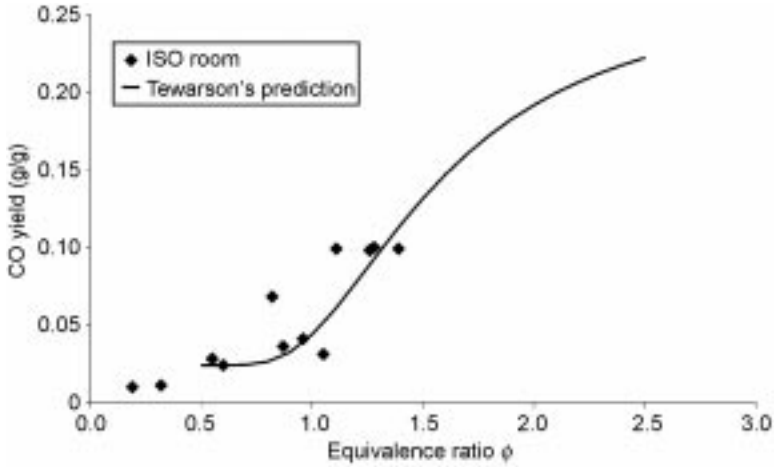
Fire propagation apparatus[36]

This method (Fig. 12.16) is similar in principle to the cone calorimeter but the fire zone is contained within a 172 mm diameter vertical silica tube allowing better control of the fire atmosphere, and keeping it out of contact with the heaters, which are outside the tube. Horizontal test specimens, typically 100 mm square and up to 25 mm thick, or vertical specimens 100 mm wide, 305 mm high and up to 25 mm thick, are exposed to thermal radiation and a pilot flame. The effluent flows through an instrumented duct and the rate of heat release is determined from oxygen consumption. Again the effluent yields can be directly related to the ISO fire stages. As well as obtaining heat release rates, it is also suited to obtaining toxicity data, and yield data have been published as a function of equivalence ratio, and have been used to calculate FED and LC_{50} values. A significant advantage of this method is that the air flow and composition in the fire zone is controlled and consequently the apparatus could be used with pre-determined values of equivalence ratio (ϕ) to generate effluent yield data for the different ISO fire stages.[37,38]

Using data from the fire propagation apparatus, Tewarson[37] has reported formulae for the prediction of toxic product yields as a function of equivalence ratio. For polypropylene, this is given by:



12.16 Fire propagation apparatus.



12.17 Comparison of carbon monoxide yield from polypropylene in the ISO room with that predicted from data from fire propagation apparatus.

$$Y_{CO} = Y_{CO_{well-ventilated}}\left(1 + \frac{\alpha}{e^{2.5\phi^{-\xi}}}\right)$$

$$Y_{CO} = 0.024\left(1 + \frac{10}{e^{2.5\phi^{-2.8}}}\right)$$

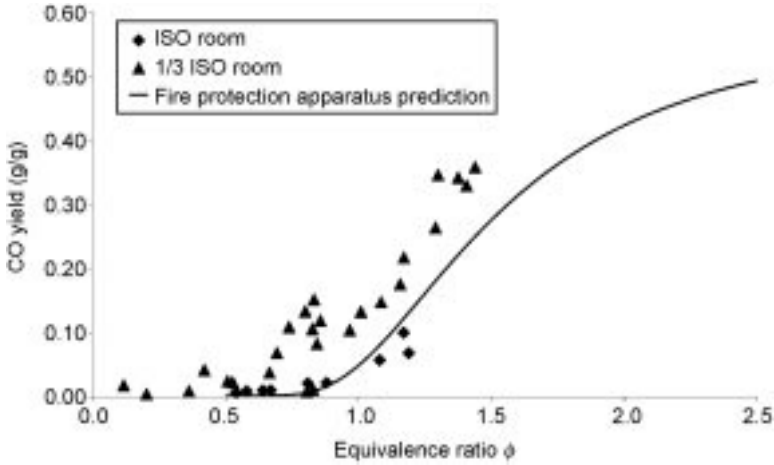
where $Y_{CO_{well-ventilated}} = 0.024$, $\alpha = 10$ and $\xi = 2.8$.

The predicted yields of carbon monoxide for polypropylene have been plotted in Fig. 12.17 alongside the same large-scale ISO room data,[31] showing good agreement. However, Tewarson's yield of carbon monoxide continues to increase with the increasing ϕ, reaching a somewhat higher plateau.

The predicted yields of carbon monoxide for polyamide-6.6 (Fig. 12.18) have been calculated using the above equation with $Y_{CO_{well-ventilated}} = 0.038$; $\alpha = 36$; $\xi = 3.0$. The data have been plotted alongside the same large-scale ISO room data,[31] showing good agreement. Again, Tewarson's yield of carbon monoxide continues to increase with the increasing ϕ, reaching a somewhat higher plateau. Unfortunately Tewarson has not reported a similar correlation for hydrogen cyanide yield from polyamide-6.6.

12.4.2 Steady-state flow-through or steady-state tube furnace methods

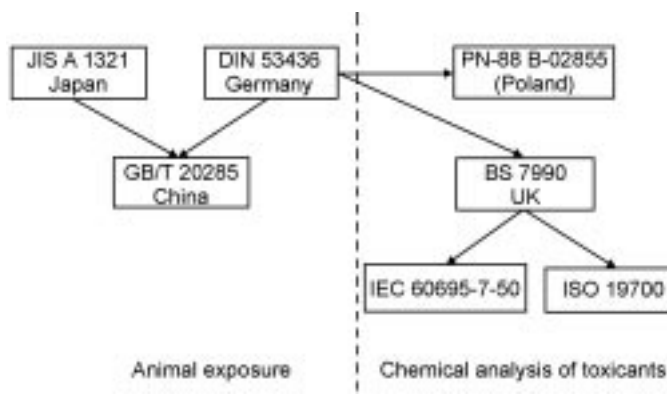
The difficulty of replicating the conditions of fully developed and under-ventilated flaming on a bench scale is caused by two practical problems. In fully developed fires in under-ventilated conditions, the high heat flux is large enough for burning to continue at low oxygen concentrations (e.g. ~5%); in bench-scale experiments the heat flux is usually constant, and often insufficient to sustain



12.18 Comparison of carbon monixide yield from polyamide-6.6 in ISO room with that predicted from curve-fitting data from fire propagation apparatus.

flaming at such low oxygen concentrations. In fully developed fires, mixing and recirculation of the fire effluent ensure that all the oxygen present passes into the fire plume; in many bench-scale apparatuses, such as the controlled atmosphere cone calorimeter or smoke chamber, an unknown quantity of fresh air bypasses the fire plume, so the ventilation condition remains undefined.

The steady-state tube furnace approach addresses both of these problems by feeding the sample into a furnace at a fixed rate, under a fixed air supply, inside a narrow horizontal tube, to ensure adequate mixing of fuel and oxidant. These methods force combustion by feeding the sample into a furnace of increasing heat flux at a fixed rate, thus replicating each fire stage by steady-state burning. Figure 12.19 shows the development of the steady-state tube furnace group of standards.



12.19 Evolution of the steady-state tube furnace family of standards.

DIN 53436

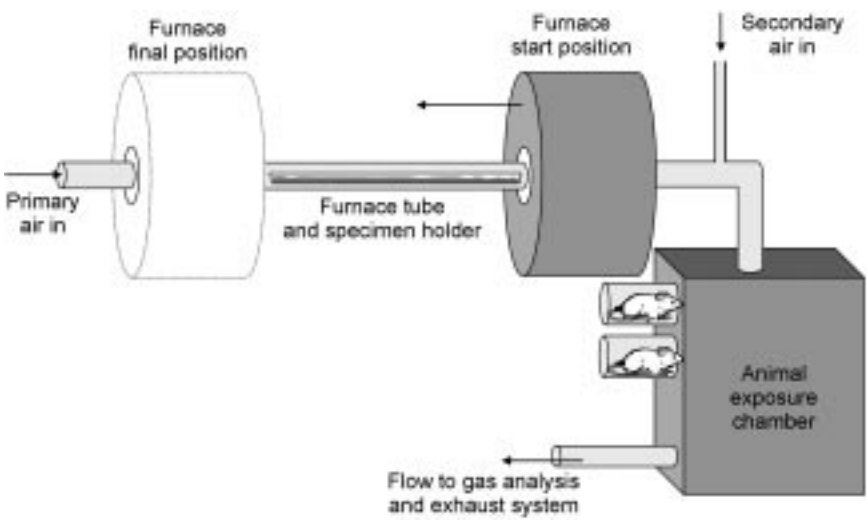
The approach was first used in the German DIN 53436[39] (Fig. 12.20), in which a narrow, annular tube furnace was moved counter to the direction of primary air flow ($2\,l\,min^{-1}$). The effluent is then diluted with secondary air, and the toxicity assessed using animal exposure. The method, in particular the use of animal exposure, is becoming obsolete, superseded by later versions of the steady-state tube furnace and avoiding test protocols using live animal exposure. The UK's BS 7990 method is based on the DIN 53436, with three important modifications:

- The furnace is static with the sample being driven into the furnace – this is mechanically easier, but requires a longer bench space.
- The furnace and boat are both longer reducing rapid quenching of the fire effluent, and char oxidation, which occurs when the DIN moving furnace passes over the sample.
- The replacement of animal exposure in the protocol by chemical analysis is the primary means of toxicity assessment.

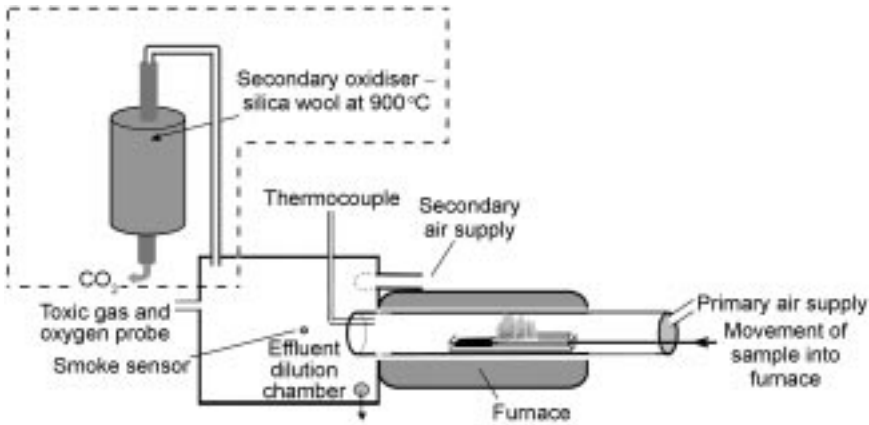
This method is now being adopted as the only international standard specifically designed for toxicity assessment, as ISO 19700, and in the electrotechnical sector as IEC 60695-7-50.

The Purser furnace BS 7990,[40] ISO TS 19700[41] and IEC 60695-7-50[42]

This method has been designed to generate data for input to ISO 13344,[43] ISO 13571,[44] BS 7899[45] and fire risk assessments, particularly those which are



12.20 Schematic of the DIN 53436 furnace.



12.21 Diagram of apparatus of ISO TS 19700. The secondary oxidiser (inside dotted line) shows one method for determination of total hydrocarbons specified in the ISO standard.

specifically related to the ISO fire stages. The methods use the same apparatus and protocol, although the ISO 19700 apparatus is more closely specified, and the earlier potential ambiguities have been removed. The apparatus is shown in Fig. 12.21, with the air flow and temperature required to replicate each fire stage shown in Table 12.1.

An initial run, followed by adjustment of temperature, air flow or specimen introduction rate may be required to simulate a specified ISO fire stage. A strip

Table 12.1 Furnace conditions corresponding to characteristic stages of burning behaviour

File type	Temperatures (°C)	BS 7990 Primary air flow ($l\,min^{-1}$)	ISO TS 19700 Primary air flow ($l\,min^{-1}$)	IEC 60695-7-50 Primary air flow ($l\,min^{-1}$)
1b Smouldering (non-flaming fires)	350	2	2	1.1
2 Well-ventilated flaming	650	10*	10*	22.6
3a Small under-ventilated flaming fires	650	Twice stoichiometric fuel/air ratio	Twice stoichiometric fuel/air ratio	–
3b Full developed under-ventilated fires	825	Twice stoichiometric fuel/air ratio	Twice stoichiometric fuel/air ratio	2.7

* Subject to verification of ventilation condition.

specimen or pieces are spread in a long silica boat over a length of 800 mm at a loading density of 25 mg mm^{-1} and fed into a tube furnace at a typical rate of 1 g min^{-1} with flowing air. Secondary air is added in a mixing chamber to give a total gas flow of 50 l min^{-1}. This narrows the analytical range – if less primary air is used the concentration of toxic products tends to be greater, and provides enough sample for analysis. The toxic potency of the effluent assessed during the steady state burn period, after the initial peak, but before the final tail off.

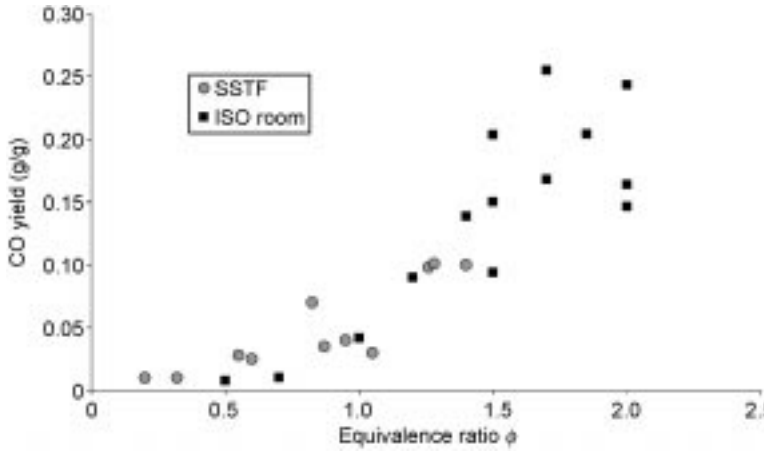
This protocol enables the toxic potency of a material of unknown composition to be determined under known, steady-state fire conditions (temperature and equivalence ratio) which relate directly to the end-use fire hazard. The use of a high secondary air flow usually permits the required gas samples to be taken during a single run. Smoke obscuration may also be determined. Unlike the closed box methods which may give toxic product data for a continuum of fire stages, in this method a separate run is required for each fire stage. In addition to analysis of the gases specified in ISO 13344 (carbon dioxide, carbon monoxide, oxygen, hydrogen cyanide, NO_x, hydrogen chloride, hydrogen bromide, hydrogen fluoride, sulphur dioxide, acrolein and formaldehyde) there is a requirement to determine the total hydrocarbons. This may be achieved by passing part of the air-diluted test effluent through a secondary combustion furnace to allow the determination of the products of incomplete combustion. This also enables the equivalence ratio to be calculated directly.

Correlation of steady-state tube furnace with large scale

Crucially, the steady-state tube furnace method has been shown to replicate the toxic product yields from large-scale tests. Comparison of the yields of carbon monoxide from burning polypropylene (Fig. 12.22) and polyamide-6.6 (Fig. 12.23) shows a strong dependence on equivalence ratio and consistency between bench and large scales.[46]

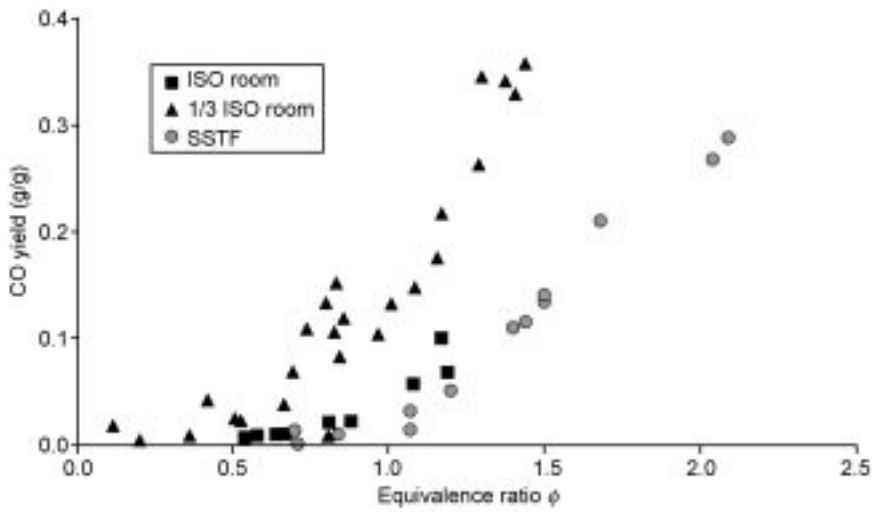
Figure 12.22 shows a comparison of carbon monoxide yield from polypropylene obtained in the steady-state tube furnace[46] with that obtained by Blomqvist and Lonnermark in the TOXFIRE project,[32] which has already been presented in Fig. 12.13. In well-ventilated conditions, both the tube furnace and the large-scale fire give carbon monoxide yields around 0.02–0.03 g/g, rising to 0.17 g/g in the tube furnace and 0.1 g/g in the large-scale test for under-ventilated flaming.

Figure 12.23 shows a comparison of the carbon monoxide yield for polyamide-6.6, as a function of equivalence ratio, for the steady-state tube furnace[46] with data reported by Andersson *et al.* from the TOXFIRE project,[32] as presented in Fig. 12.14 in comparison with the controlled atmosphere cone calorimeter. Given the generally very poor correspondence between bench and full-scale toxic product yields, particularly for carbon monoxide under less well-

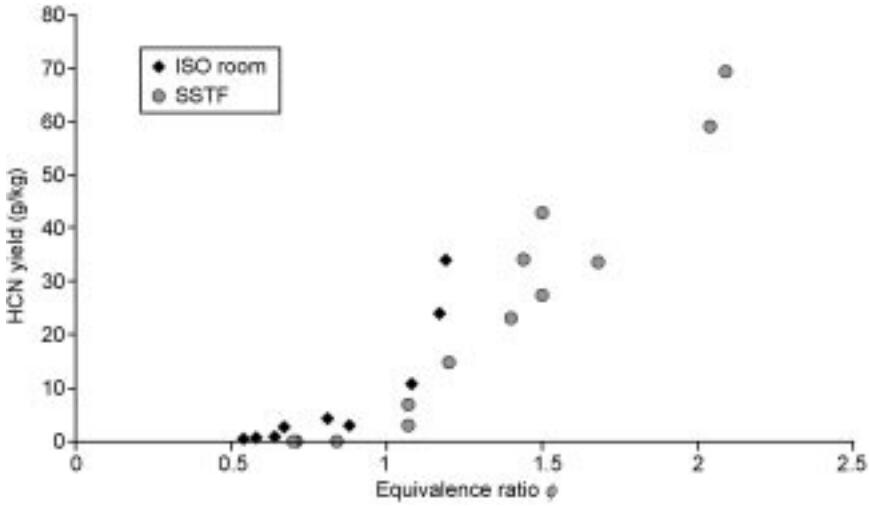


12.22 Comparison of tube furnace carbon monoxide yields with large scale for polypropylene.

ventilated conditions ($\phi > 1$), the large-scale test data (from the ISO room test) show very good agreement with the steady-state tube furnace data. At higher equivalence ratios the scatter of the data points is more evident. Pulsation of flaming was observed as the fire gases hunted for oxygen in the $\frac{1}{3}$ISO room, where sporadic flaming was observed in the effluent dilution chamber. This may lead to a higher degree of scatter between the individual experiments in under-ventilated conditions.



12.23 Comparison of carbon monoxide yield for polyamide-6.6 from steady-state tube furnace with ISO room and $\frac{1}{3}$ ISO room as a function of equivalence ratio ϕ.



12.24 Comparison of hydrogen cyanide yield for polyamide-6.6 from steady-state tube furnace with ISO room as a function of equivalence ratio ϕ.

Figure 12.24 shows a comparison of the hydrogen cyanide yields from the steady-state tube furnace with those from the same ISO room experiments. Again this shows a dramatic increase associated with under-ventilation in relation to the other major toxic product, hydrogen cyanide, in both the bench and large scales. This clearly demonstrates the ability of the steady state tube furnace to replicate the conditions found in large-scale fires.

PN-88/B-02855[47]

This is the Polish standard based on DIN 53634. This test uses the chemical analysis of specified gases to assess the toxicity of effluents generated in the flow-through tube furnace. Strip specimens of approximately 4 g are heated by a travelling furnace at 450, 550 and 750 ºC in a counter-current air flow of 100 $dm^3 h^{-1}$. The concentrations of specified gases, carbon dioxide, carbon monoxide, hydrogen cyanide, hydrogen chloride, nitrogen dioxide and sulphur dioxide, are determined by gas chromatography and results are expressed as a toxicity index (related to a 30 min exposure period) which is used to classify materials as 'very toxic', 'toxic' and 'merely toxic'.

GA 132-1996[48]

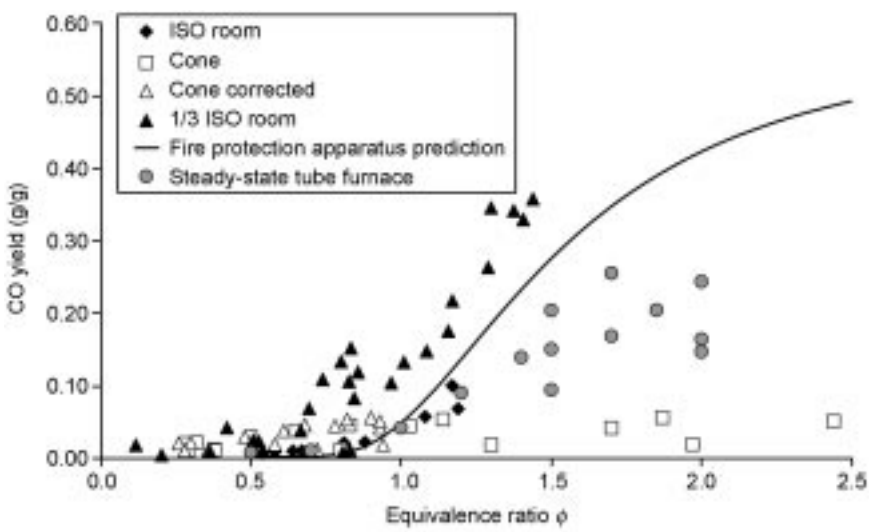
This is a standard test of the People's Republic of China and uses the same state moving furnace system as DIN 53634 in combination with the mouse exposure chamber and rotary cages of JIS A 1321. The results are given as LC_0 which is

the concentration in mg litre^{-1} which does not cause the death of any of the exposed animals within a 30 min exposure. The LC_0 is compared to a specified value.

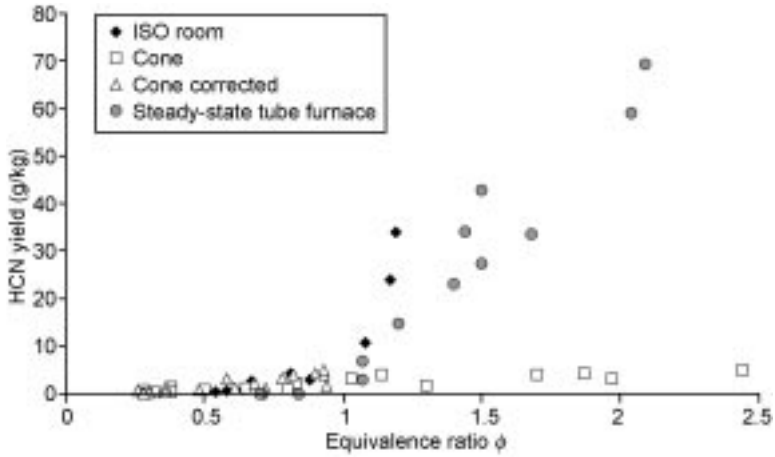
12.5 Overall comparisons between bench and large scales

The data already presented separately, of carbon monoxide yields from polyamide-6.6 as a function of equivalence ratio, comparing the controlled atmosphere cone calorimeter, fire propagation apparatus and steady-state tube furnace with the ISO room and the 1/3 scale ISO room, are shown in Fig. 12.25. This shows a significant increase in the carbon monoxide yield as the fire moves from well ventilated to under-ventilated, using all methods except the controlled atmosphere cone calorimeter.

Figure 12.26 shows the hydrogen cyanide yields from polyamide-6.6 as a function of equivalence ratio for comparison between the controlled atmosphere cone calorimeter and the steady-state tube furnace with the large-scale ISO room. It is apparent that the controlled atmosphere cone calorimeter also fails to replicate the higher yields of the other major asphyxiant, hydrogen cyanide in under-ventilated fires. The yields of toxicants and their relationship to fire conditions are discussed further in Chapter 14.



12.25 Comparison of carbon monoxide yield for polyamide-6.6 from steady-state tube furnace, controlled atmosphere cone calorimeter, fire propagation apparatus, with ISO room, and with $\frac{1}{3}$ ISO room as a function of equivalence ratio ϕ.



12.26 Comparison of hydrogen cyanide yield for polyamide-6.6 from steady-state tube furnace and controlled atmosphere cone calorimeter, with ISO room, as a function of equivalence ratio ϕ.

12.6 Conclusions

There are a large number of different methods used for bench-scale assessment of combustion toxicity, and some confusion surrounds the applicability of test data to fire hazard assessment. Toxic hazard data should not be used in isolation but should either be a part of a classification scheme or as part of the input to fire risk and fire safety engineering assessments. It is important that uncertainty or confidence limits should be used with toxic hazard data, because they are often relatively large. Fire effluent toxicity does not have a unique value but is a function of the material and the fire conditions, particularly temperature and oxygen availability in the fire zone, and also the fire environment (enclosure, geometry and ventilation). In order to assess the fire hazard, toxic hazard data must be relevant to the end use fire situation, which can be defined using the ISO classification of fire stages.

Globalisation of trade and relaxation of national barriers drive the need for international harmonisation of toxicity testing. ISO specifications and standards provide a common basis on which to determine toxic hazard. A number of standard fire smoke toxicity tests are available and it is important to consider their relevance and limitations before selecting a method. Some of these tests do not appear to represent any fire stage; some represent several fire stages separately; others represent the progress of a fire through an indeterminate number of stages. Further, some test methods produce data, which are a function of both the flammability of the specimen and the yield of toxic products, while others provide toxic product yield data, which are independent of the burning behaviour. Finally, although this has been discussed in earlier chapters, chemical

methods of assessment provide a breakdown of the concentrations of individual toxicants, from which the toxic hazard of each component can be calculated, while animal-based assays give an overall estimate of the toxicity of the fire smoke. It has been argued that animal-based methods are more likely to identify any new unusually high toxic potency (UHTP) products, provided the human and test animal responses were similar, though it should be noted that there have only been two such instances (trimethylol propane phosphate[49] (TMPP), and PTFE) in the last three decades, and neither product would be expected to be toxicologically significant in a real fire.

The general trend has shifted from standard tests, which include precise details of apparatus, procedure, method of assessment and specification of results, to, more recently, approaches which define the apparatus and procedure necessary to obtain data relevant to end use fire situations. The latter requires the involvement of suitably qualified personnel to define the necessary test conditions, effluent analyses, and to interpret results to ensure they are relevant to the end use application.

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13

Large-scale generation and characterisation of fire effluents

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Abstract: The characterisation of fire effluents from large-scale fire tests is important for assessing the risks associated with specific scenarios regarding buildings and transport, and also for validation of effluent data from small-scale tests. This chapter describes some of the most important standard large-scale test scenarios and modifications of these tests including gas analysis. It will further describe some specially designed tests with a focus on how these tests can be used to obtain information concerning the emission of toxic species. The standard tests described include tests with building materials, cables and tests of extinguishing systems on ships. The specially designed tests discussed include various tests with land vehicles, marine vehicles and different industrial applications. A discussion of methods for sampling and analysing toxic species of interest with a focus on large-scale applications is also included.

Key words: fire effluents, large-scale fire tests, smoke characterisation, toxic fire gases.

13.1 Introduction

Fires represent a variety of hazards that, in unfortunate circumstances, may lead to injury or death. The heat and flames from fires are obvious risks but the evolution of toxic gases also presents a significant hazard. Indeed it is accepted that the inhalation of toxic smoke is one of the greatest risks posed to people by fires. This knowledge has, however, in general not been adequately reflected in research activities in the fire community, or in standards or codes. While building codes have regulated the fire performance of structures, building material, escape routes and, in recent years, even furnishing, they have generally not regulated emissions except in some specific applications, e.g. passenger vessels, as described in more detail later in this chapter. The fire safety assessment of material and products is therefore largely based on testing and standards considering parameters such as ignitability, heat release, flame spread and in some cases rate of smoke obscuration but seldom on toxicity. The basic principle is to mitigate the fire risk by minimising the risk for ignition and restricting

the flame spread, thereby reducing the amount of combusted material that might produce smoke and toxic gases.

Much of our knowledge of materials and products has been gained through standard product testing but there are few mandatory standards that address the toxicity of smoke gases. Naturally this varies between countries and regions; however, as an example, the European fire classification system for construction products[1] does not include any requirement on combustion toxicity.

In the International Maritime Organisation (IMO) regulations for the classification of surface materials for use in the interiors of ships, however, there are detailed requirements on smoke toxicity.[2] This is a direct reaction to the fire on the *Scandinavian Star* in 1990 when 159 people lost their lives largely through smoke inhalation.[3] Similarly, for materials intended for use in aircraft, there are regulations on smoke toxicity (Airbus).[4] Although the concept of focusing on the basic fire properties of materials and products must be the foundation of fire safety, there does appear to be a gap between the information gained from testing and the behaviour of real materials and products in real fires. This issue was the focus of a project conducted by NIST, where it was concluded that the proper treatment of smoke toxicity in standards and codes has not yet been solved.[5]

Fires produce a complex cocktail of gases, all with varying modes of action and toxicity. Traditionally, carbon monoxide (CO) is recognised as the main toxicant in fires,[6] although numerous other gases are acknowledged as potentially important in determining the outcome of any given fire exposure. Hydrogen cyanide (HCN), elevated levels of carbon dioxide (CO_2) and oxygen vitiation are also important in their contribution to the asphyxiating characteristics of smoke gases. There are other components in smoke gases that cause sensory irritation to eyes and the upper respiratory tract. These compounds include acid gases produced from the combustion of halogen-containing materials (where hydrogen chloride, HCl, is the most common), and a variety of organic compounds, such as: formaldehyde, acrolein and isocyanates. Irritant gases may have their greatest influence in reducing the speed of egress in the evacuation of people from a fire. But at higher concentrations of irritants, lung damage and oedema may result in death some time after exposure.

Generally, the danger from fire gases is a combination of the toxic potency of the smoke and the time of exposure (i.e. dose-related effects from asphyxiants). However, for irritants the sub-lethal effects are concentration related. In addition to gaseous species, condensed phase components in the fire effluents constitute a threat. Such aerosols (smoke) reduce visibility, obstruct breathing and may contain nano-sized particles that can be transported deep into the pulmonary tract.

Although there are few frequently applied standard test methods assessing the content of fire smoke, knowledge has been gained from research activities in recent years. There is information available in the literature on the occurrence

and production of various fire gases, especially on important lethal gases such as carbon monoxide[6–9] and hydrogen cyanide,[10–12] but also to a lesser extent on sub-lethal organic compounds,[13–15] which in some cases may have a more significant long-term effect. Owing to the complexity of an uncontrolled combustion process (i.e. a fire), and the high costs associated with detailed chemical characterisation, there are still many issues that remain unsolved.

Most existing studies of smoke gas toxicity have relied solely on data from small-scale physical fire models. It is, however, generally not straightforward to interpret such data in terms of smoke gas composition in real-scale fires. There is generally a lack of quantitative chemical data concerning fire effluents from real-scale fires. As an example, in recent work conducted at NIST, it has been concluded that time-dependent yield data for fire-generated gases from room fires are almost non-existent and are much needed.[16]

The consequences of fires in terms of their direct threat to people in the vicinity of a fire, and the economic losses associated with fires in terms of damage to buildings and infrastructure are naturally of great societal interest. The correct characterisation of emissions from real fires is a difficult (some might say impossible) task. Our understanding of the emissions from fires is, therefore, largely reliant on laboratory testing. In many cases standard tests have been used and will be used in the future to allow the ready comparison of results from different material but such tests have the disadvantage of not necessarily being representative of real scenarios. Complementary to such testing it is important to conduct large-scale (approaching real-scale) ad hoc tests that replicate real-life scenarios to an acceptable degree. Such tests give us a glimpse of real fire data but are not as generally applicable as standard tests. In both cases, however, characterisation of fire gases is a task whose complexity increase with the number of species being monitored.

This chapter will describe some of the most important standard large-scale test scenarios and some specially designed tests with a focus on how these tests can be used to obtain information concerning the emission of toxic species. In this context, methods for sampling and analysing toxic species of interest will also be discussed.

13.2 Fire characterisation

A fire is dependent on and controlled by, the interaction of three constituents: a fuel, an oxidiser and energy. Heat is necessary to pyrolyse the fuel, and the oxidiser is necessary for the combustion of the pyrolysis gases. The exothermal combustion reactions produce heat, thereby continuing the cycle from heat to pyrolysis to combustion. A change in one of the components (i.e. interference in the chain of events) has a major influence on the fire conditions and the products from the fire. It is therefore important to define the conditions in a fire in any study of its emissions. One parameter commonly used to describe the ventilation

conditions during combustion is the equivalence ratio ϕ, discussed in Chapter 2, which may also be defined in Equation 13.1 below as:

$$\phi = \frac{\dot{m}_{\text{fuel}}/\dot{m}_{\text{oxygen}}}{\left(\dot{m}_{\text{fuel}}/\dot{m}_{\text{oxygen}}\right)_{\text{stoich}}} \quad \begin{array}{ll} \phi = 1 & \text{stoichiometric combustion} \\ \phi < 1 & \text{well-ventilated combustion} \\ \phi > 1 & \text{under-ventilated combustion} \end{array} \quad 13.1$$

where $\dot{m}_{\text{fuel}}$ is the mass loss rate of the fuel, $\dot{m}_{\text{oxygen}}$ is the mass flow rate of oxygen, and the subscript 'stoich' refers to the quotient under stoichiometric conditions.

The equivalence ratio describes the relationship between the actual fuel/oxygen ratio and the stoichiometric fuel/oxygen ratio. In cases where the overall combustion process is studied, as opposed to spatial variations in, for example, an enclosure, ϕ can be defined in a more general sense using the equivalence ratio for the total combustion process. This is usually referred to as the global equivalence ratio (GER). In cases where spatial variations in the fire are of interest one defines the equivalence ratio for each particular position in a fire as the local equivalence ratio (LER).

13.3 Sampling and analysis of fire gas from large-scale tests

The characterisation of gases from a fire is complicated by a number of factors: a fire is a dynamic and turbulent process and the concentration of specific compounds in the smoke plume may change from ppm levels to percentage levels during the course of the fire, or from one part of the plume to another. Further, fire gases are most often hot at the sampling point, which introduces complications such as continued chemical reactions, or condensation of gases in cold parts of the sampling equipment, or on surfaces in the test set-up.

Depending on the species to be measured it can be necessary to choose an online method which allows time resolution of species concentration or a cumulative method which provides average concentrations. In the case of online methods, the development of the species concentration can be monitored and compared with the development of the fire itself which can provide important insight into when a certain species is most important during a fire. Such methods do not, however, typically allow the measurement of very low concentrations which ignores a large number of important toxic species produced in very low concentrations.

Cumulative methods do not allow time resolution of results but they do allow the determination of very low concentrations which is particularly important in the case of certain highly toxic organic species such as halogenated dibenzo dioxins and furans. In the case of cumulative sampling the smoke is continuously drawn through a medium designed to retain the species studied. The

species concentration in the sampling medium is subsequently determined using a suitable analysis technique.

In fire gas characterisation, the presence of high concentrations of particles creates additional challenges in sampling. The sampling methodology is, therefore, an important part of the total measurement scheme, irrespective of the analysis method employed. The aim of sampling is to collect a representative sample of the fire gases for subsequent analysis. To accomplish this, the sampling equipment typically consists of a probe, a particulate filter, tubing and a pump. The particulate filter and the sampling tubing are normally heated to avoid condensation of water.

This section will contain an outline description of methods which are suitable for the measurement of toxic species in large-scale fire tests. Other methods may be available but those presented here have been applied in a large number of research projects and their usefulness is well established. Further information regarding sampling and measurements of chemical species from fires can be found in ISO 19701[17] and ISO 19702.[18]

13.3.1 Sampling

Sampling from a duct, where the smoke gases are well mixed, is the traditional and most controlled situation. The rule of thumb is that the fire gases are sufficiently well mixed at a distance of five times the duct diameter and that one can use a single-hole probe. When moving from the vicinity of the fire to the duct, e.g. in the opening of an enclosure or inside a fire enclosure the fire gases are more concentrated and not as well mixed particularly before they have been diluted with external air. Here, the sampling conditions are more severe.

Which sampling strategy is chosen depends on whether one is interested in a characterisation of fire gases both temporally and spatially or whether it is sufficient to obtain average values for an entire enclosure. The choice of sampling strategy has a significant impact on the design of the probe. Probes can be broken into single-hole or multi-hole probes. In cases where the gases are well mixed a single sampling point can give a representative sample for a given situation but if the fire gases are not well mixed a single sampling point will only provide information concerning the gas concentration at that single point which may be difficult to interpret. Alternatively, a multi-hole probe can be employed to extract a representative sample from stratified gases.

It is difficult to design a multi-hole probe so that it takes a representative sample when gas concentrations are stratified. One example of such probe design was used in the TOXFIRE[19] and SAFIR projects[20] where sampling in the door of the ISO room was chosen to maximise the concentration of certain species. In the TOXFIRE project a probe was designed to hang diagonally across the upper part of the door opening to extract gas samples from the different strata leaving the upper part of the door (the lower part of the door acted as a

natural fresh-air inlet). This probe was closed at one end and contained between 7 and 10 holes with 10 cm spacing (⊘ 3 mm). Calculations conducted using the Bernoulli equation as a part of the SAFIR project,[21] however, showed that the pressure drop in the probe meant that only the holes furthest from the closed end were actually extracting gas while the others were essentially closed. To avoid this situation a probe was designed with 10 cm spacing and increasing hole size: 1.5, 1.6 , 1.8, 2.1, 2.5, 3.2, 5.0 mm (the largest hole closest to the closed end of the probe). This probe was able to extract a representative sample from the stratified gases exiting the door opening. Thus, if such sampling is to be attempted one should make similar calculations for the specific sampling situation and design the probe for the experiment in question to ensure representative sampling.[21]

Gas flow is not significantly dependent on the mass of the molecules and samples can be extracted at a constant velocity. However, if particulate matter is to be sampled it is important to take into account the mass of the particles to avoid over-sampling the lighter species. This is done using isokinetic sampling. Isokinetic sampling is a technique for collecting aerosols in which the sampling device has a collection efficiency of unity for all sizes of particles in the sampled gases, regardless of the gas stream velocity and direction of the instrument. The gas stream entering the collector has a velocity (speed and direction) equal to that of the gas stream just ahead of the sampling part of the collector. Isokinetic sampling should always be used when sampling particulate matter.

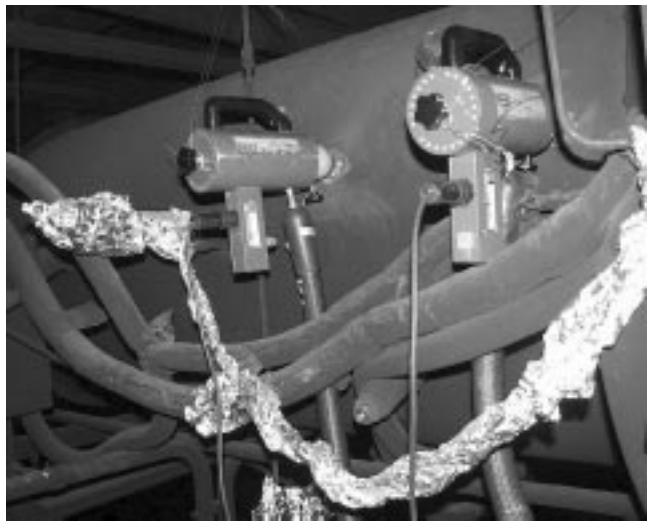
It is important to realise that the sampling system extends beyond the probe. In cases where hot gases are extracted and transported from the sampling point to an online instrument it is generally necessary to ensure that water does not condense between the sampling point and the measurement instrument. Experiments conducted during the SAFIR project recommend that a temperature of 150–180 ºC should be maintained across the whole sampling line. Any cold spots allow the condensation of water which could scrub important species from the fire gases.

In some cases, sensitive instruments will need to be protected from particulate matter in the fire gases, and a filter will be included in the sampling line. This filter should also be heated and its capacity should be carefully chosen to ensure that it does not become clogged during the experiment. Sampling probes with heated filter units mounted for sampling from a smoke gas duct are shown in Fig. 13.1.

13.3.2 Online methods

Fourier transform infrared (FTIR) spectrometry

By using online FTIR (Fourier transform infrared) spectrometry (discussed in more detail in Chapter 11), it is possible to simultaneously measure the time-



13.1 Sampling probes with heated filter units mounted to a smoke gas duct.

resolved concentration of many gases in a large-scale fire experiment. The main advantage of the FTIR technique is that information from all spectral elements is measured simultaneously; another advantage is that the measurement is made with a high optical throughput.[22] The practical measurement procedure is to continuously extract smoke gases to the FTIR from the sampling point through a heated sampling system. The gas sample is passed through a heated IR absorption cell of the FTIR, in which the specific absorption patterns of IR-active gases are recorded by a detector and are presented as an absorption spectrum. The frequency at which the absorption spectra are scanned determines the time resolution of the measurement. The concentration data of individual gas components are evaluated from the absorption spectra by various mathematical methods. Guidance for using FTIR for analysis in fire tests is given in ISO 19702.[18] Only a brief introduction to the technique is given here.

The gas sampling system often consists of a probe for sampling fire effluents from the sampling point, a filter system for removing particulates from the sampled gas, tubing for transporting the gas to the FTIR, and a pump draw the gaseous sample through the sampling system. The parts of the sampling system placed before the FTIR must be heated to avoid condensation and consequent losses of certain water-soluble compounds (e.g. hydrogen chloride). A sampling system temperature between 150 and 180 ºC has proved adequate.[18]

Suitable spectrometer resolutions are normally between 0.5 and 4 cm^{-1}. The advantage of a higher resolution (i.e. lower wavenumber) is that more of the spectral fine structure is resolved. However, a scan at a higher resolution takes proportionately more time. It is also advantageous to average a number of scans for each spectrum, as the noise is reduced as a function of the measurement time.

The scanning time (and noise level) varies for different FTIR instruments and appropriate settings for each instrument must be individually determined to optimise the sensitivity and time resolution.

The spectral range of the measurement determines the amount of information acquired. In order to collect information concerning all compounds that are generally of interest in a fire test a wavenumber range from 4500 to 500 cm^{-1} is appropriate.

To make quantitative measurements of gases, special calibration of the instrument is necessary since most gases do not give linear concentration/absorption profiles. Calibration must be made for each gaseous species to be quantified. Further it is necessary to calibrate other species with significant interference in the spectral region used for quantification. The most important interference species are water and carbon dioxide. The composition of the smoke gases is often very complex and changes rapidly with temperature and ventilation conditions. Hence, one needs a calibration covering a broad concentration range. Compounds that are suitable for measurement using FTIR include: carbon dioxide, carbon monoxide, hydrogen chloride, hydrogen fluoride, hydrogen bromide, sulphur dioxide, hydrogen cyanide, nitric oxide, nitrogen dioxide and some organic compounds such as acrolein.

Mathematical analysis of the fire smoke gas spectra is necessary for extracting quantitative data. The analysis of a spectrum may be based on the peak height or the area of a limited region of the spectrum. It is advisable to avoid regions where other gases overlap if possible. A calculation routine is used to simplify the analysis. There are a number of possible mathematical methods that can be used for the analysis, including multivariate methods such as classical least squares (CLS) and partial least squares (PLS). A more detailed discussion of different quantification methods is available in the SAFIR final report.[20]

Specific analysers

Different types of online analysers for a certain gaseous species or group of gaseous species are used in large-scale fire testing. These types of specific analysers include: analysers for carbon dioxide and carbon monoxide, analysers for oxygen, analysers for nitrogen oxides (NO_x), and analysers for unburned hydrocarbons. These methods and their applicability to the analysis of fire effluents are described in ISO 19701.[17]

Non-dispersive infrared (NDIR) analysers are used for the measurement of carbon dioxide and carbon monoxide. These are often combined in a single instrument. Some analysers require dried gases to be subjected to analysis. This is different from FTIR which often measures hot wet gas mixtures. Measurement ranges vary depending on the specific analyser, e.g. a typical commercial instrument might have a range up to 1% for carbon monoxide and up to 10% for

carbon dioxide. The analyser should be chosen to reflect the range of concentrations one expects to obtain. The output from the analyser is designed to be proportional to the gas concentration; however, at ppm levels of carbon monoxide, deviations from linearity are often found, and FTIR is in many cases more reliable for these low concentrations.

Analysers for oxygen utilise the property of paramagnetism originating from the relatively unusual unpaired electrons in the oxygen molecule. Commercial instruments generally measure over the complete range of 0–100%, but it is often possible to use a more narrow range, such as 0–25%. The performance of modern instruments is often very good with accuracy in the 0.01% range. It is important to allow an oxygen instrument to work at normal pressure, as these instruments are often very sensitive to changes in pressure.

Dedicated analysers for nitrogen oxides (because of their ease of interconversion, NO and NO_2 are sometimes referred to collectively as NO_x) utilise the fact that a portion of the nitrogen oxide becomes excited and emits electromagnetic light (chemiluminescence) when exposed to ozone. In the reaction chamber of the instrument, the sample gases are mixed with ozone (O_3) and reaction between nitrogen oxide and ozone takes place. The emitted light is measured by a photomultiplier detector. Some commercial instruments are heated which facilitates the analysis of hot fire gases without drying the sample gas. Standard commercial instruments typically have a measurement range of 0–10 000 ppm and a detection limit of the order of 0.1 ppm. The main reason for using a dedicated NO_x analyser simultaneously with FTIR, is the superior minimum detection limit of the chemiluminescence detector compared with FTIR.

The total amount of unburned hydrocarbons (THC) can be measured using a heated flame ionisation detector (FID) instrument. In an FID, organic components are burned in a hydrogen/air flame. The detector signal is, to a first approximation, directly proportional to the number of carbon atoms oxidised to carbon dioxide. The FID response for carbon atoms attached to one or more heteroatom, i.e. chlorine and sulphur, is, however, significantly reduced. For carbon monoxide the response is virtually zero. The FID response is normally linear over several orders of magnitude and the detection limit is approximately 1 ppm.

Light extinction

The smoke gases from a fire contain particles resulting in visual obscuration that may impair the ability of victims to escape from the fire as well as adding to the toxicity. The smoke properties that are important for the assessment of visual obscuration are light extinction and visibility. A short definition of important properties and dependencies will be given here. For a full account of the topic see, for example, the review of Mulholland.[23]

The smoke property normally measured is the light extinction coefficient (K). Measurements of K are based on Bouguer's law, which gives a relation for the intensity of the incident monochromatic light, $I_0(\lambda)$, of a wavelength λ and the intensity of the light, $I(\lambda)$, transmitted through a pathlength L through the smoke, i.e.:

$$I(\lambda)/I_0(\lambda) = \mathrm{e}^{-KL} \tag{13.2}$$

The smoke production rate (SPR) is the quantity often used in standard fire testing. SPR is the product of the light extinction coefficient (K) and the volume flow in the smoke gas duct for the measurement. The unit of SPR is m^2/s. The total smoke production (TSP) in a test is expressed as:

$$\mathrm{TSP} = \int_0^t \mathrm{SPR}\ \mathrm{d}t \tag{13.3}$$

Particles

The characterisation of particles (aerosols), which are highly dependent on agglomeration, and hence most likely to differ in a large-scale fire, can be made using accumulative methods such as low pressure cascade impactor technique. Mass size distributions and particle number concentrations can, for example, be obtained by using a DLPI (Dekati low pressure impactor) or the more advanced online technique, ELPI (electrical low pressure impactor).

In a cascade impactor, particles are separated according to their 'aerodynamic size'. The term aerodynamic size is used to provide a simple means of categorising the sizes of particles having different shapes and densities with a single dimension. The aerodynamic diameter of an arbitrary particle is equal to the diameter of a spherical particle having a density of 1 g/cm^3 that has the same inertial properties in the gas as the particle of interest. An advanced cascade impactor, such as a low pressure impactor, consists of several such impaction plates with nozzles of gradually decreasing diameters.

The stages of an impactor are characterised by their cut-off sizes. The *cut-off size* ($D_{50\%}$) is related to the Stokes number (i.e. particle inertia) that gives 50% collection efficiency, i.e., an impactor plate does not have perfect collection characteristics, and thus some under-sized particles are collected and some over-sized particles are admitted to the next plate. As some larger particles escape the designated plate and are collected on the following plate, the *geometric mean diameter* (D_i) is commonly used as an alternative description of collector plates. If there is a risk for 'overloading' of large particles, a pre-cyclone is used before the impactor to reduce the number of such large particles.

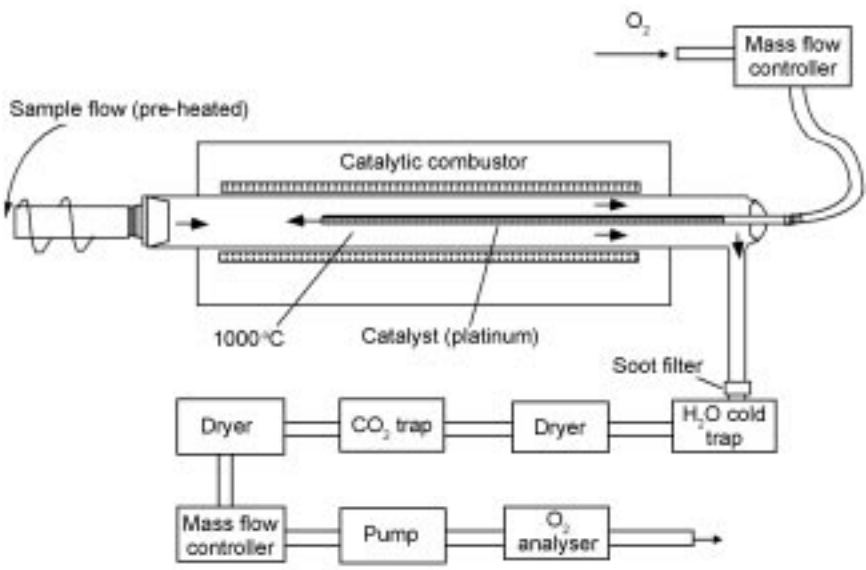
Measurement with the DLPI gives average data over the sampling period. The particles in the sampled aerosol are collected on the pre-weighed impactor plates, and the sampled mass distribution within the available size ranges is then

determined gravimetrically after the test. The online ELPI, however, determines the particle number concentrations continuously. The sampled particles are charged in the instrument's corona charger before reaching the electrically isolated collector stages of the low pressure impactor. The charged particles are continuously quantified at each stage by a sensitive multi-channel electrometer.

Particle number, distribution and respective particle mass distribution are calculated by assuming an aerodynamic particle diameter, i.e. a spherical particle with a density of 1 g/cm^3, having the same terminal velocity as the particles studied.

Phi meter (equivalence ratio)

To measure the GER in the room containing the fire, a *phi meter*[24,25] can be used. The essential parts of the phi meter are the combustor, into which the fire gases and additional pure oxygen are introduced, and the oxygen analyser (see Fig. 13.2). In the combustor, complete combustion of the fire gases is achieved using a catalyst (platinum) and additional oxygen. The readings on the oxygen analyser are compared with background measurements without fire gases through the phi meter. A simple computation gives the equivalence ratio. The phi meter was originally constructed and calibrated for hydrocarbons, but it has since been applied to substances containing atoms of other elements (nitrogen, sulphur and chlorine).[26]



13.2 The phi meter, an instrument for online measurement of the equivalence ratio.

13.3.3 Cumulative methods

Specific, organic species of high toxicity are particularly difficult to identify using online methods and generally one relies on cumulative methods for such study. The drawback of cumulative methods relative to online methods such as FTIR is that no time resolution is possible although much lower concentrations can be detected. Cumulative methods are also sometimes used for inorganic species, e.g. sampling of hydrogen halides using bubblers, and subsequent analysis of the sampling solution. These techniques are described in ISO 19701.[17]

A variety of cumulative methods are available. This section presents different methods based on which organic species are to be quantified.

Volatile organic compounds (VOC)

VOC can be measured by sampling of fire gases on commercially available Tenax® adsorbent tubes. The definition of VOC species using this method includes a range of non-polar or slightly polar small-medium sized hydrocarbon species with a molecular weight of approximately 75–200 amu. The adsorbents are subsequently analysed by thermal desorption and often high resolution gas chromatography with mass spectrometric detection. To capture even smaller gaseous species, commercially available activated carbon sampling tubes can be used. Relatively small sampling flows are used for these types of commercial adsorbent tubes.

An alternative sampling method developed for large-scale fire gas analysis,[27] uses a sampling set-up consisting of one tube containing XAD-2 (Amberlite XAD-2 resin, suitable for higher molecular weight species), a cooled U-tube (approx. −10 ºC) to condense and trap water, and one activated carbon adsorption tube cooled to −50 ºC to collect lower molecular weight species. In the method involving XAD-2 adsorbent and activated carbon, adsorption tubes with greater amounts of adsorption material can be used. A relatively high sampling flow can therefore be used without risking losses in the sampling. Chemical desorption, using suitable solvents, was used for this alternative sampling method. One advantage of this method is the possibility of performing multiple analyses on the same sample extract. A disadvantage of this method, however, is that the chemical solvent may interfere with the species to be quantified depending on the analysis method, or that the solvent may dilute the samples below the minimum detection limit. In the case of thermal desorption no dilution occurs and no interference can be experienced from a solvent. The main disadvantage to thermal desorption is that the entire sample is spent in a single analysis.

Aldehydes

Aldehydes present particular problems in the analysis of fire gases due to their high irritancy and their reactivity, aldehydes must be stabilised prior to analysis.

They can be sampled on Sep-pack® cartridges containing silica gel coated with 2,4-dinitrophenylhydrazine (DNPH). During sampling, they are therefore derivatised by reaction with DNPH in order to form hydrazones. The cartridges are subsequently extracted with acetonitrile and the collected hydrazones are separated by reversed-phase high performance liquid chromatography (HPLC) and can be analysed using, for example a UV/VIS detector for formaldehyde and acetaldehyde[28] or by atmospheric pressure chemical ionisation–mass spectrometry (APCI-MS) which is preferable for acrolein.[29]

Isocyanates

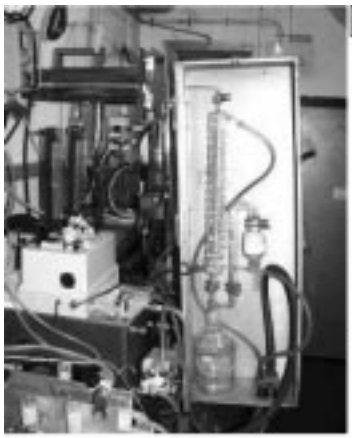
Isocyanate compounds (including isocyanates, aminoisocyanates and amines) can be sampled using an impinger-filter sampling system. The system samples airborne isocyanates in an impinger flask containing a reagent solution of DBA (di-*n*-butylamine) in toluene to form specific DBA–isocyanate derivatives. A glass fibre filter should be placed in series after the impinger. It has been shown that large particles (>1.5 μm) are retained in the impinger solution, whereas smaller particles (0.01–1.5 μm) pass through the impinger solution and are collected by the filter.[30] Analyses should be conducted separately for the impinger solution and the filters. Liquid chromatography–mass spectrometry (LC-MS) detection results in a highly sensitive measurement of isocyanates, equivalent to 0.0005 of the Swedish threshold limit value.

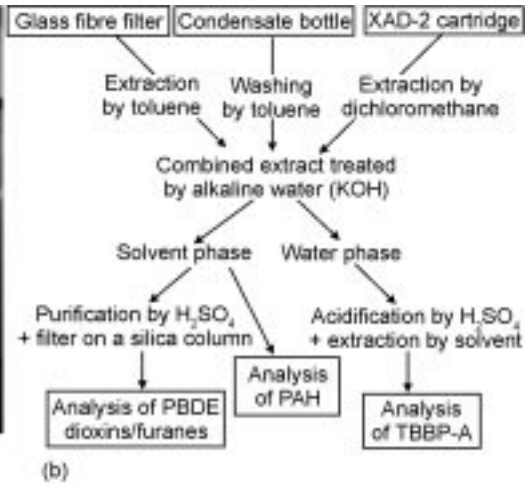
Semi-volatile/condensed phase organics

Organic compounds with high boiling points tend to be adsorbed on particles in smoke gases. Hence, it is of importance that the sampling method used collects a representative sample concerning particle size distribution. The diameter of the sample-probe tip should, together with the sampling flow, be adjusted to attain a sampling speed in the orifice of the tip that is equal to that of the gas speed in the smoke gas collector duct. In this manner isokinetic sampling can be achieved.

Large organic compounds, such as polycyclic aromatic hydrocarbons (PAHs) and chlorinated or brominated dibenzo-dioxins and furans (PCDDs/PCDFs and PBDDs/PBDFs), are best collected using a system with a large sampling volume. The sampling system can consist of a heated glass fibre filter, a water-cooled condenser with a condensate bottle, and a large adsorbent cartridge containing XAD-2. A sampling system mounted for analysis is shown in Fig. 13.3(a).

This type of sampling system is commonly used in Scandinavia and is in close agreement with the recommendation in EN 1948[31] for sampling of PAHs and PCDDs/PCDFs. The difference to the EN 1948 standard is that an adsorbent cartridge is used to replace the impinger bottles that are described in the standard. Such samples can also be analysed for the presence of PAH and certain





13.3 (a) Photograph of sampling system for PAHs and dioxins and (b) schematic of extraction and analysis of the dioxin sample.

flame retardants. A schematic of the extraction and analysis methodology for the analysis of dioxins, furans, PAH, PBDE and tetrabromo bis-phenol A (TBBP-A) is given in Fig. 13.3(b).

13.4 Large-scale testing

13.4.1 Standard tests and modifications thereof

Numerous important large-scale tests have been developed in recent decades. Although there are very few standard tests that include the measurement of toxic species as part of their basic protocol, several standard tests have been modified to include a certain degree of fire gas characterisation. Those tests that either presently include the measurement of certain toxic species or have often been modified to include some degree of fire gas characterisation are described in more detail here.

ISO 9705: Room corner test

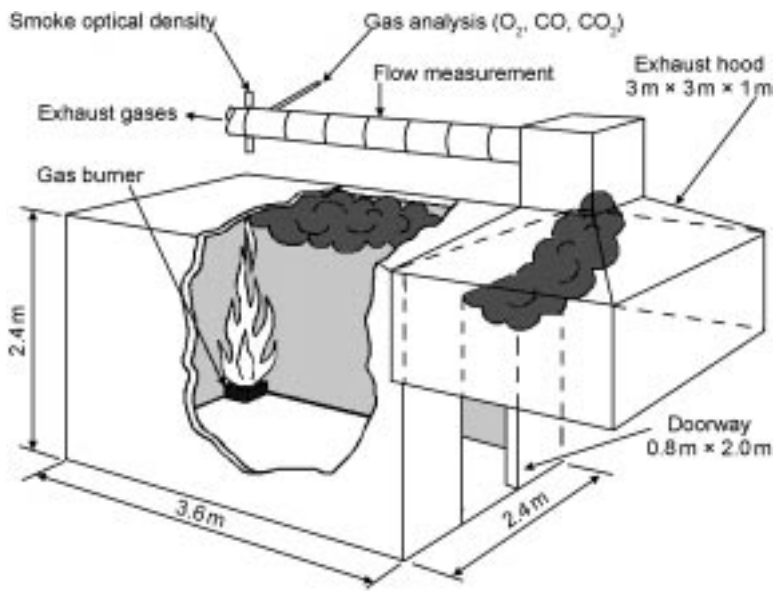
The ISO 9705 room corner test[32] is presently used as a reference scenario for the classification of building material within the Euroclass system and it has, over the years, been a reference standard for a number of important small-scale classification standards. The standard itself only contains provisions for the determination of oxygen, carbon monoxide and carbon dioxide for the determination of the heat release rate (HRR) and the determination of the optical density of the smoke emitted from the room. It does not contain provisions for the determination of other combustion products, but it has often been modified to

allow the determination of toxic species. Further, within the scope of the standard it is cited that while the method is intended to describe the fire behaviour of products under controlled laboratory conditions it may also be used as part of a fire hazard assessment which takes into account all pertinent factors for any particular end use. This could, therefore, include the measurement of toxic species.

The room is $3.6 \times 2.4 \times 2.4\,m^3$. It contains one opening, $0.8 \times 2.0\,m^2$, centrally located on one of the short walls. Ignition is performed in one of the back corners of the room and the test sample is typically used to line the walls and ceiling of the test room. All fire effluents are collected using a hood system and gaseous species and optical density are measured in the exhaust duct connected to the collection hood. The prescribed flow rate for the collection system is a minimum of $3.5\,m^3/s$. Figure 13.4 shows a schematic view of the ISO 9705 test set-up.

The standard test can be easily modified to include the measurement of many toxic species in the same position in the duct where the other gas measurements are conducted. In this manner one ensures that a representative sample is obtained, as laminar flow should have been established at this point. These gas samples can be used for fire gas characterisation using all of the methods described in Section 13.3 on the sampling and analysis of fire gases from large-scale fires.

Data on the chemical characterisation of fire effluents from standard ISO 9705 tests have been published in numerous cases, e.g. from tests conducted at the BRE in the UK.[33] Results from tests with furniture within the ISO 9705 room are



13.4 The large-scale experiment set-up used in the ISO 9705 room.

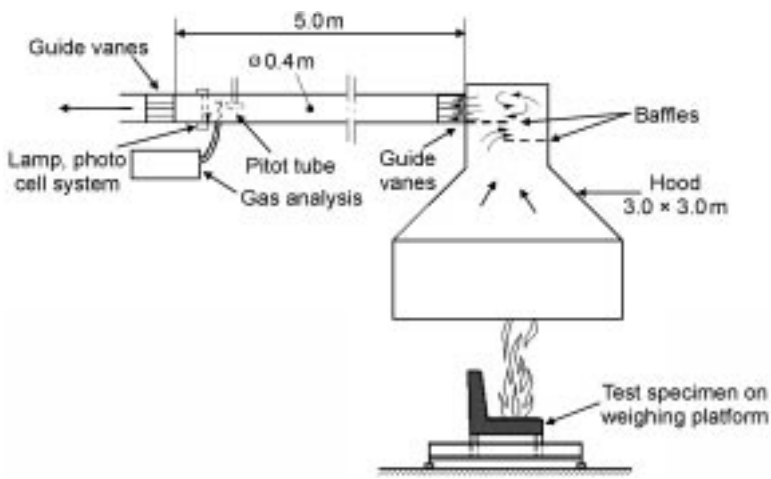
available from the EU-project CBUF.[34] Tests with pure polymers and chemicals placed in the ISO 9705 room, and with restriction of the opening to vary the ventilation conditions, are available from the TOXFIRE project and described in detail by Lönnermark and co-workers.[19,25,26] The ventilation condition can be easily modified by restricting the opening on the doorway to replicate under-ventilated flaming. TOXFIRE data are reported later in this chapter.

ISO 24473: open calorimeter

Open calorimeters are described in ISO 24473.[35] In this type of test the product is placed under a calorimeter hood and the fire effluents are collected by the hood, which makes measurement of toxic gases possible. ISO 24473 specifies a series of test methods that simulate a real-scale fire with a test object or group of objects under well-ventilated conditions. A range of different fire sizes can be studied depending on the scale of the equipment available.

The hood, duct and exhaust system are the basis of the calorimeter. The standard prescribes that the volume of the hood should be as small as possible to minimise time lag and smear-out of gas concentrations reaching the calorimeter analysis station. However, the inlet area is prescribed to be large enough to collect the plume gases without any losses.

The ISO 9705[32] system is given as an example in ISO 24473[35] of a full-scale calorimeter that has been standardised and is applicable as an open calorimeter. The ISO 9705 system is suitable for studying the burning behaviour of medium sized objects such as furniture and sections of construction with a maximum heat release of 1–2 MW. An application using the ISO 9705 hood system as an open calorimeter for studying the fire behaviour of furniture is shown in Fig. 13.5.



13.5 An example of an open calorimeter: the ISO 9705 hood system.

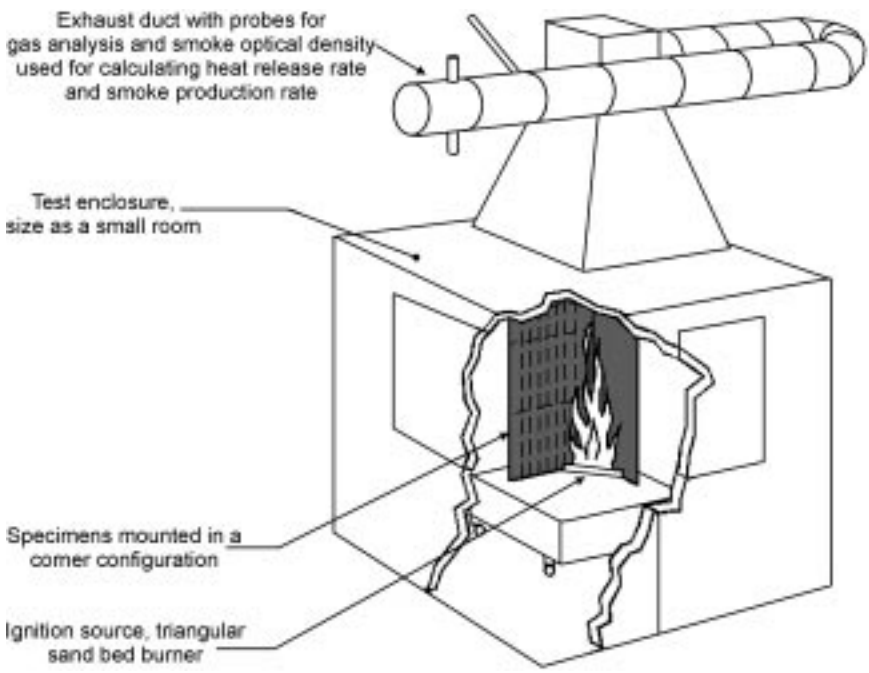
Samples of fire gases can be extracted a suitable distance from the hood as described for the ISO 9705 test.[32] These gas samples can be used for fire gas characterisation using all of the methods described in Section 13.3 concerning the sampling and analysis of fire gases. The test specimen can be placed on a balance to monitor the weight-loss during the test, thereby making it possible to calculate yields for selected periods of the test.

Larger calorimeters have been used for the collection of fire effluents from large-scale fire tests where the characterisation of fire gases was an object. Several examples are given in Section 13.5. The fire scenario in the open configuration is essentially well ventilated.

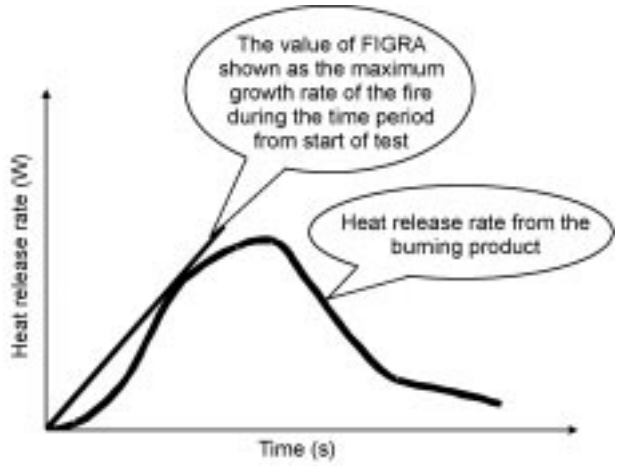
EN 13823: single burning item (SBI)

EN 13823,[36] the single burning item (SBI) test (Fig. 13.6), is the major test method for classification of lining products according to EN 13501-01.[1] EN 13823 evaluates the potential contribution of a lining product to the development of a fire, based on the fire scenario that a single item is burning in the corner of a room. The reference scenario for EN 13823 is the room corner test, ISO 9705.

The SBI test is an intermediate-scale method. Two test samples, 0.5 × 1.5 m^2 and 1.0 × 1.5 m^2, are mounted in a corner configuration where they are



13.6 Schematic figure of EN 13823, SBI.



13.7 Schematic figure explaining the FIGRA index.

exposed to a 30 kW gas flame ignition source. The smoke exhaust system of the SBI shall be capable of continuously extracting a normalised volume flow of 0.50–0.65 m^3/s. Measurement of fire growth, HRR, light obscuration and the smoke production rate (SPR), are the principal results from a test. The occurrence of burning droplets/particles and the maximum flame spread are also observed.

The index FIGRA, FIre Growth RAte, is used in EN 13823 to determine the Euroclass of the tested product. Euroclasses are defined in EN 13501-1. In this standard a product is classified based on its tendency to support fire growth. FIGRA is a measure of the maximum growth rate of the fire during an SBI test. A graphical presentation of the calculation principle for FIGRA is shown in Fig. 13.7. An additional classification for smoke is based on the index SMOGRA, SMOke Growth RAte. This index is calculated in a similar manner to FIGRA.

The EN 13823 SBI test[36] can be easily modified to include the measurement of toxic species in the same position in the duct where other gas measurements are conducted in the standard test (see Fig. 13.6). These gas samples can be used for fire gas characterisation using all of the methods described in Section 13.3 concerning the sampling and analysis of fire gases. The advantage of using this test for the measurement of toxic gases is that data concerning gas production can be assessed together with data concerning the product's reaction to fire, which is acquired from the normal test procedure. The main disadvantage with this method is that the SBI test only describes a well-ventilated fire, and that the dilution of the fire effluents in the exhaust duct is large during periods in the test with limited flame spread and burning.

IEC 60332-3-10/EN 50266-1: large-scale cable test

IEC 60332 specifies test methods for the assessment of flame spread of vertically mounted bunched wires or cables. IEC 60332-3-10[37] specifies the test apparatus for a large-scale test where mounted cables of 3.5 m length are evaluated.

CEN has adopted an equivalent test method which is labelled EN 50266-1.[38] This test standard bases classification on damaged length only which provides a coarse division of different cable fire performance at best. The proliferation of cables in buildings has led to the modification of this method to include not only damaged length but also important parameters such as HRR, SPR and TSP. In the supplementary test standard prEN 50399:2007[39] the measurement of these parameters is described, and FIGRA and SMOGRA are used as part of the product classification. Much of the developmental work behind the present design of the cable test is based on research conducted within the EU project FIPEC. For details concerning the background to the test and its development the reader is referred to the project report.[40]

The cables are mounted on a ladder which is vertically mounted inside a test chamber with the dimensions 2 m (l) × 1 m (w) × 4 m (h). A volumetric flow in the exhaust system in the range 0.7–2 m^3/s is recommended in prEN 50399:2007 depending on the exhaust duct diameter. A schematic of the test set-up is given in Fig. 13.8.

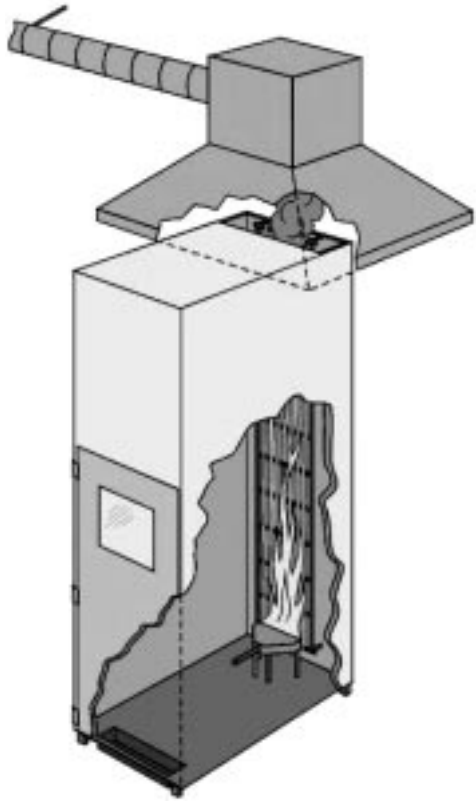
The test can be easily modified to include the measurement of many toxic species in the same position in the duct where gas measurements are conducted in the prEN 50399:2007 test. These gas samples can be used for fire gas characterisation using all of the methods described in Section 13.3 concerning the sampling and analysis of fire gases.

Results from the measurement of toxic gases in the IEC/EN large-scale cable test have been published by Hull *et al.*[41] Modified test where the ventilation to the cable fire was restricted and detailed characterisation of the fire effluents was made have been reported by Simonson *et al.*[42] and by Van Hees *et al.*[43]

IMO: fixed gaseous extinguishing agent systems test

The IMO's MSC/Circ.848[44] contains provisions for the measurement of certain toxic species. This is a large-scale test of the function of fixed gaseous extinguishing agent systems. The test is used both for halocarbon agent systems and for inert gas systems. In the first case 95% of the design concentration should be discharged in 10 s or less, and in the latter case the time should not exceed 120 s for 85% of the design concentration. One reason for the short discharge time required in the first case is the minimisation of toxic degradation products from the halocarbon agent.

The fire test method requires a series of four fire test scenarios. Test 1, which is performed at 83% of the design concentration of the extinguishing agent, is



13.8 Schematic view of the large-scale IEC/CEN cable test.

intended to evaluate new nozzles and distribution system equipment. Tests 2–4, which are performed at the design concentration, are intended to evaluate the extinguishing concentration of the agent.

The test enclosure should have a nominal volume of 100 m^3. The exterior of the test enclosure is shown in Fig. 13.9. Inside the test compartment, an engine mock-up is installed (see Fig. 13.10(a)), and both pool (see Fig. 13.10(b)), and spray fires are arranged using flammable liquids.

The guidelines require that the system must function safely regarding the toxicity of the agent and its decomposition products. It further states that provisions should be made to ensure that escape routes, control stations and other locations that require manning during a fire situation have hydrogen fluoride and hydrogen chloride concentrations below 5 ppm. Finally, concentrations of other products should be kept below hazardous levels.

Therefore, the test requires the analysis of decomposition products within the enclosure. Detailed analysis methods are not described in the guideline, but sampling with bubblers and subsequent analysis of trapped F^- and Cl^- from the

13.9 The exterior of the IMO test enclosure.

corresponding hydrogen halides is a possible method. FTIR has also been used for the analysis of decomposition products, and a fast scanning FTIR instrument with a small cell can also be suitable for measurement of firefighting agent concentration in tests with halocarbon agents.

Su *et al.*[45] used FTIR for measurement during fire suppression tests of two halon replacements. The 121 m^3 test enclosure used resembled the IMO test described above. The two agents tested were HFC-227ea and a mixture of HCFC-22, HCFC-124, HCFC-123 and D-limonene, referred to as HCFC Blend A. The FTIR measurements showed that toxic and corrosive degradation products were produced in the fire suppression tests. Species such as hydrogen fluoride and carbonyl fluoride (COF_2) were found from both agents, and hydrogen chloride was also found in the tests with HCFC Blend A. The

13.10 Inside the IMO test enclosure: (a) the engine mock-up and (b) a liquid pool-fire.

production of the degradation products increased with increasing fire size, extinguishing time and discharge time. The production decreased with increased agent concentration.

IMO: sprinkler test

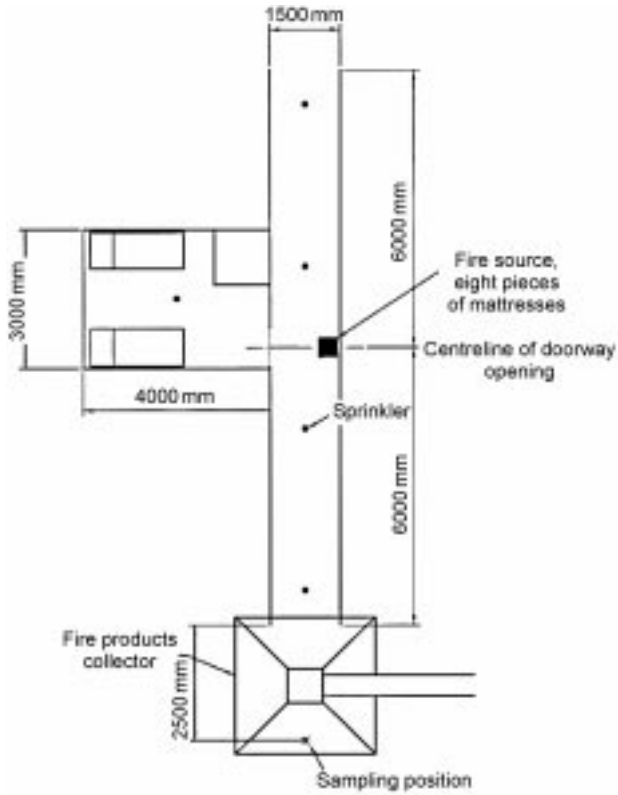
The IMO's Resolution A.800 (19) – appendix 2[46] was adopted at the 83rd meeting of the Maritime Safety Council (MSC) and tests the approval of sprinkler systems equivalent to that described in SOLAS Regulation II-2/12. This test contains no requirements concerning the measurement of toxic species. The test set-up can, however, be modified to allow the measurement of a variety of species depending on the aim of the measurements. In this test procedure polyurethane (PUR) mattresses are used as a fire source to produce heat and smoke for sprinkler activation.

In an investigation of exposure to isocyanates from fires with PUR material, measurements were conducted in connection with a series of sprinkler tests conducted according to IMO Resolution A.800(19). Analyses were made of the air close to the fire test at locations where laboratory staff were positioned, and also of urine samples from such staff members to determine whether they had increased levels of isocyanate metabolites in their body after the test series. Air sampling was conducted according to the procedures described in Section 13.3.3.

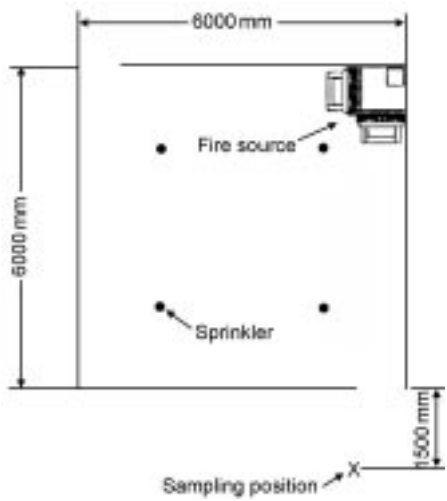
Measurements of isocyanates were conducted for two different test scenarios. In the first test scenario (test A) the fire source consisted of eight pieces of 400 $\times$ 400 $\times$ 76 mm^3 mattress sections, piled on top of each other. The fire source was placed in the middle of a 12 m long corridor. The sampling point for isocyanates was placed 2.5 m from one end of the corridor. There was no forced ventilation in the corridor during the test. The experimental set-up for test scenario A is shown in Fig. 13.11.

In the second test scenario (test B) the fire source consisted of a wood crib (6.9 kg spruce wood) and two large pieces of mattresses (each, 914 $\times$ 1016 $\times$ 76 mm^3) to simulate a piece of furniture. The fire source was placed in the corner of a larger cabin. The cabin had two 80 cm wide door openings and the sampling point for isocyanates was located outside one of these openings. The experimental set-up for test scenario B is shown in Fig. 13.12. The sprinklers were activated 1 min after ignition but did not extinguish the fire. There was no forced ventilation in the cabin during the fire test, although the cabin was vented from smoke gases with a fan after extinction.

Two test subjects carried sampling equipment during the tests and provided urine samples before and after the tests: the test leader who actively participated in all tests at the observation position during the tests and represented a high risk of exposure, and a person who spent most of the time away from direct exposure and represented a low risk of exposure.



13.11 Top view of test scenario A.



13.12 Top view of test scenario B.

The concentration of isocyanates and amines found in the air sample from test A was close to 10 ppb, the short-term hygienic limiting value for 5 min exposure in Sweden. In test B the concentration was almost five times higher. Isocyanic acid was the dominating species together with lower amounts of 2,4-toluene diisocyanate and 2,6-toluene diisocyanate. In test B where wood was included in the fire, the ratio of isocyanic acid to toluene diisocyanate was much higher indicating a more complete combustion chemistry in this test.

There were no traces of isocyanates found in either of the urine samples taken before the tests. In the samples taken after the test series low but detectable levels of 2,4-toluene di-isocyanate and 2,6-toluene di-isocyanate were found in the urine from the person representing the greatest risk for exposure. The conclusion from these measurements was that, although a protective mask was used most of the time during the tests, exposure to isocyanates was present for the high risk subject.

13.5 Specially designed tests

Standard fire tests are important for the classification of products and determination of their safety and utility on the marketplace. Such tests are specifically designed to optimise repeatability and reproducibility and are often a schematic representation of a standard fire scenario. They are seldom a faithful representation of a real-life fire scenario. Specially designed tests have the advantage that a specific fire scenario can be recreated and specific risk assessments can be conducted. Interesting information can be obtained pertaining to very specific scenarios but such information can be difficult to generalise and should be used with care.

This section contains some examples of test series with specially designed tests that have been conducted in recent years, their advantages and limitations. The number of specially designed tests that have been conducted internationally is considerable and this chapter cannot hope to provide meaningful information concerning all such tests. Owing to the availability of data to the authors, information is presented mainly from tests conducted by SP Technical Research Institute of Sweden. The information presented here has been chosen to be illustrative rather than exhaustive. The presentation of the various tests is based on the scenarios they have been designed to investigate: buildings, land vehicles, marine vehicles and industrial applications.

13.5.1 Buildings

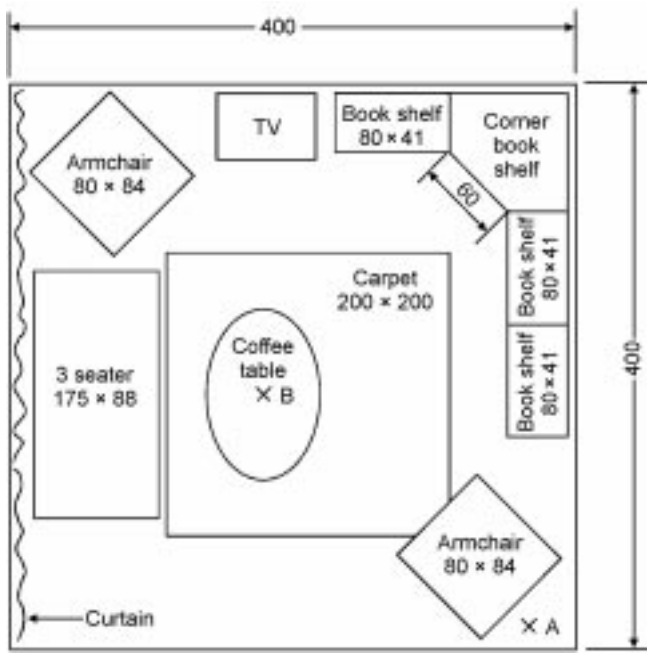
Fire in a furnished room

Fire incidents in private residences are common, but detailed quantitative data on the emissions from such fires are seldom reported. The data reported in the

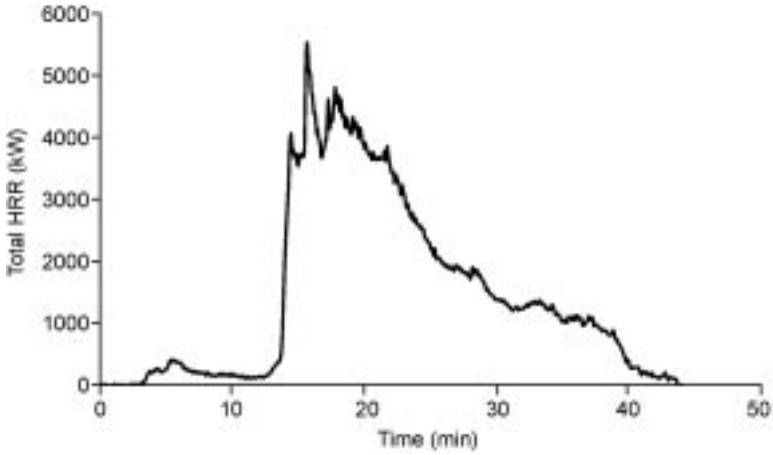
literature on emissions of, for example, PAH and PCDD/F are normally not related to the total emission but are reported as concentrations on contaminated surfaces from wipe sampling, or concentrations in collected ash samples.[47] A series of simulated room fires conducted at SP Technical Research Institute of Sweden contains unique information concerning emissions from room fires. In these tests the contents of the combustion gases were quantified in detail.[48] The room fire experiments were conducted as a part of a project aimed at studying the emissions from TV sets throughout their life cycle.[49] Three simulated room fires were conducted with a test room containing a typical domestic fuel load.

The measurement of the fire effluents included inorganic species such as carbon dioxide, carbon monoxide, hydrogen bromide, hydrogen chloride, hydrogen cyanide, NO_x and antimony (Sb), and various organic species such as VOCs, PAH, PCDD/F, PBDD/F and selected brominated flame retardant agents. The combustion gases leaving the room were quantitatively collected and the HRR from the room fire was measured.

The test room had a floor area of $4 \times 4\,m^2$ and the height to the ceiling was 2.4 m. The door opening was centrally located in the front wall with a height of 2.0 m and a width of 1.2 m. A schematic representation of the test room can be found in Fig. 13.13. Thermocouple trees were used to measure the temperature



13.13 Schematic representation of experimental layout for the room experiments. 'A' and 'B' denote thermocouple trees. The door was placed centrally in the front wall of the room (bottom of figure). All measurements in cm.



13.14 Total HRR measured in the room experiments.

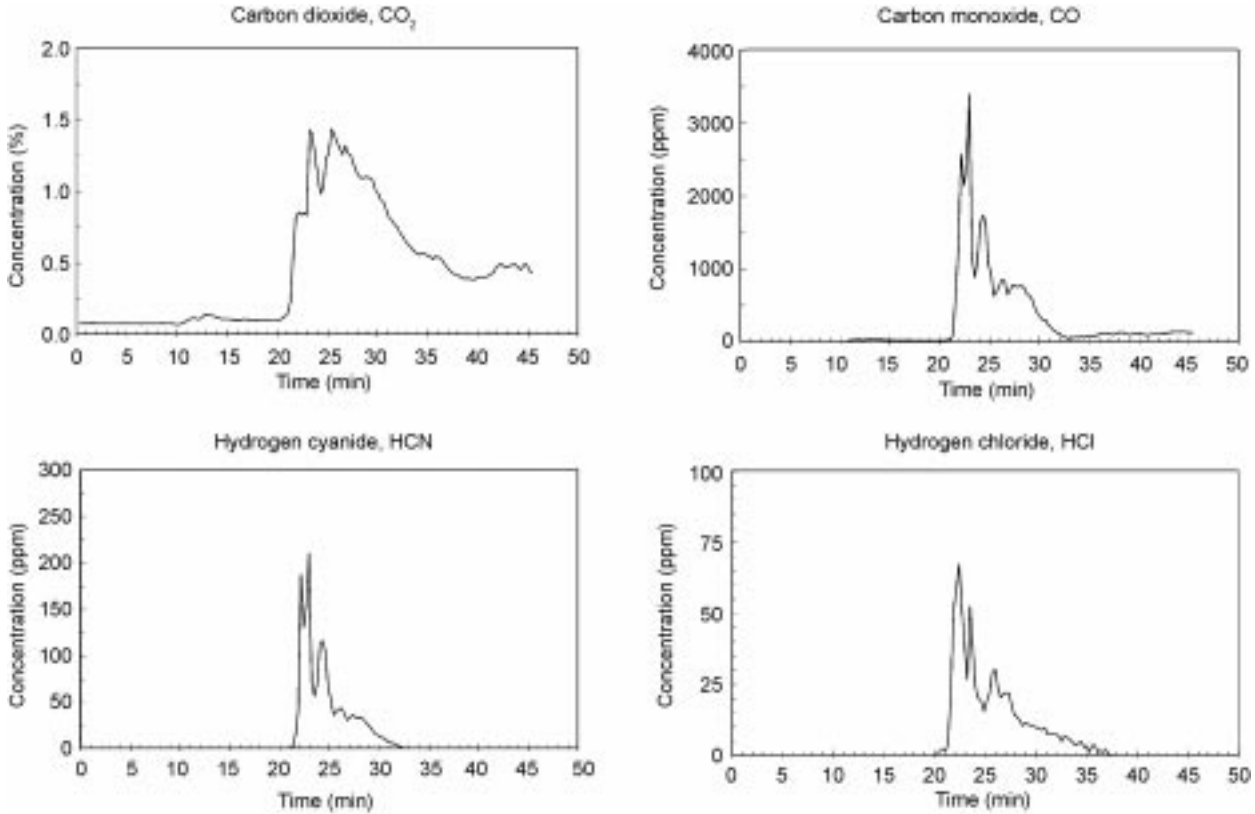
in the room during the fires. The material load used in the three room experiments was essentially equivalent except for the TV. The furniture was chosen as typical for Europe. The total weight of the materials was approximately 550 kg in each of the tests.

In all experiments the fire spread from the object first ignited to engulf the complete room which eventually led to flashover. The total heat release measured from the first room test conducted with a European TV set without flame retardants in the outer casing is shown in Fig. 13.14. Similar results are available for all three room experiments that were conducted within the fire life-cycle assessment TV case study. Full details can be found in the project publications.[48]

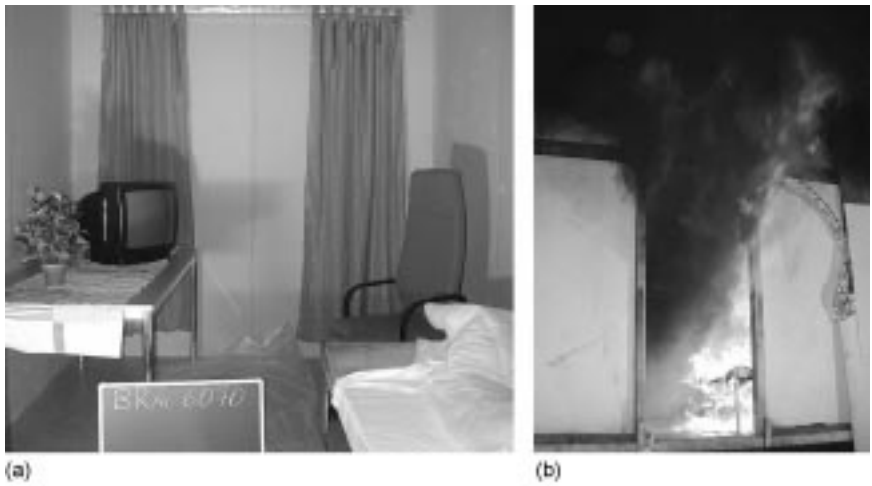
The detailed quantitative characterisation of the combustion gases from this series of room fires forms a unique source of emission data for fire incidents in buildings. Full emissions data are available in the project report.[49] A selection of toxic emissions is given in Fig. 13.15 for the same room experiment described in Fig. 13.14.

Investigation of hospital fire

Two patients were killed and several more were injured in an arson fire in a Swedish psychiatric detention clinic in 2003. Two of the victims were found in a room at the end of a long connecting corridor, quite a distance from the fire room. It was reported by the fire rescue services that the smoke had been exceptionally dense and had been a major obstacle for the firefighters. An investigation including a large-scale fire test was initiated to reconstruct the room fire and to identify toxic components in the fire effluents.[50,51]



13.15 Emissions data for a domestic room fire test.[49]

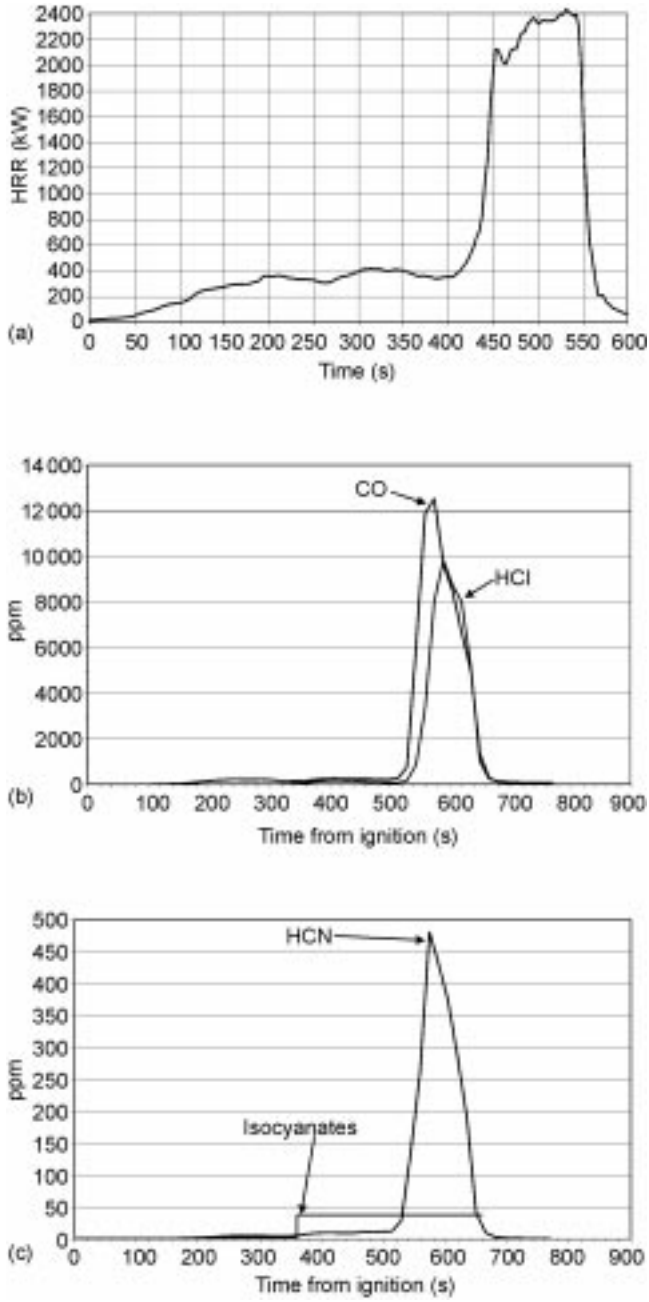


13.16 (a) Content of the test room arranged to reconstruct the clinic fire. (b) Flames exiting the test room at flashover.

The room used for the reconstruction had the dimensions of the ISO 9705 room, which was somewhat smaller than the real fire room. The room was furnished with a PVC floor covering, a bed with a mattress which was taken from the clinic, a TV, a desk, a piece of upholstered furniture and a set of curtains. The furniture was chosen to replicate conditions in the clinic at the time of the fire. The contents of the test room can be seen in Fig. 13.16(a). It should be noted that the actual room in the clinic contained additional combustible objects, but the experiment was simplified to include those objects thought to have been the major sources of heat and smoke. The door to the corridor was open in the real fire, but a difference between the experiment and real fire was that a window was broken at some point during the real fire. In the experiment, only the door of the test room was open.

The experiment was started by ignition of the mattress and the TV simultaneously using wood-cribs as ignition sources. The door opening of the room during flashover is shown in Fig. 13.16(b). Note the sampling line at the upper right hand side of the door. Fire effluents were sampled using a probe that was traversing the upper part of the door opening.

Some selected results from the measurements in the reconstruction test are shown in Fig. 13.17. Figure 13.17(a) shows the HRR, Fig. 13.17(b) the concentration profiles of carbon monoxide and hydrogen chloride which were both measured continuously using FTIR, and Fig. 13.17(c) the concentration profile of hydrogen cyanide, also measured by FTIR, and for the concentration of isocyanates. Note that isocyanates were measured using cumulative sampling. The average measured concentration for the measurement period is shown.



13.17 (a) Measured total HRR; (b) concentration profiles of carbon monoxide and hydrogen chloride; (c) concentration profile of hydrogen chloride and average concentration of isocyanates.

The reconstruction indicated a highly flammable mattress provided sufficient heat and radiation to ignite the PVC flooring material which then became the main source of heat and smoke. Analysis of soot from the fire site and measurements during the reconstruction showed that the fire smoke contained large amounts of irritants (hydrogen chloride and isocyanates) that might have had an important impact in the tragic outcome. Comparison of the toxicity of smoke gases produced during the reconstruction suggested that irritants in the fire smoke were as dangerous as, or more dangerous than, the common asphyxiant gases present, carbon monoxide and hydrogen cyanide.

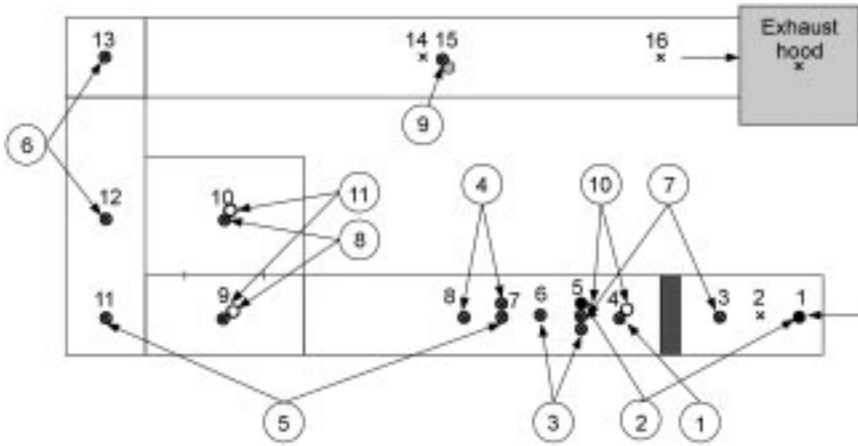
Spread of fire effluents in a corridor

A series of fire tests was conducted in a full-scale corridor designed specifically for these tests. Different types of cable were used as the fire source under a variety of ventilation conditions. The purpose of the tests was to investigate the conditions, including gas concentrations, smoke and temperatures, inside a full scale corridor during a fire. The results of the tests were later used as validation for computational fluid dynamics (CFD) modelling.[52,53]

The tests were conducted indoors in the large fire test hall of SP Technical Research Institute. Inside the fire hall, a U-shaped corridor with a total length of 44.6 m (centreline) was constructed. The nominal inner height of the corridor was 2.4 m. The nominal inner width of the corridor was 2.0 m. At the inner corner, between the first and the second corridor, a room was connected to the corridor through a $2 \times 0.4\,m^2$ opening at ceiling level. The room had inner floor dimensions of $3.0 \times 4.0\,m^2$ and the same ceiling height as the corridor. The corridor also had four soffits installed at different locations, extending 0.4 m from the ceiling. The fire source, a cable installation, was located about 3.9 m from the 'inlet end' of the corridor. The inlet gable had a $1\,m^2$ opening situated at floor level. In order to obtain a restricted air flow, some tests were performed with this opening closed and completely sealed. The corridor exit was positioned below a calorimeter system, making it possible to measure the heat release rate using oxygen depletion calorimetry.

In order to record the fire development and the generation and transportation of smoke gases, extensive measurements were made along the corridor during each test. Gas analyses were performed at 13 positions along the corridor and in general, the sampling location was 0.2 m below the ceiling. Concentrations of carbon monoxide, carbon dioxide, hydrogen chloride and oxygen were measured at a number of locations. In addition, smoke obscuration and temperatures were measured. The layout of the corridor and the principal instrument arrangement are shown in Fig. 13.18.

Owing to the large number of sampling locations, most gas analysis instruments were connected to two sampling probes at two different positions (not the FTIR). A remote-controlled valve was used to switch the gas sampling between

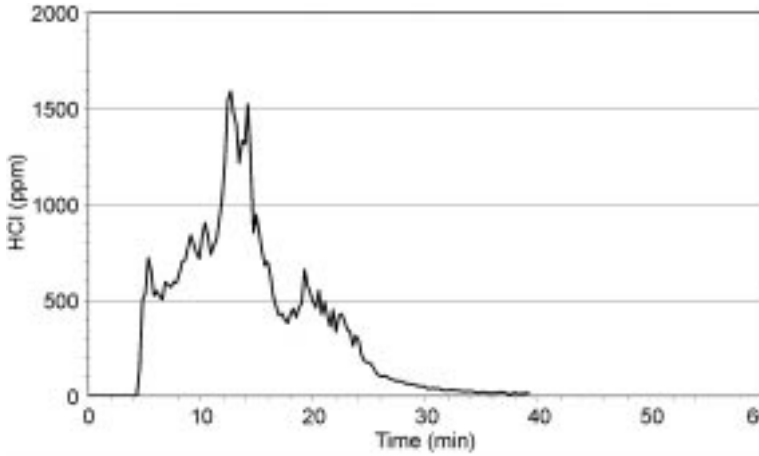


13.18 Schematic sketch of the arrangement of gas analysis instruments and positions (×) for carbon monoxide (black), carbon dioxide (grey) and oxygen (white) measurements.

the probes nominally every 30 s. The valves were controlled by an electric signal allowing two common sampling sequences for all instruments.

Measurements of carbon dioxide, carbon monoxide and hydrogen chloride were made using online FTIR at sampling position 4 (see Section 13.3.2 for sampling procedure for the FTIR). The average concentration of hydrogen chloride was further determined at sampling positions 4 and 15 using impinger bottles. Smoke gases were sampled via a heated filter and a short heated sampling line (1.5 m) to an impinger bottle with a second bottle connected in series. Both the filter and the gas sampling line were heated to 180 ºC. A controlled volume of smoke gases was sampled using a diaphragm pump and the air was dried before the volume was measured using a calibrated diaphragm gas meter. The impinger bottles contained a sodium hydroxide solution and the total content of chlorine captured in each bottle was determined after the tests using ion chromatography (HPIC). The filters for the FTIR and the impinger bottles were analysed separately for any captured HCl in all tests containing PVC cables. Further, the sampling lines to the impinger bottles were washed with sodium hydroxide solution and analysed for chlorine.

The results from one of the tests, where a PVC cable was used as the fire source and the ventilation was restricted (test no. 9 in the test series), is presented in Fig. 13.19 as an example of the type of results obtained from each test. The results given in Tables 13.1 and 13.2 show that the agreement between the FTIR and the impinger bottle measurement in position 4 was fairly good in this test. It further shows that it was necessary to correct the results for losses in filters, as these were significant.



13.19 Concentration profile measured by FTIR in sampling position 4.

Table 13.1 Results for hydrogen chloride from impinger bottles including filter (sampling time 3–26 min)

Gas washing bottles	Sampled volume (l)	Cl^-, bottle A (mg)	Cl^-, bottle B (mg)	Cl^-, filter (mg)	Cl^-, total (mg)	Resulting HCl conc. in smoke gases (ppm)
Pos. 4	43.3	44	< 0.05	5.9	49.9	795
Pos.15	36.6	18	< 0.05	5.6	23.6	445

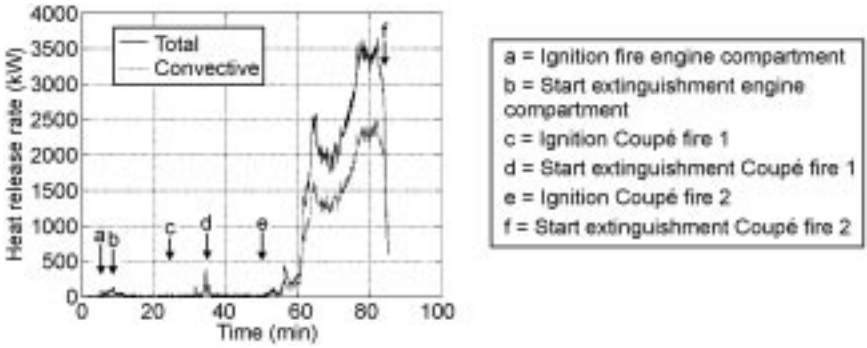
Table 13.2 Results for hydrogen chloride from FTIR including filter (3–26 min)

FTIR	Cl^-, filter (mg)	Volume trough FTIR filter (l)	Calculated HCl lost in filter (ppm)	Average HCl from FTIR (ppm)	Resulting HCl conc. in smoke gases from FTIR including filter (ppm)
Pos. 4	6.1	92	46	580	627

13.5.2 Land vehicles

Automobile fire

Automobile fires are numerous and there is a need for information on the emissions from such fires, both for incident planning and for estimates of total emissions. When fires occur in enclosures such as car parks or tunnels such



13.20 Measured heat release during the different phases of the full-scale test.

emissions are much more dangerous. To gain more knowledge of the emissions from automobile fires, experimental work was commissioned by the Swedish Rescue Services Agency (SRV)[54] and conducted at SP Technical Research Institute of Sweden.

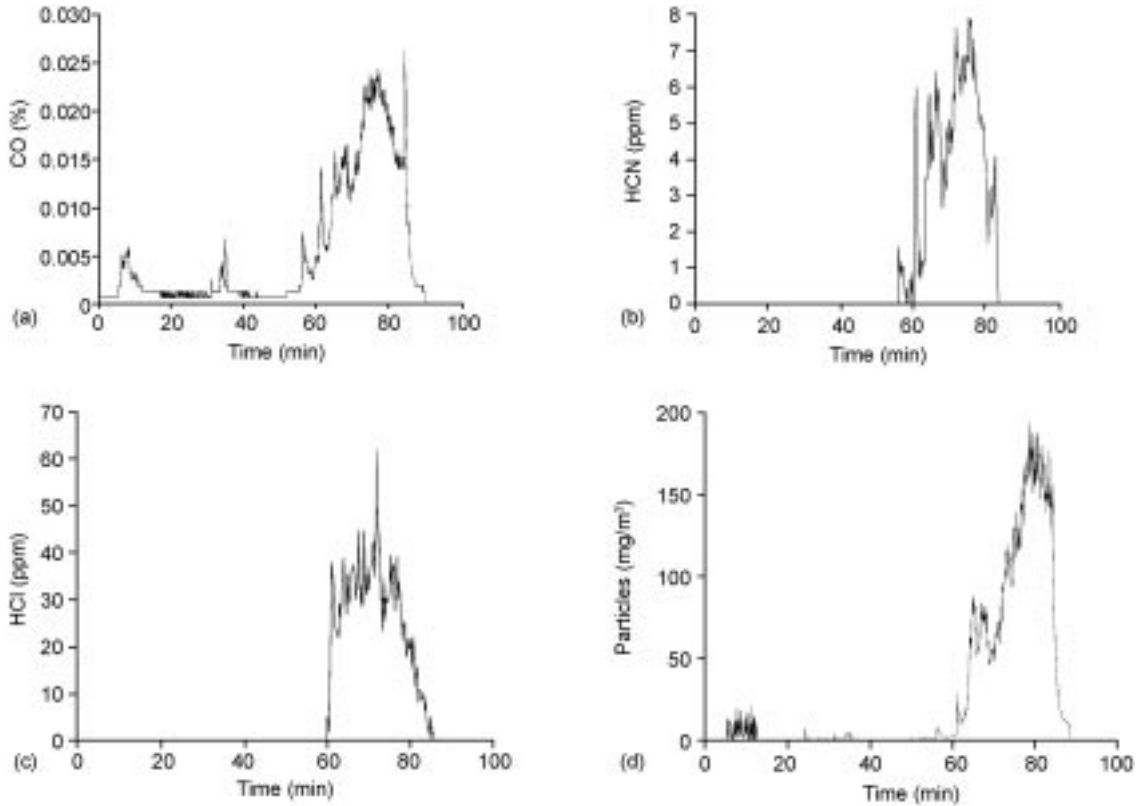
The work included an experimental series where a complete automobile was burned in a full-scale fire test, and detailed measurements were made on the emissions from the fire, including the characterisation of gas phase components, particulates and run-off water from extinguishing activities. The automobile was placed under the hood of a large calorimeter in which the fire effluents were quantitatively collected. Different types of fires were investigated in the same experiment with the automobile and the experiment ended with a full-scale fire. The heat release measured from the fire is given in Fig. 13.20.

The quantitative analysis of the smoke gases from the experiment showed that emissions with a chronic toxic effect on humans or with a potentially negative impact on the environment were produced in significant quantities. These emissions included hydrogen chloride, sulphur dioxide, volatile organics, PAHs and PCDDs/PCDFs. Analysis of run-off water indicated that it was severely contaminated, containing elevated levels of both organic compounds and metals.

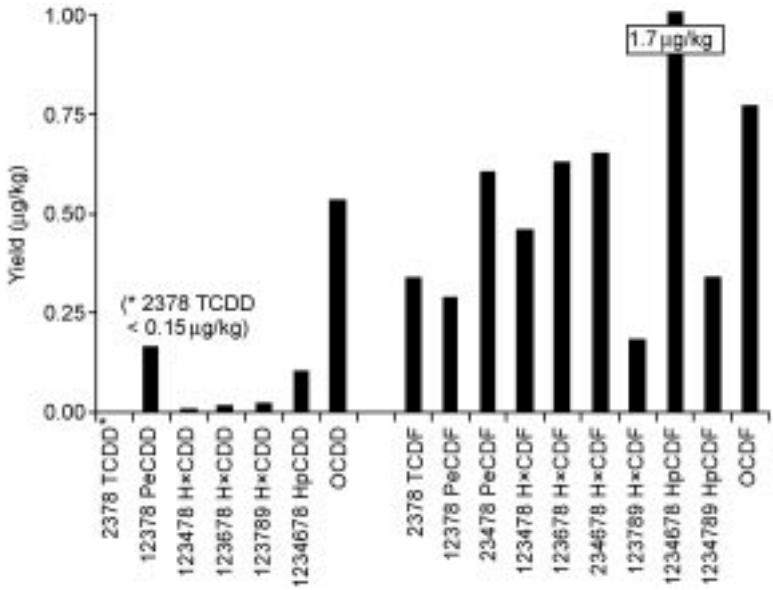
FTIR was used for the measurement of smaller inorganic gas species in the duct (see Fig. 13.21(a–c)). Particulate concentration was measured continuously using ELPI in the duct (see Fig. 13.21(d)). It can be seen that hydrogen chloride was produced at the earlier stages of the full-scale fire and that the particle production coincided with the peak in HRR.

Chlorinated dioxins were found from the analysis of collected fire effluents. The total concentration found from the fire test was 87.0 μg TCDD (2,3,7,8-tetrachlorodibenzodioxin) I-TEQ*, and expressed as yield, 0.8 μg/kg TCDD I-

*I-TEQ refers to the International Toxic Equivalent Scheme set up by NATO.



13.21 Concentration profiles of (a) carbon monoxide, (b) hydrogen cyanide, (c) hydrogen chloride, all measured with FTIR and (d) mass concentration of particles measured with ELPI.



13.22 Individually quantified chlorinated dioxins, PCDDs/PCDFs.

TEQ (see Fig. 13.22). Wichmann *et al.*[55] have previously determined the total emissions of chlorinated dioxins from automobile fires to 32 μg TCDD I-TEQ and 44 μg TCDD I-TEQ, from experiments with two different automobiles in tunnel fire experiments.

Bus fire

Fires involving modern buses and coaches can have serious consequences. Such fires have led to the loss of lives in several countries recently.[56] The Swedish and Norwegian road transport authorities have evaluated and examined the fire properties of materials common in modern buses in a research project that started during 2005.[57] The project included a full-scale fire experiment with a complete modern coach, in which measurements of toxic gases were made.

The fire test was divided into three parts using the same coach placed under a large calorimeter in the main fire test hall at SP Fire Technology. The first part of the test involved fire detection and fire resistance during fuel leakage and the resulting fire in the engine compartment. The second phase involved fire resistance of windows exposed to a fire involving the tyres and wheel housing. The third and last phase involved the measurement of toxic gases using FTIR, when the fire was initiated in the rear luggage compartment. The test was conducted to evaluate the production and spread of toxic gases, smoke spread and gas temperatures during a fully developed fire.

13.23 (a) The interior of the coach 3 min after ignition and (b) the exterior of the coach.

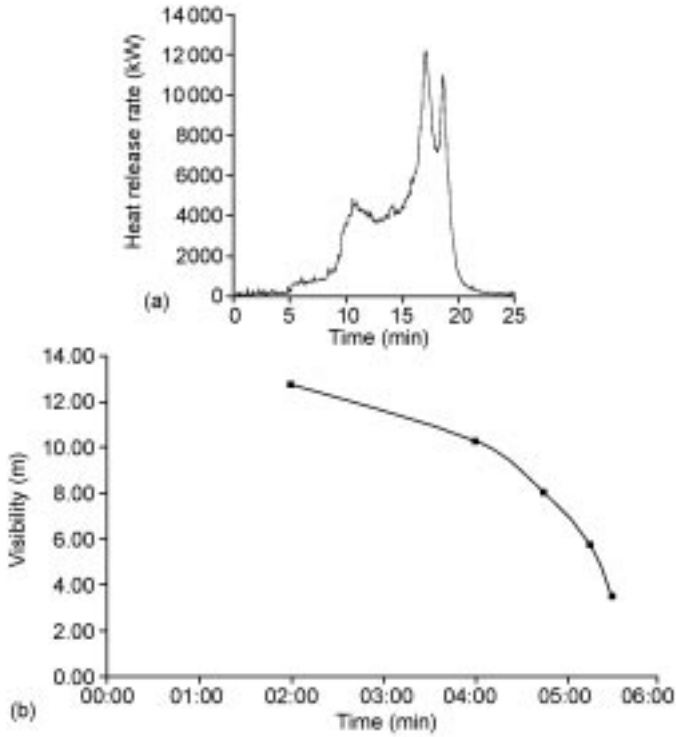
The sampling point for the FTIR (single-hole probe) was located in the back of the compartment at head height for a person standing in the passage between the two rows of seats. The sampling point was at a height between mark 1 and mark 2 in front of the rear sign post in Fig. 13.23(a), which shows the interior of the coach 3 min after initiation of the fire. Fire effluents were sampled and transported to the FTIR using a long, heated PTFE sampling line. The exterior of the coach is shown in Fig. 13.23(b).

The fire in the rear luggage compartment increased steadily during the first 10 min of the test and the interior of the coach was gradually filled with smoke. The total heat release from the fire is shown in Fig. 13.24(a) and the measured visibility in the compartment is shown in Fig. 13.24(b). It can be seen that the visibility quickly decreased to a few metres after 5–6 min. Toxic gases were detected around 4 min, and the concentrations increased rapidly at about 5 min to reach incapacitating levels. The measured concentrations of the asphyxiant gases carbon monoxide and hydrogen cyanide are shown in Fig. 13.25(a) and (b), before the fire had grown significantly.

The main conclusion from the fire test with the coach was that incapacitating conditions were reached in the coach after 4–5 min. This would be sufficient time for evacuation during normal conditions, but in a post-crash situation where the bus may have been overturned, this could have been disastrous. It was further concluded that the fast fire growth of the bus would have led to danger for people in a tunnel or an underground station.

Simulated vehicle fire in road tunnel

Fires in European tunnels have clearly shown the risks and consequences of tunnel fires with large vehicles. In the Mont Blanc tunnel fire in 1999, for example, over 20 lorries were destroyed, and several people lost their lives. Knowledge of the growth and spread of fires in lorries has been very limited. To

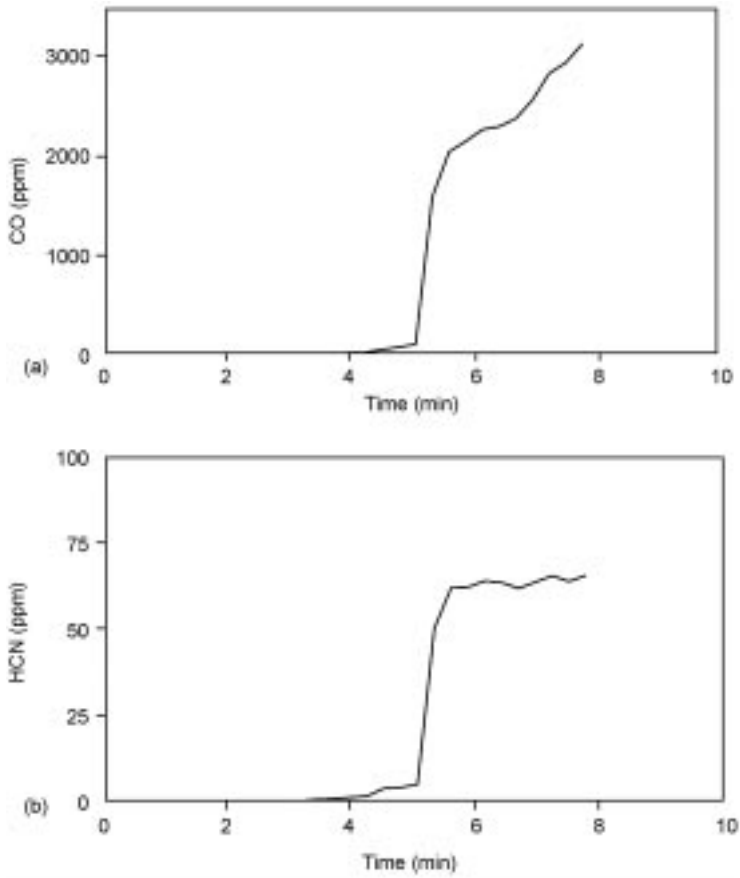


13.24 (a) Total heat release from the bus fire and (b) measured visibility in the compartment during the test.

gain more knowledge in this area, a research project was initiated within the framework of Swedish national and European research programmes on tunnel safety. Comprehensive large-scale fire tests were conducted in 2003 in the abandoned Runehamar road tunnel in Norway. The test series included semi-trailer fires similar to the size of the recent real fire incidents. The purpose of the fire tests was to measure the rate of fire growth of various types of lorries cargoes and to investigate the heat exposure to the tunnel linings. The purpose was also to obtain information to assist a new approach to fighting fires in tunnels. The measurement of selected toxic gas components was conducted during these tests.

The results from the test series were first reported at the International Symposium on Catastrophic Tunnel Fires, held in Borås in November 2003.[58] Lönnermark and Ingason have later published detailed accounts of the temperatures[59] and heat release rates[60] measured in the test series. Further, fractions of incapacitating doses for asphyxiant gases were determined as part of Lönnermark's PhD thesis.[61]

The Runehamar tests were run using a mock-up of a heavy goods vehicle (HGV) trailer as the fire load. Four tests were run. Full details of the tests are



13.25 Concentration profiles in the compartment measured with FTIR: (a) carbon monoxide and (b) hydrogen cyanide.

provided in the documentation cited above. In one test (T2), the fire load consisted of wood pallets and PUR mattresses. The total mass of combustible material was 6920 kg. The Runehamar tunnel has a length of 1600 m, a height of 6 m and a width of 9 m. The HGV mock-up was placed 563 m from the west entrance, and there was an initial (forced) longitudinal ventilation flow of ~3 m/s in the east-to-west direction. Figure 13.26 shows the burning load on the HGV mock-up in one of the tests.

Measurements were made at different heights, at a height of 2.9 m from the tunnel floor in the tunnel 105 m from the west entrance, and included: temperatures, velocities, oxygen, carbon dioxide, carbon monoxide and hydrogen cyanide. The data were used to calculate the fractional effective dose (FED) of asphyxiant gases.[62] The HCN concentrations were considered more uncertain and are treated separately below.[61]

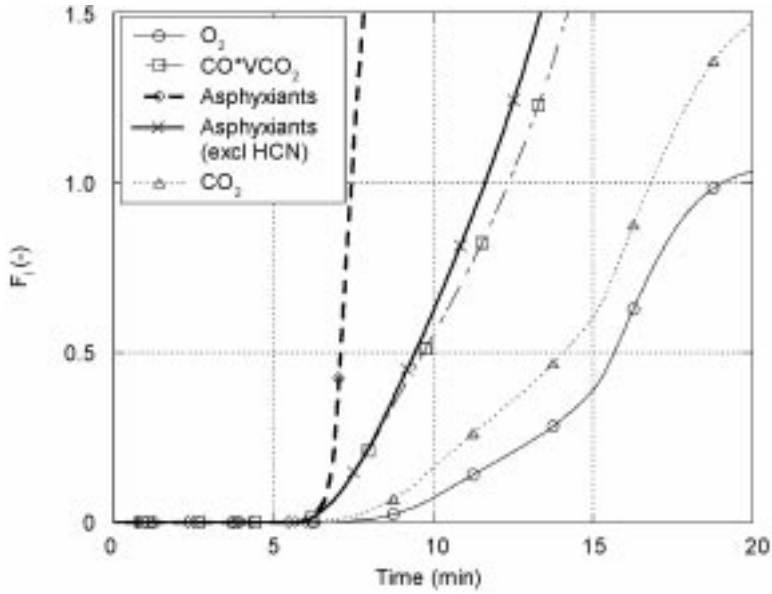
13.26 Burning load on HGV mock-up in one of the Runehamar tests.

In tests, the peak HRR was measured to 157 MW, approximately 14 min after initiation of the HGV fire. Peak values were: $CO_2 = 9.2\%$, $CO = 2430$ ppm, $HCN = 218$ ppm, and $O_2 = 8.6\%$. The effects of asphyxiant gases on a person exposed to the fire effluents at the position 458 m from the fire source, was estimated using the model by Purser.[63] The resulting FED for incapacitation (F_I) acquired during the course of the fire tests (T2) is given in Fig. 13.27, where the timescale starts from the time of ignition of the HGV mock-up. This shows the predicted time of incapacitation for each of the components listed above, and the cumulative effect of CO, HCN, $CO_2 + O_2$ depletion (as asphyxiants), as the time when $F_I = 1$.

In tests, the conditions in the tunnel at the measurement position, become incapacitating ($F_I = 1$) from the effects of asphyxiant gases only a few minutes after ignition. The contribution to the asphyxiant effect from hydrogen cyanide decreases the time for incapacitation by approximately 5 min. Note that a person remaining at that position in the tunnel would have been incapacitated long before the fire had reached its peak.

Fire in railway carriages

The FIRESTARR project was conducted to support CEN work on a European standard with requirements on the fire behaviour of materials and components of

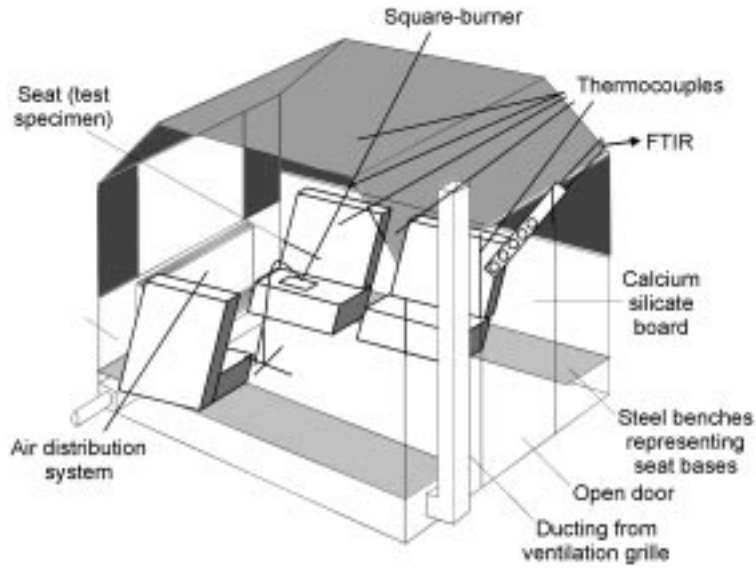


13.27 Fraction of an incapacitating dose for asphyxiant gases analysed in the Runehamar tunnel.[61]

passenger trains. The programme included a series of tests to evaluate, in large and real scale, the fire behaviour of a representative range of furniture products used on European trains. As indicated by statistical research on fires in trains and reports on the most frequent fire scenario in railway vehicles, the seats represents the most dangerous part of the compartment; and this was the furniture product selected for evaluation within the project. Details of the project are available.[64]

The large-scale tests included the assessment of ignitability, spread of flame, heat release, smoke generation and toxic gas species generation, as well as the evaluation of the tenability limits which are directly related to a fire's effect on passengers. Real-scale tests were carried out taking into account the end use conditions of material in a carriage. A range of different seats were tested and the test set-up used is shown in Fig. 13.28.

The tests were conducted with different degrees of 'vandalism', i.e., of exposure of the seating material, beginning with the seat not vandalised, extending the degree of vandalism in four stages. Measurements of toxic gases were made with FTIR sampling from one probe placed in the exhaust duct, collecting all effluents from the carriage, and from one probe placed at nose level in the door of the carriage. Full details of the test results have not been published in the open literature but they have provided the basis for modern European test methods and requirements for trains.



13.28 Layout of full-scale train compartment tests in the FIRESTARR project.

13.5.3 Marine vehicles

Cabin fire in lightweight constructed ship

The use of lightweight construction materials for shipbuilding is an important topic internationally. This use was previously prohibited by the SOLAS requirement for 'steel or equivalent' construction material, but has been made possible through the new (2002) Regulation 17 on 'Alternative design and arrangements'. An equivalent safety level has to be demonstrated and a series of large-scale fire experiments was made with a real-scale passenger cabin to evaluate the performance of a composite superstructure conducted in 2007. The test series is described in detail by Arvidson *et al.*[65]

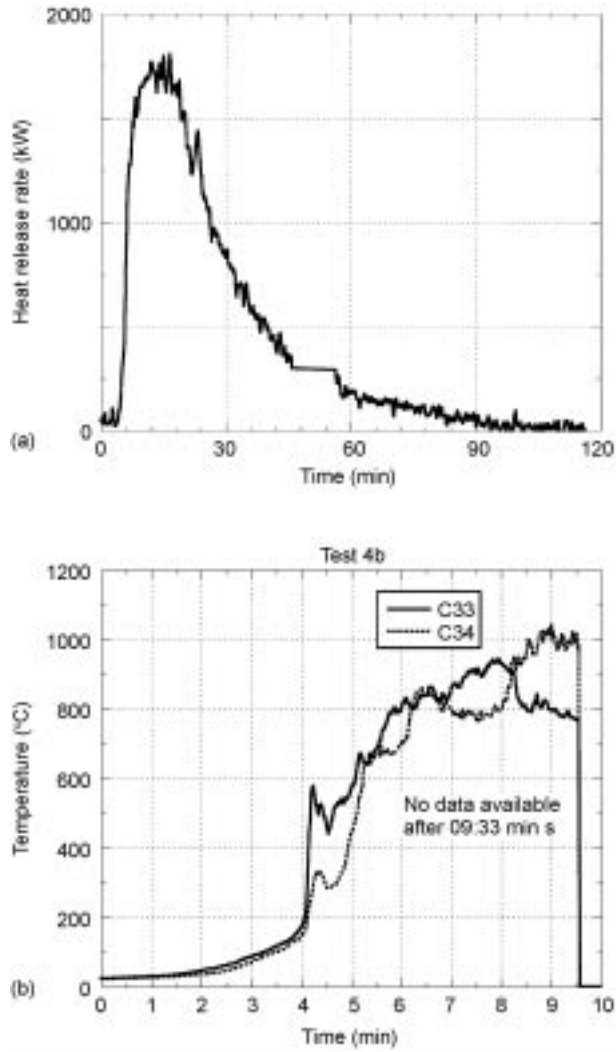
The results of the test series show that the composite structure can withstand more than 60 min of uncontrolled cabin fire without critical damage, and that an outside drencher system is efficient in preventing fires from propagating through broken windows. The tests also show that normal approved cabin interiors can produce a very severe fire in a short time if all safety systems malfunction. One of the tests, which include the measurement of toxic gas components of the fire effluents leaving the cabin, is described here.

Two cabins and a corridor were constructed within a section of fire insulated PVC + GFRP (glass fibre reinforced polyester) composite decks and bulkhead. They were constructed using realistic designs and materials. Each of the cabins measured 4300 mm (l) × 2995 mm (w). The ceiling height was 2100 mm and the

corresponding volume of each of the cabins was 27 m^3. The interior of the cabins consisted of the following items: two bunk beds, mattresses and bedding material associated with the bunk beds, a small table and a chair, a hat rack, windows curtains, light fixtures, personal belongings and luggage (PVC suitcases). The experiments were conducted to investigate the effect of ventilation, fire detection and sprinkler systems.

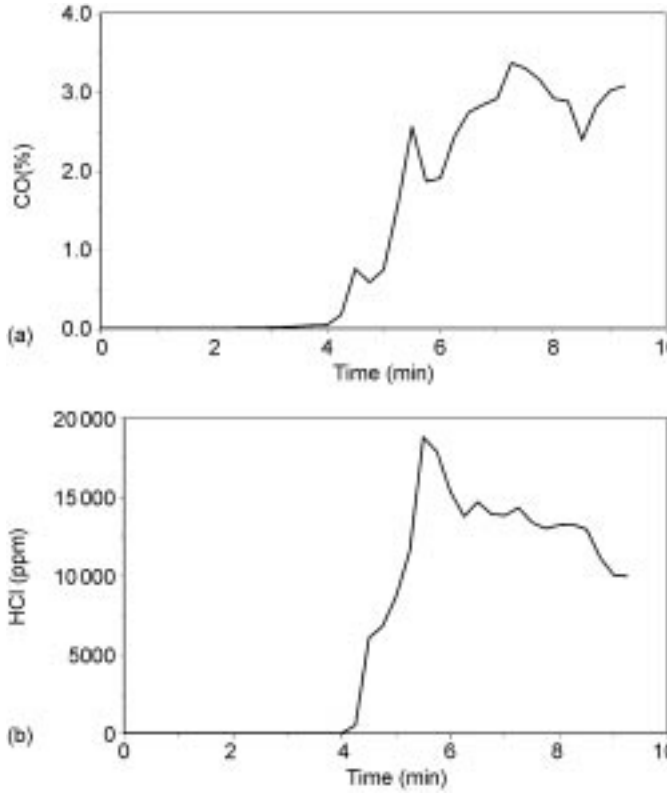
The fire test described here was set in the cabin closest to the opening of the corridor, and the door to the cabin was fully open. Windows were closed and both the cabin sprinkler nozzles and the corridor nozzles were disconnected. During this test, an FTIR was used to analyse the fire effluents leaving the cabin. A sampling probe was placed across the corridor doorway, diagonally over the top 100 mm of the opening. The multi-hole probe was designed to sample uniformly over the 100 mm height. The FTIR measurement continued for approximately 9.5 min into the test, approximately 4 min into the flashover phase, where the sampling filter and pump had to be removed due to strong radiative heat. The opening of the corridor with the sampling line, and protected probe and filter units, are shown in Fig. 13.29. The fire in the cabin has already reached flashover at the time this photograph was taken.

13.29 Opening of corridor instrumented with sampling probe for FTIR during full-scale cabin fire.



13.30 Data from full-scale cabin fire: (a) HRR and (b) temperatures close to the ceiling in the cabin.

The heat release measured from the fire and gas temperatures close to the ceiling in the cabin is shown in Fig. 13.30. Measured gas concentrations from the corridor opening are shown in Fig. 13.31. It can be seen from the heat release and the cabin temperatures in Fig. 13.31 that flashover was reached after about 5 min. The concentration profile of carbon monoxide is increasing steeply until the occurrence of flashover and then levels out. The concentration of hydrogen chloride peaks just after flashover and then declines slowly, this is probably because all interior PVC foil was consumed a short time after flashover and the



13.31 Concentration profiles from FTIR measurement in the corridor opening: (a) carbon monoxide and (b) hydrogen chloride.

floor carpet starts burning soon after flashover. The wall foil was very thin, but the total amount in the cabin was almost 9 kg, the floor represented 38 kg of PVC carpet. The measured maximum of hydrogen chloride at 5 min was almost 20 000 ppm which means immediate incapacitation if inhaled. Concentrations of hydrogen cyanide and nitric oxide were also recorded but the spectral interference was too large to make accurate interpretations of the spectra after 5 min. However, both hydrogen cyanide and nitric oxide reached above 100 ppm within 5 min which is close to the limit for incapacitation. Maxima were probably significantly higher and data indicate that hydrogen cyanide might have reached levels above 3000 ppm.

13.5.4 Industrial applications

Fire in storage of chemicals and polymers

In the European project Guidelines for Management of Fires in Chemical Warehouses, TOXFIRE (1993-1996), SP Technical Research Institute of

Sweden conducted controlled large-scale combustion experiments with fuel amounts in the 100 kg range.[19] A series of indoor, controlled large-scale combustion experiments was conducted with material with different chemical composition. The degree of ventilation was varied from well ventilated to under-ventilated, and was determined using a phi meter. In addition to measuring the traditional fire-related parameters, extensive chemical characterisation of the smoke gases was carried out. Two series of tests were performed, where both the scale and the experimental configuration were varied.

Five different materials were included in the large-scale tests. To obtain reasonable complexity in the composition of the smoke gases, the elemental composition, in addition to just carbon–hydrogen–oxygen, included nitrogen, sulphur and/or chlorine. The materials studied include two polymers, polypropylene and nylon-6,6 (Ny); two crystalline organic compounds, tetramethylthiuram monosulphide and 4-chloro-3-nitrobenzoic acid; and a fairly volatile liquid, chlorobenzene.

Four individual experiments were performed in a modified ISO 9705 room with each of the materials. The fuel was put in a pan in the room, and the ventilation conditions were varied by restricting the size of the door opening. The weight loss of the fuel was monitored throughout the tests. The restricted door opening of the ISO 9705 room is shown in Fig. 13.32.

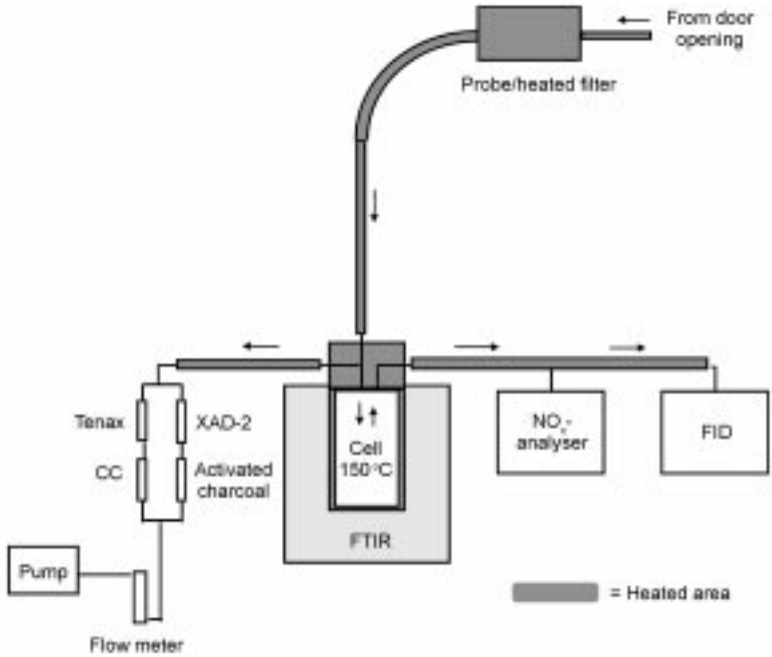
13.32 Restricted door opening of the ISO 9705 room in TOXFIRE.

13.33 The larger storage configuration enclosure in TOXFIRE.

In the larger storage configuration enclosure, the fuels were packed in paper bags and put in cardboard boxes. The boxes were positioned on steel shelves in a two-tiered post-pallet system within the large storage enclosure. Single tests were carried out with this scenario. The storage configuration enclosure is shown in Fig. 13.33.

It was expected that continued oxidation would occur of the hot unburned gases as they leave the enclosure, particularly for under-ventilated fires. Further, substantial dilution of the smoke occurred as it was drawn through the smoke gas duct. Therefore, sampling in the duct for the measurements of equivalence ratio and for the characterisation of the smoke gas components was considered unsuitable in these tests and sampling in the opening of the enclosures was chosen as the preferred strategy.

Samples were taken diagonally across the upper half of the opening through two stainless steel probes, with the suction end of the probes in the top corner; for a more detailed description, see the experimental reports.[26,66] The probe for the phi meter sampling had its holes inwards to include the soot with the sampled gas, whereas the other probe had the holes turned outwards to exclude the soot as far as possible.



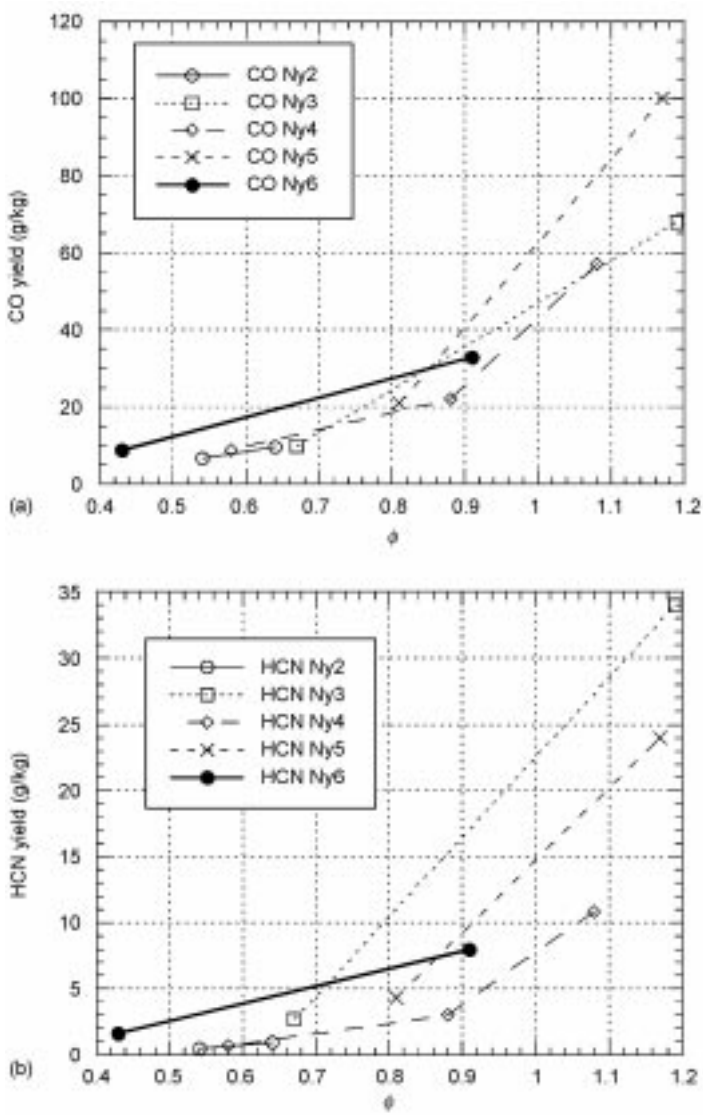
13.34 Sampling system for the characterisation of species in the fire effluents leaving the opening of the test enclosure.

Detailed characterisation of the individual products of combustion was the most important task in these experiments. Both online and cumulative sampling and measurement techniques were used. An overview of the main system for sampling of the smoke leaving the test enclosure is shown in Fig. 13.34.

It was shown in these experiments that it is possible to attain under-ventilated conditions on a scale as large as that in the ISO 9705 room, and that larger-scale fires such as those in the storage configuration facility do not appear to alter the outcome of the combustions significantly. Indeed, a clear correlation was found between the two configurations regarding the yields of the combustion products and their dependence on the degree of ventilation, in many cases. Nylon-6,6 is an example of a material, which exhibited correlated behaviour for all the combustion products measured. Yields of hydrogen cyanide and carbon monoxide versus the degree of ventilation are shown in Fig. 13.35, as an example.

Smouldering fires in silo storage

Solid biofuels are porous materials susceptible to heat generating processes from microbiological growth and chemical oxidation. These materials are therefore prone to self-heating which can result in spontaneous ignition. Owing to the low



13.35 Yields of carbon monoxide (a) and hydrogen cyanide (b), respectively, for nylon-6,6 from four ISO room tests with different sizes of door opening (Ny2–Ny5) and one storage configuration test (Ny6).

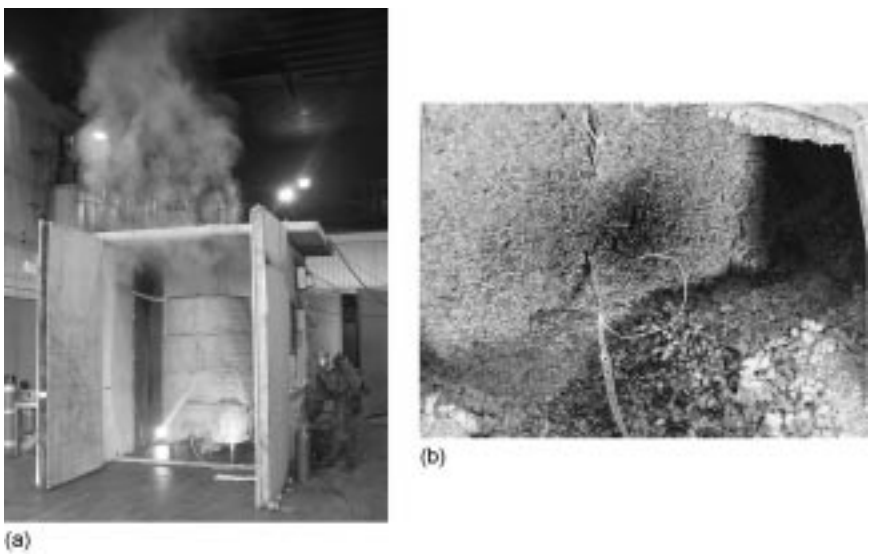
moisture content of wood pellets, the growth of microorganisms is normally limited, but temperature build-up is often observed from chemical oxidation, especially in newly produced material. Several incidents of spontaneous ignition of wood pellets in storage have occurred in Sweden and elsewhere.[67] Apart from the risk of fires, there is an additional risk are from the low-temperature produc-

tion of carbon monoxide and organic irritants in storage. Incidents with fatal outcomes in ocean transport of wood pellets with cargo ships have been reported.

Laboratory experiments have been conducted to study spontaneous ignition of wood pellets.[68] Experiments were conducted within physical scales from 1 dm^3 to 4 m^3. Small-scale basket heating tests were conducted to derive kinetic data for high temperature oxidation reactions which was used in the planning for the large-scale experiments. Experiments in the 1 m^3 scale were set up basically as an enlargement of the basket tests to obtain spontaneous ignition in experiments with controlled conditions in a reasonably large scale. In experiments close to real scale with 4 m^3 wood pellets in a 6 m high silo,[67,69] pyrolysis spread and gas production was mapped using a large number of measurement points in the pellet bulk and in the top of the silo. These test series have been discussed in some detail in Blomqvist and Persson[68] and Blomqvist *et al.*[70] The two large-scale test set-ups are shown in Figs 13.36 and 13.37.

The aim of the test series with 1 m^3 tests was to create strictly controlled conditions for self-heating that would result in spontaneous ignition. Detailed instrumentation in the tests provided data concerning temperature and gas transport (carbon monoxide, carbon dioxide, oxygen) in the bulk of the pellets during the heating process. For the size and boundary condition of the test set-up used, a temperature of 105 ºC (pellet bulk and boundary temperature) proved to be above critical, and spontaneous ignition occurred.

The series of large-scale tests with wood pellets stored in a reduced size silo were conducted to increase the knowledge of emissions, fire development,



13.36 The 1 m^3 sized spontaneous ignition experiments: (a) the test set-up and (b) close-up of the centre of the wood pellet bulk after spontaneous ignition.

13.37 The 4 m^3 test conducted in a 6 m high test silo.

detection and inert gas extinction in silo fires. The silo used for the tests was built using concrete rings with a diameter of 1 m, and a total height of almost 6 m. The silo experiments were not 'spontaneous ignition experiments' as it was recognised that the pre-heating/burning period before extinguishing would have been excessively long. Instead, a local auto-ignition was initiated by a coiled heating wire placed in the pellet bulk centrally in the silo. The silo was instrumented with almost 100 thermocouples to follow the development of the pyrolysis zone and ultimately the efficiency of the extinguishment. Gas analyses were made, both in the free space in the top of the silo, and at four different height levels in the pellets bulk. The gas analysis included oxygen, carbon dioxide and carbon monoxide, both in the pellet bulk and in the top of the silo. Additionally, in the top of the silo the concentrations of unburned hydrocarbons (THC) and VOCs were measured.

Some general observations were made from the gas measurements made in the large-scale test referred to above, and also from measurements in two real silo fires.[68] The concentration of carbon monoxide was normally below approximately 1 vol% in the emissions from self-heating of wood pellets in storage. However, when self-heating resulted in pyrolysis in the bulk, the

concentration of carbon monoxide in the emissions increased considerably. An increased concentration of carbon monoxide is normally accompanied by increased concentrations of carbon dioxide and THC, and a decreased concentration of oxygen. Regarding organic compounds, the same groups of compounds were found from all scenarios investigated. In all cases aliphatic hydrocarbons, terpenes and aldehydes were found. Reactive compounds such as mono-terpenes and hexanal were found in high concentrations and explain the irritant emissions often experienced from a self-heating storage of wood pellets.

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14

Effects of the material and fire conditions on toxic product yields

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Abstract: Fire gases contain a mixture of fully oxidised products, such as carbon dioxide, partially oxidised products, such as carbon monoxide or aldehydes, fuel or fuel degradation products, including aliphatic or aromatic hydrocarbons, and other stable gas molecules, such as nitrogen and hydrogen halides. The yields of most of the species depend on the material composition, the decomposition conditions (non-flaming or flaming) and, for flaming, the ventilation conditions. This chapter examines the effects of the main parameters determining product yields, illustrated with data for six common polymeric materials obtained using the ISO 19700 tube furnace, which is found to provide an excellent method for exploring the relationship between combustion conditions and product yields.

Key words: toxic product yields, combustion conditions, equivalence ratio, polymers, carbon monoxide, hydrogen cyanide, hydrogen chloride.

14.1 Introduction

Fire gases contain a mixture of oxidised products, partially oxidised products, fuel or fuel degradation products, and other stable gas molecules, such as nitrogen and hydrogen halides. The development of toxic hazards in fires depends upon the time–concentration curves of the toxic products, which in turn depend upon:

- the mass burning rate of the fuel (kg/s) and its dispersal volume, to give the mass loss concentration (kg/m^3) at different locations and times during the fire;
- the yields of each toxic product (kg/kg) from different fuels at different locations and times during the fire.

The yields of toxic gases vary considerably during different types and stages of full-scale flaming compartment fires.[1] For different fire stages the yields of fire gases will depend upon:

- material composition;
- fuel/air equivalence ratio (ϕ);

- temperature;
- oxygen concentration in the flame zone.

For non-flaming fires equivalence ratio is considered not to be a meaningful concept, but temperature and to some extent air supply affect product yields.

For any material, a major determinant of the yields of all the important toxic compounds is the fire condition; whether decomposition is non-flaming or flaming and the extent to which combustion is well-ventilated or under-ventilated for flaming decomposition. Other variables found to have some effect on the product yields are temperature (in particular whether combustion is under pre- or post-flashover conditions) and oxygen concentration. For any particular material, the yields of toxic products in fire therefore depend upon the interactions between the material composition (elemental and structural) and the fire conditions.[2]

Full-scale compartment fires can be classified into a range of different types or stages depending upon the combustion conditions, so it is important when measuring toxic product yields in any test apparatus, either bench or large-scale, to ensure that the combustion conditions are relevant to the full-scale fire scenario of interest. The different stages of full-scale fires and their general effects on toxic product yields are described in Chapter 2, in which Table 2.3 provides a method for specifying combustion conditions in fire tests into four main categories:

- non-flaming or smouldering fires;
- early well-ventilated fires;
- under-ventilated fires
  - pre-flashover,
  - post-flashover.

14.2 Toxic product yields for common materials and fire conditions

The fuel in most unwanted fires does not consist of small molecules, like petrol or paraffin, but is predominantly based on natural or synthetic polymers. This section examines the relationships between thermal decomposition or combustion conditions and yields for specific classes of natural and synthetic polymers. The data presented are mainly as measured in a bench-scale apparatus, the steady-state tube furnace (ISO 19700)[3] for which yields of a number of materials have been validated against full-scale fire conditions.[4–7]

Thermal decomposition and combustion processes have been shown to produce a very wide variety of products with varying toxic effects and potencies. In the following section consideration has been limited to those products considered most significant in causing incapacitation and death in fire victims (see Chapter 3–5 and 8). These consist predominantly of asphyxiant gases (carbon monoxide, hydrogen cyanide, carbon dioxide, nitric oxide and lowered

oxygen) and irritants, which include acid gases (hydrogen fluoride, hydrogen bromide, hydrogen chloride, sulphur dioxide, nitrogen dioxide, phophoric acid) and organic irritants. The identities of all the important organic irritants have not been fully established, since in practice fire atmospheres, especially those produced under non-flaming or under-ventilated flaming conditions, have been found to be considerably more irritant to exposed animals than could be explained in terms of the measured effluent composition. In addition, the decomposition conditions are so radically different from those used in conventional chemistry that it is possible that new, uncharacterised molecules are also present. In general it has been found that thermal decomposition atmospheres rich in partially oxidised organic species, such as carbonyl compounds, organic acids and other organic species such as stryrene monomer, tend to have a high irritant potency (see Chapter 8). Specific classes of compounds, such as isocyanate derivatives have also been found to be highly irritant.[8] In the following section yields of specific organic products are not reported, but an indication of overall irritant potential is provided in terms of the yield of carbon in the effluent present as organic carbon and carbonaceous particulates (see Chapters 3, 7 and 8 for a discussion of irritant products).

14.3 Generalised mechanism of polymer decomposition

The pyrolysis of a polymer involves decomposition, turning polymer chains of 10 000–100 000 carbon atoms into species small enough to be volatilised. In some cases, the chain releases groups most easily from its ends, which is known as end-chain scission or unzipping. In many more cases the chain breaks at random points along its length, known as random chain scission. A third process, where stable molecules, attached to the backbone as side chains, are lost, is known as chain stripping. The resulting chain may undergo scission to volatiles or lose further substituents forming double bonds, which cross-link and undergo carbonisation, ultimately leading to char formation. Thus, the conversion of organic polymer to volatile organic molecules may follow four general mechanisms. While some polymers fall exclusively into one category, others exhibit mixed behaviour.[9] Examples of common polymers and decomposition products are presented in Table 14.1.

The products of pyrolysis and combustion are strongly linked to heat and the availability of oxygen. This affects the chemical reactions that occur, releasing different types of volatile components that not only continue to thermally degrade, but also oxidise or react with other chemical species present in the combustion mixture, with the result that at different temperatures different types of combustion products are formed.

Under non-flaming oxidative thermal decomposition conditions, especially for polymers containing aliphatic carbon chains, low molecular weight aliphatic

Table 14.1 Generalised mechanisms of polymer decomposition[9]

Mechanism	Examples of polymer	Typical products
Random chain scission	Polyethylene	Alkanes, alkenes, very little monomer
	Polypropylene	Alkanes, alkenes, very little monomer
	Polystyrene	Styrene monomer, dimer and trimer
	More generally	Monomers and oligomers
End chain scission	Polymethylmethacrylate	90–100% monomer
	Polytetrafluoroethylene	90–100% monomer
	More generally	Monomer
Chain stripping	Polyvinyl chloride	Hydrogen chloride, aromatic hydrocarbons and char
	Polyvinyl alcohol	Water and char
	Generally	Small molecules and char
Cross-linking	Polyacrylonitrile	Char (hydrogen cyanide, nitrogen oxides, ammonia)
	Generally	Much char, few volatile products

carbon compounds such as methane, ethane, ethene, propane and propene tend to comprise a high proportion of the organic component of the effluent, with lower yields of partially oxidised organic compounds and a proportion of aromatic compounds including benzene and various other derivatives (see Chapter 2). Even under these conditions most carbon is released as carbon monoxide and carbon dioxide, while under flaming conditions carbon monoxide yield is low in well-ventilated conditions and increases in favour of decreased carbon dioxide yields as conditions become under-ventilated.[5]

As the most toxicologically significant fire gas, and as a good indicator of fire condition, the range of conditions favouring the formation of carbon monoxide has been considered in Chapter 2. Carbon monoxide results from incomplete combustion, which can arise from insufficient heat, quenching of the flame reactions, the presence of stable breakdown products or insufficient oxygen. For fuel nitrogen the main product is nitrogen gas. In under-ventilated conditions a proportion is released as hydrogen cyanide, while in well-ventilated conditions a proportion is released as nitrogen oxides, mainly nitric oxide with a very low yield of nitrogen dioxide.[7]

14.4 Material composition and the effect of ventilation condition on toxic product yields

In practice the yields of toxic products from different materials vary considerably, depending mainly upon their elemental composition and the efficiency with which different elemental components are converted to specific gaseous products.[4] When compared under similar combustion conditions the yields of

products from different materials vary depending upon the mass fractions of the main elements present in the base material (fuel), but if yields are normalised and reported in terms of conversion efficiency, then the decomposition chemistry of different materials can be compared more directly.

As a general guide to the typical variation of toxic product yield with material, decomposition and ventilation condition, the yields of toxic gases in the steady-state tube furnace (ISO 19700) are presented here. For non-flaming decomposition conditions some examples are presented of the effects of temperature and air flow on product yields, while flaming combustion conditions are expressed in terms of the fuel/air equivalence ratio, ϕ. The principle of operation of the tube furnace is described in Chapter 12. The relationship between the carbon monoxide yield and the equivalence ratio under flaming conditions in compartment fires was described for a variety of fuels in work reviewed by Pitts[10] (see also Chapter 2). For the tube furnace, the relationships between equivalence ratio and yields have been validated against compartment fire data for carbon monoxide, hydrogen cyanide, nitric oxide, smoke and total organic carbon for a variety of materials.[4–7]

For flaming conditions examples are presented for six different natural and synthetic polymer classes demonstrating the relationship between the equivalence ratio and the product yields. The main carbon-containing products: carbon dioxide, carbon monoxide, soot particulates, organics (VOCs) and char residue are reported. The organic fraction is measured as total organic carbon in the gas phase and is expressed as the yield of CH_2. In addition, the yields of nitrogen-containing products (hydrogen cyanide, nitric oxide and nitrogen dioxide), where nitrogen is present in the polymer, and the hydrogen chloride yield from a material with a high chlorine content (polyvinyl chloride, PVC), are presented. Yields for all gas phase products and residues are expressed as g/g (i.e. grams of product per gram of material on a mass charge or mass loss basis). Equivalence ratios are varied from 0.5–2.5 in separate experiments representing the conditions in stage 2 (well-ventilated) and stage 3a (under-ventilated) fires (see Table 2.3). Additional data are presented to illustrate the effects of higher decomposition temperatures representing combustion conditions in stage 3b post-flashover under-ventilated fires and also the effect of varying oxygen concentration at specific equivalence ratios.

As described for generic types of compartment fires in Chapter 2, for most fuels (combustible gases, liquids, natural and synthetic polymers) the yields of toxic products such as carbon monoxide are very low under well-ventilated combustion conditions, but increase steeply in under-ventilated combustion conditions as ϕ increases above 1. This results in a sigmoid relationship between ϕ and yield, so that the yields of products of incomplete combustion can increase by factors of approximately 50 between well-ventilated flaming conditions ($\phi < 1$) and fuel-rich conditions ($\phi > 1$). An inability to control or determine the equivalence ratio during most small-scale toxicity tests or to allow for its

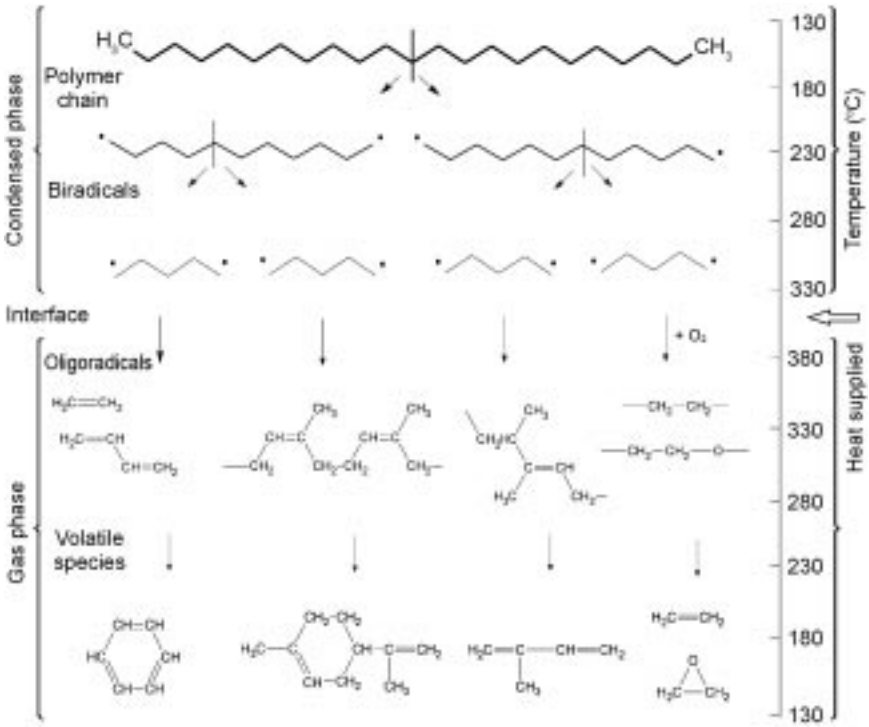
effects on toxic product yields in engineering calculations can therefore lead to considerable variability in estimations of toxic product yields and toxic fire hazard (see Chapters 12 and 13). The increase in products such as carbon monoxide, hydrogen cyanide, organic irritants and smoke particulates with ϕ is matched by a corresponding decrease in the products of more complete combustion, principally carbon dioxide, water, nitrogen and NO_x. Superimposed on this basic pattern of decomposition and yields are lesser effects of decomposition temperature and oxygen concentration, and specific effects related to the polymer composition. One important composition-related effect is char formation in some natural and synthetic polymers, and in products containing fire retardants acting in the solid phase (such as phosphates), which leads to reduced yields of airborne products. Other important yield modifiers are halogenated fire retardants, which act in the gas phase, resulting in increased yields of products of incomplete combustion throughout the range of equivalence ratios. The examples shown in the next section have been chosen to illustrate the effects of these variables on product yields for six common synthetic and natural polymers.

14.4.1 Aliphatic CH polymer: polyethylene

The thermal decomposition of polyethylene (PE) is a random chain scission process comprising several steps, presented schematically in Fig. 14.1. The temperature increase causes random scission of the polymer backbone, resulting in the formation and release of a larger amount of smaller molecules and radicals. Formation of cyclic hydrocarbons and aromatic rings occurs at higher temperature by Diels–Alder cyclisation reactions of alkenes (olefins or molecules with C=C double bonds). The aromatic content increases with increasing temperature. The thermal decomposition in air produces hydrocarbons and aromatic compounds, partially oxygenated products such as aldehydes, ketones and also major combustion products (carbon monoxide, carbon dioxide, water, etc.).[9]

Under non-flaming oxidative thermal decomposition conditions (Table 2.3, Stage 1b) the product yields are affected by both the decomposition temperature and the air flow over the polymer surface. Table 14.2 shows that for low density polyethylene (LDPE), the yields of all major products increased as the temperature was increased in separate experiments between 250 and 350 ºC, with a very large increase in organic mass yield at 350 ºC and high air flow rates.[11]

Figure 14.2 presents yields for LDPE under flaming combustion conditions (shown as g/g mass loss for airborne products and g/g mass charge for residue).[12,13] A similar basic pattern of product yields occurs in this and all the other non-fire retarded natural and synthetic polymers. Under Stage 2 (see Table 2.3) well-ventilated combustion, at equivalence ratios of less than 1, combustion is relatively efficient, so that the main carbon-containing product is carbon

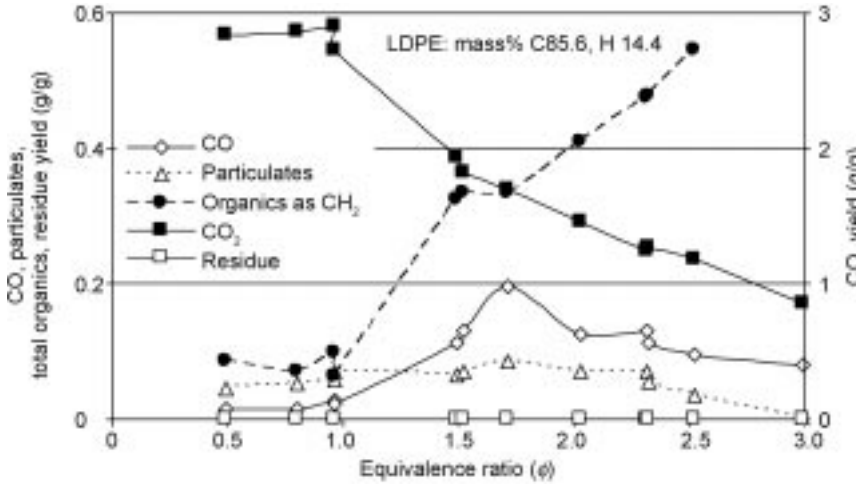


14.1 Low density polyethylene (LDPE) decomposition processes.[9,14]

dioxide, at yields approaching 3 g/g, representing a high proportion of the carbon in the original polymer. However, combustion is not complete, even at equivalence ratios around 0.5, since significant yields of organic carbon, particulates, and a small amount of carbon monoxide are also formed. As ϕ increases, there is little change in product yields until ϕ exceeds 1, from which point there is a steady decrease in carbon dioxide yield, with increases in unconsumed organic products and carbon monoxide. The carbon monoxide yield reaches a peak at $\phi = 1.75$ of 0.2 g/g, while carbon dioxide yield decreases

Table 14.2 Yields of major products from LDPE during non-flaming decomposition as a function of temperature

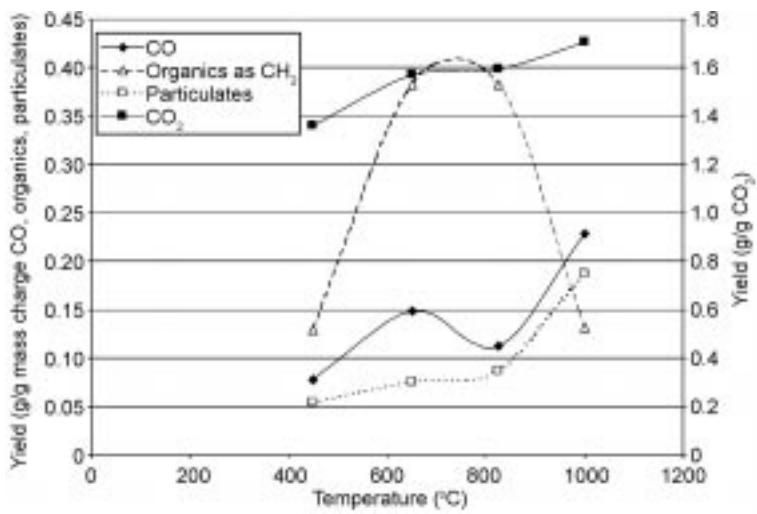
Temperature (°C)	Air flow (l/min)	CO (g/g)	CO_2 (g/g)	Particulates (g/g)	Organics as CH_2 (g/g)
250	1.1	0.002	0	0.015	0
350	1.1	0.079	0.038	0.032	0
350	22.5	0.158	0.031	0.094	0.831



14.2 Yields of the main combustion products for LDPE in the steady-state tube furnace.

by approximately $\frac{2}{3}$ at $\phi = 3$, as might be predicted from the lack of oxygen. Carbon monoxide yield also decreases above $\phi = 1.75$, presumably due to limited oxygen availability.

The effect of temperature on the yields during under-ventilated combustion of LDPE is shown in Fig. 14.3. At an equivalence ratio of 1.6 the results show some increases in yields of carbon monoxide, carbon dioxide and smoke



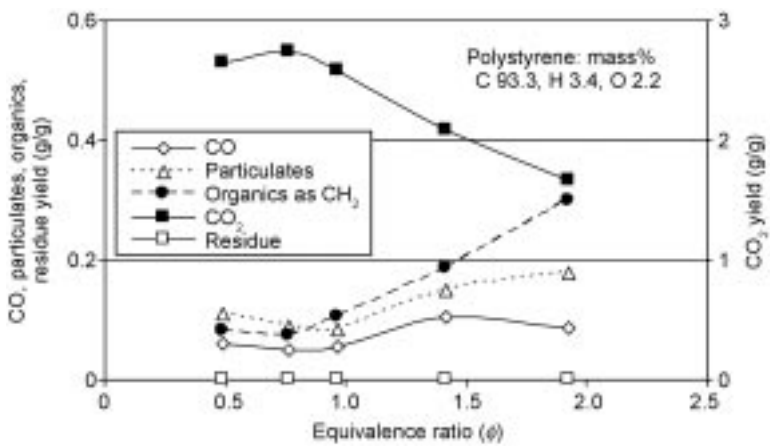
14.3 Effect of temperature on yields under flaming conditions for LDPE at $\phi = 1.64$.

particulates, while the total airborne organics reach a peak between 650 and 850 °C, then decrease at 1000 °C.[11]

14.4.2 Aromatic CH polymer: polystyrene

Polystyrene (PS) has a similar carbon content to LDPE, but a higher carbon/hydrogen ratio. The combustion product yield pattern (Fig. 14.4),[13,14] is similar to that of LDPE, but with less sensitivity to the ventilation conditions. It shows a high carbon dioxide yield at low equivalence ratios, decreasing as ϕ exceeds 1, but there is a greater propensity to form carbon-rich soot throughout the ϕ range and especially at high equivalence ratios. This is matched by a lower yield of gaseous hydrocarbons at high equivalence ratios. At low equivalence ratios there are higher yields of carbon monoxide and particulates than from LDPE and overall a somewhat less efficient combustion.

For PS the carbon monoxide yields appear to be controlled by two processes. The first, breakdown of the aromatic ring, appears (from carbon dioxide and carbon monoxide data) to be incomplete at 650 °C. The second, oxidation of carbon monoxide to carbon dioxide, is more efficient at higher temperatures, particularly 850 °C. The relatively high carbon monoxide yields under well-ventilated combustion conditions and low carbon monoxide yields in under-ventilated conditions at 650 °C suggest the presence of stable aromatic molecules, and low hydrogen ratio, resulting in inefficient oxidation. At temperatures of 750 and 850 °C, carbon monoxide yields increase more with increase of equivalence ratio. The higher carbon monoxide yield and correspondingly higher soot yield for aromatics and unsaturated fuels burning in well-ventilated conditions is well known. The lower carbon monoxide yield under fuel-rich



14.4 Main combustion products for PS measured in the steady-state tube furnace.

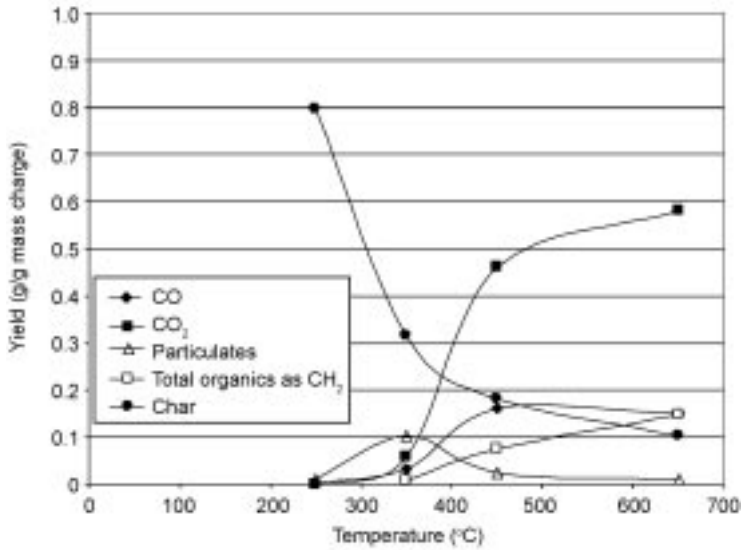
conditions is more interesting. Beyler, as reported by Pitts,[10] discusses a carbon monoxide yield of 0.11 g/g for toluene under fuel-rich conditions, and attributed it to the thermal stability of the molecule. This results in a further reduction in combustion effiency as the aromatic hydrocarbons are not converted to carbon monoxide.[15] Since the main product of decomposition of polystyrene is the monomer, with smaller quantities of dimer, trimer and tetramer,[14] these are also likely to show similar enhancements in thermal stability, limiting the availability of OH· radicals.

14.4.3 Cellulosic natural polymer CHO products: wood (*Pinus sylvestris*) and medium density fibreboard (MDF)

Two major differences between cellulosic materials such as medium density fibreboard (MDF) or wood and CH polymers are that they contain oxygen, and therefore less carbon per unit mass, and that oxygen can be lost as water, leaving a carbon-rich char under both non-flaming and flaming combustion conditions. For char-forming materials, decomposition is a two-stage process. Initial application of heat results in a mainly endothermic pyrolysis and oxidative thermal decomposition, resulting in flaming, leaving a carbon-rich residue. The carbon residue may then continue to be decomposed by exothermic oxidation in the solid phase. If the air supply is sufficient a glowing char may be formed. This constitutes smouldering decomposition, whereby the residual carbon is oxidised mainly to carbon monoxide and carbon dioxide. In self-sustained smouldering both processes occur simultaneously. The exothermic oxidation of the hot smouldering coal drives endothermic oxidative thermal decomposition of adjacent unheated material, so that the overall product yield depends upon the combined effects of the two processes.

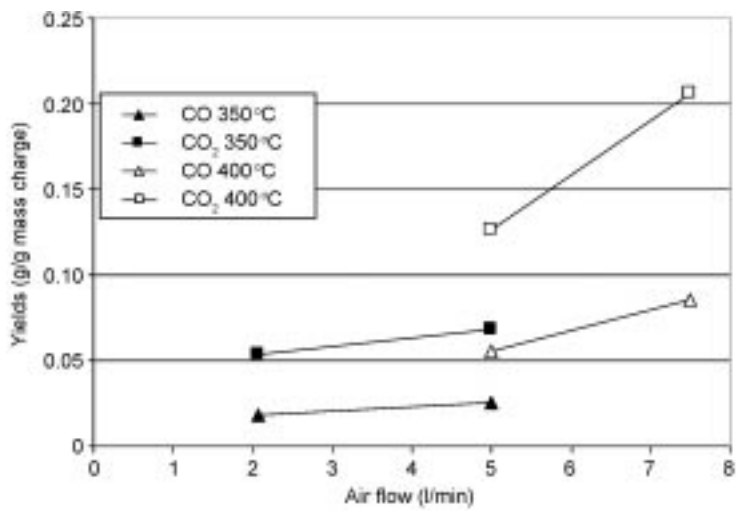
Both processes can also be accelerated by additional externally applied heat. At a given temperature species yields and rates of decomposition increase under more highly ventilated conditions. For char formers, increased ventilation can considerably increase the specimen temperature and rate of decomposition.

The effects of increasing temperature on product yields for a char-forming material (wood) under constant air flow conditions are shown in Fig. 14.5. As the temperature increases there is an increase in yields of carbon monoxide, carbon dioxide, particulates and total organics (expressed as CH_2) and a decrease in char residue. Significant yields are obtained above approximately 350 ºC. Figure 14.6 illustrates the effects of increasing airflow over a specimen at constant decomposition temperatures. At both 350 and 400 ºC there is an increase in yields of both carbon monoxide and carbon dioxide as the air flow is increased. The yields at 5 l/min are also increased as by increasing the temperature, and further increased by increasing the flow rate to 7 l/min. Since wood is a char former it is likely that both oxidative thermal decomposition and smouldering coexisted during these experiments.

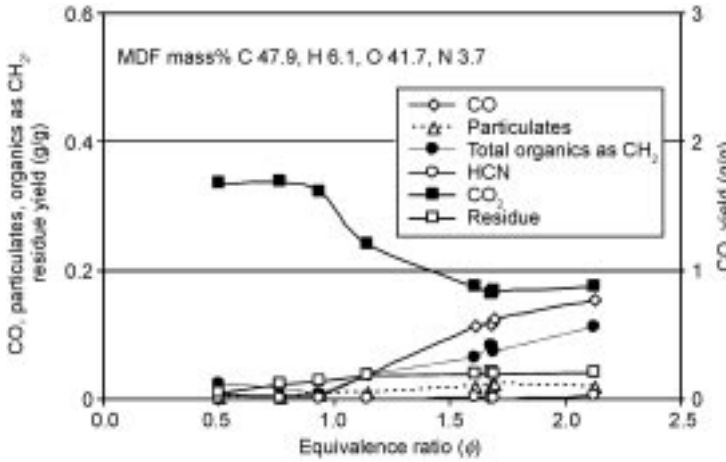


14.5 Yields (g/g mass charge) of products from wood (*Pinus sylvestris*) in the steady-state tube furnace under a constant air flow of 1.1 l/min.[11]

Although the basic yield pattern is similar to LDPE and PS, the carbon dioxide yield from MDF under well-ventilated combustion conditions is considerably lower (Fig. 14.7), corresponding to the lower carbon content. The combustion pattern is also more efficient than for the CH polymers, perhaps



14.6 Effect of changing air flow on yields of carbon monoxide and carbon dioxide from wood (*Pinus sylvestris*) under oxidative thermal decomposition in the steady-state tube furnace.[11]



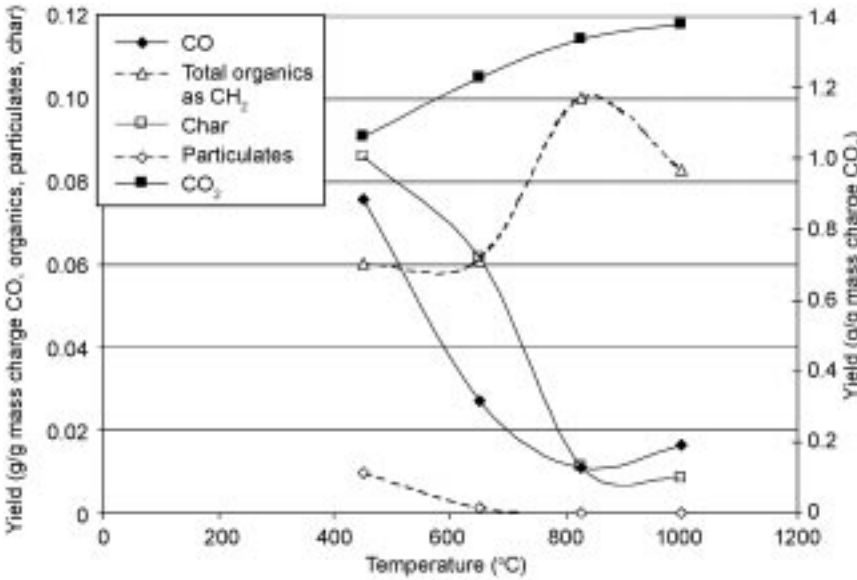
14.7 Main combustion products for MDF measured in the steady-state tube furnace.

because of the additional oxygen in the molecular structure. Another important feature of cellulosic materials is that since they are char formers, and especially in under-ventilated conditions, a significant residue remains, most of which is carbon. The yield of organic carbon is less than for the CH polymers but the conversion of fuel carbon to carbon monoxide is somewhat more efficient. MDF also contains approximately 3% nitrogen, so a small amount of hydrogen cyanide is produced, especially in under-ventilated conditions for which the maximum yield was 0.004 g/g at $\phi = 2.1$.

The combustion behaviours of MDF, plywood and wood (*Pinus sylvestris*) in the steady-state tube furnace are all very similar.[5,12,13] Figure 14.8 shows the effect of increasing furnace temperature on the yields of major products from flaming wood[11] at a ϕ of 1.0. For this char-forming material there are large decreases in the yields of char and some partially oxidised 'gas phase' products such as carbon monoxide and soot particulates, as temperature increases from 450 to 1000 ºC, with significant increases in total organics and carbon dioxide. Overall the pattern shows a somewhat more efficient oxidation at higher temperatures.

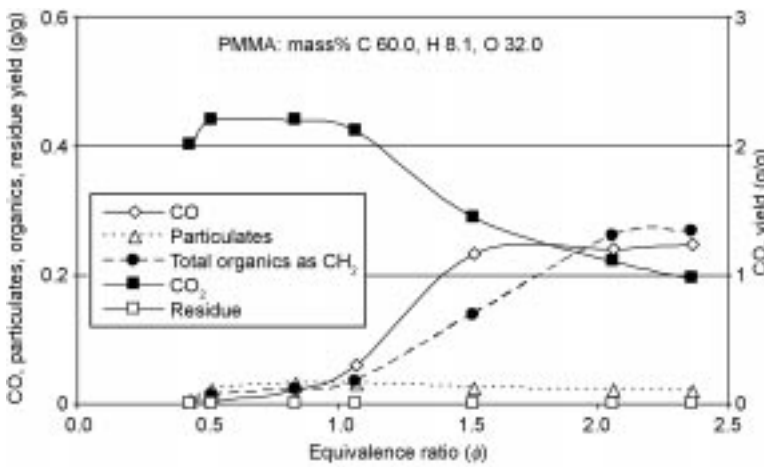
14.4.4 Synthetic CHO polymer polymethylmethacrylate (PMMA)

PMMA contains 60% carbon and 32% oxygen. It is relatively unusual in decomposing by end-chain scission, so the only reactions to take place in the gas phase are the oxidation of methylmethacrylate (the monomer of PMMA). Like cellulosic materials, it shows a very efficient combustion at ϕ below 1, with high carbon dioxide yields and very low yields of other carbon-containing products



14.8 Effect of furnace temperature on combustion product yields from wood combusted at an equivalence ratio of 1.

(Fig. 14.9). In under-ventilated combustion conditions there is a large increase in organic gases and in carbon monoxide with increasing ϕ. The efficiency of conversion of carbon to carbon monoxide is high compared with that of the CH polymers. For under-ventilated combustion conditions the yields of organics and carbon monoxide are both high compared with those from the natural cellulosic

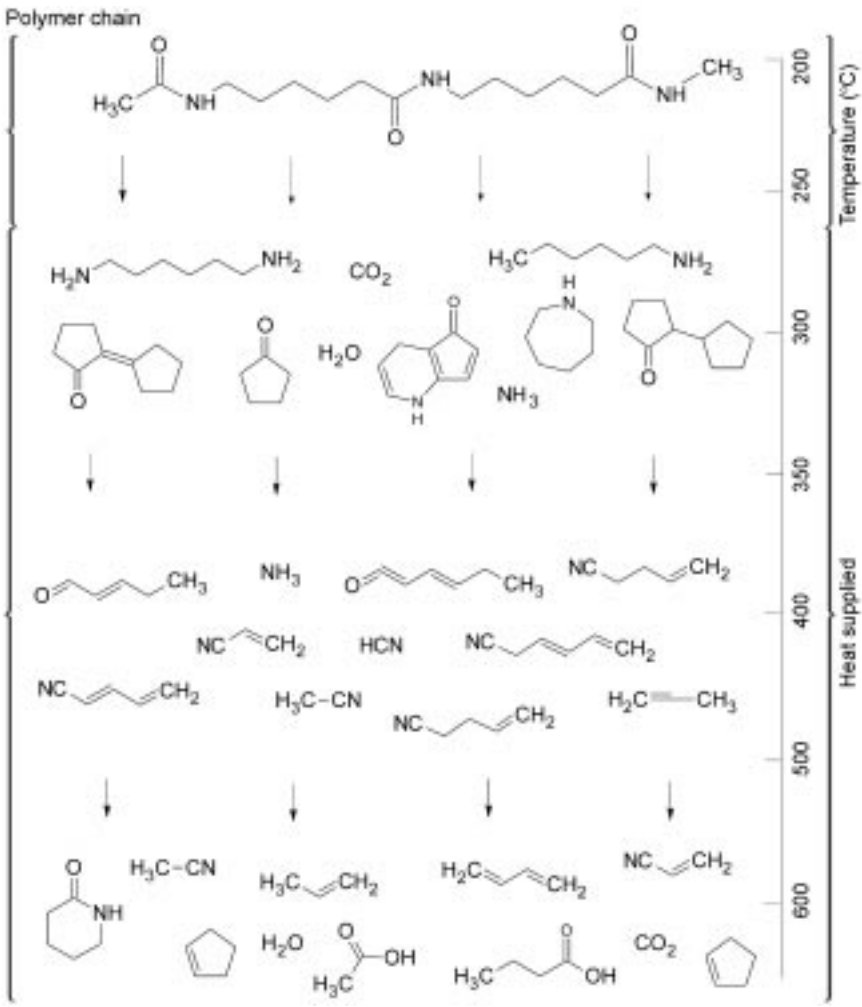


14.9 Main combustion products for PMMA measured in the steady-state tube furnace.

polymers, reflecting the fact that carbon is not retained in the form of char for PMMA, but released into the gas phase. The yield of smoke particulates is relatively low, but slightly higher than from MDF.

14.4.5 Nitrogen-containing polymer: polyamide-6

The thermal decomposition of polyamide-6 (PA-6) is also a multistep predominantly random chain scission process; presented schematically in Fig. 14.10. Numerous small aliphatic and oligomeric molecules have been identified during the thermal decomposition of PA-6,[16–18] although it has yet to be fully

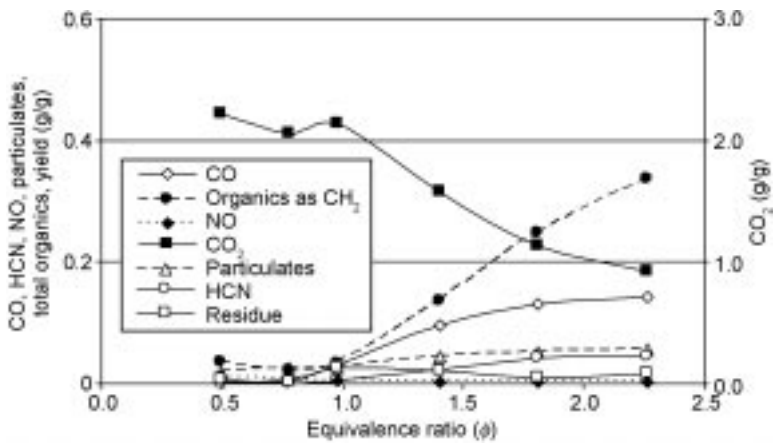


14.10 Thermal decomposition of PA-6.[14,16–21]

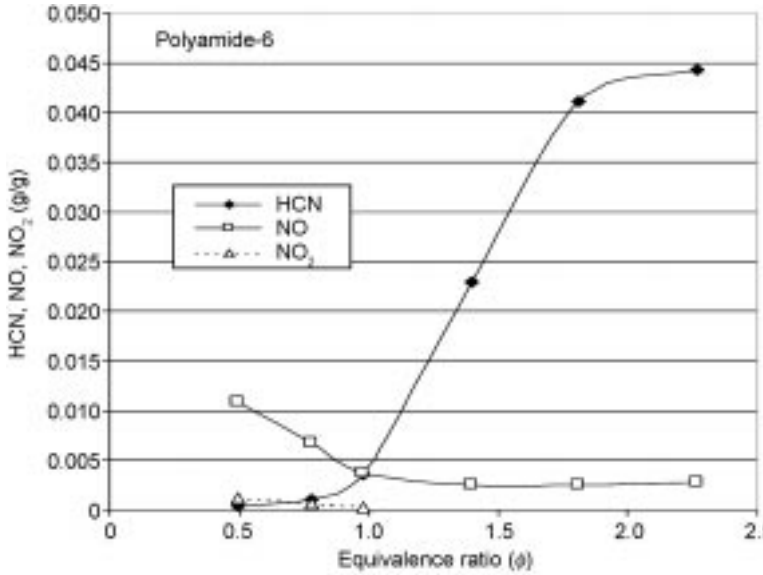
characterised. The processes are strongly linked to temperature and the presence of a nucleophile.[19] Below 300 ºC and in the absence of a nucleophile, formation of the cyclic monomer (ϵ-caprolactam) and cyclic oligomers mainly occurs.[20] The mechanism is difficult to predict, but intermolecular end group cyclisation or intramolecular and intermolecular aminolysis within the polymer chain have been suggested.[19,21] Between 500 and 800 ºC in the absence of a nucleophile, the thermal degradation results in the formation of not only monomer and cyclic oligomers, but also various small gaseous molecules (hydrogen cyanide, ammonia) and polymer chain end groups.[9,14] The most common products described in the literature from the thermal decomposition of PA-6 are presented below.

Polyamide-6 has a similar carbon content to PMMA at 64% but much less oxygen (14%) and 12% nitrogen (C: 63.7, N: 12.4, H: 9.8, O: 14.1). The yield pattern for carbon-containing products (Fig. 14.11)[7] is similar to the other materials described, the relationship between carbon dioxide yield, organics yield and equivalence ratio being almost identical to that of PMMA. Combustion is efficient at low equivalence ratios with low yields of carbon monoxide, organics and particulates, all of which increase at ϕ above 1. The efficiency of conversion of fuel carbon to carbon monoxide is lower than that for PMMA, which may be related to the lower oxygen content of the polymer.

With regard to the fate of fuel nitrogen, the products measured were nitric oxide, nitrogen dioxide and hydrogen cyanide.[7,12] The efficiency of conversion of fuel nitrogen to oxides of nitrogen was very low as shown in Figs 14.11 and 14.12. Under well-ventilated combustion conditions the main species produced was nitric oxide at a maximum yield of 0.012 g/g at $\phi = 0.5$, decreasing as ϕ increased to a yield of 0.0026 g/g in under-ventilated combustion conditions. The yield of nitrogen dioxide was approximately a factor of 10 lower than that



14.11 Main combustion products for PA-6 measured in the steady-state tube furnace.



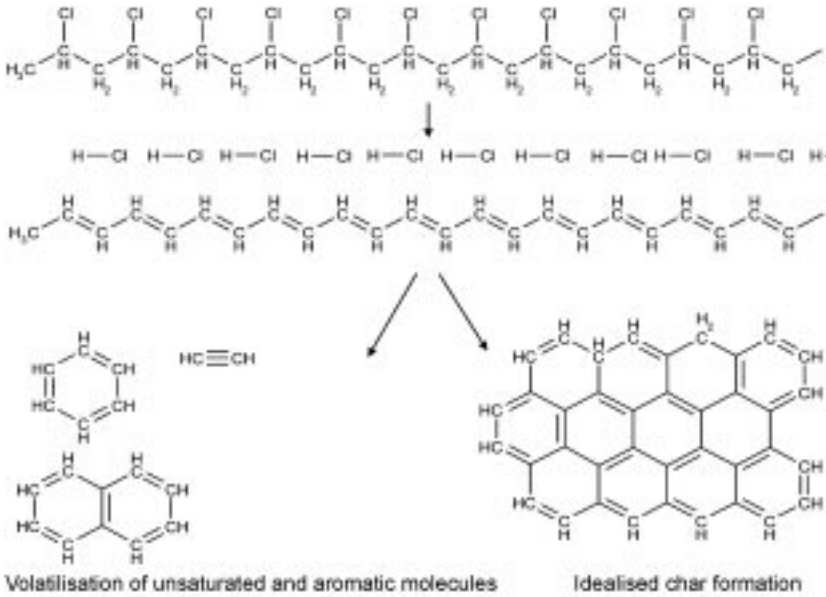
14.12 Relationship between equivalence ratio and yields of nitric oxide, nitrogen dioxide and hydrogen cyanide under flaming combustion conditions at 650 °C in air measured in the steady-state tube furnace.

of nitric oxide. Hydrogen cyanide yield showed a sigmoid relationship to ϕ, similar to that of carbon monoxide. In well-ventilated combustion conditions the yield was low, at approximately a quarter of the nitric oxide yield, but increased steeply to a maximum of 0.44 g/g at $\phi = 2.26$.

14.4.6 Chlorine-containing polymer: polyvinyl chloride (PVC)

Polyvinyl chloride (PVC) is ranked third behind polyethylene and polypropylene in terms of worldwide polymer consumption because it has a good chemical resistance and can be used in many different applications, such as cables, pipes, furniture, etc. As a synthetic material, PVC is made by polymerisation of vinyl chloride. It thus has the same chain structure as polyethene except that one hydrogen atom per ethene unit is replaced with a chlorine atom.

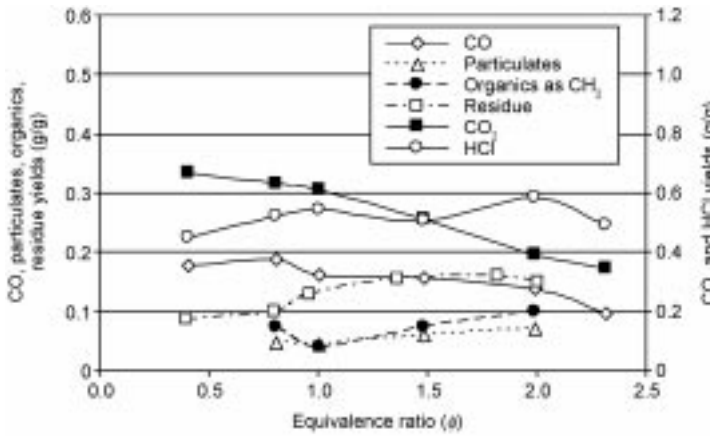
At elevated temperatures PVC undergoes a dehydrochlorination reaction to release hydrogen chloride and forms a conjugated polyene[22] which undergoes further rearrangements and product elimination at higher temperatures to produce a complex pattern of hydrocarbons with aromatic materials predominating (Fig. 14.13). At temperatures between 200 and 300 °C, 80–95% of the chlorine content of rigid PVC is released as hydrogen chloride, 70% within 1 min at 300 °C.[23] Under combustion conditions at 650 °C 75–90% of chlorine has been recovered as hydrogen chloride.[12] In some formulations, some chlorine



14.13 PVC decomposition.

may remain in the residue. For example calcium carbonate, a common filler in PVC, will react with hydrogen chloride to produce non-volatile calcium chloride, while releasing non-fuel carbon dioxide. In practice the chorine content of the residue has been found to depend to some extent on the decomposition conditions. When a plasticised PVC containing calcium carbonate was decomposed under non-flaming conditions 58% of chlorine was released as hydrogen chloride. Under combustion at 650 ºC the recovery decreased to 34%, but at 1000 ºC calcium carbonate decomposes to calcium oxide and gas phase chloride recovery increased to 43%.[11]

A small proportion of the fuel chlorine is released as other chorine-containing gas or vapour species and a number of chlorine-containing species have been identified from large-scale fires burning a high proportion of PVC, including mono- and dichlorobenzenes and other chloro-aromatic and chloro-aliphatic hydrocarbons.[24] Evidence exists to show that, depending on the fire situation, as much as 20% of the chlorine may exist in an organic form.[25] Approximately 70 compounds[26] including benzene, toluene, xylene, indene and naphthalene have been identified, but among these hydrogen chloride is the principal toxicant. However, under non-flaming decomposition conditions the irritant potency of the mixed effluent has been found to be considerably greater than could be explained on the basis of the hydrogen chloride content (see Chapter 8), so that additional organic irritants more potent than hydrogen chloride must be present.

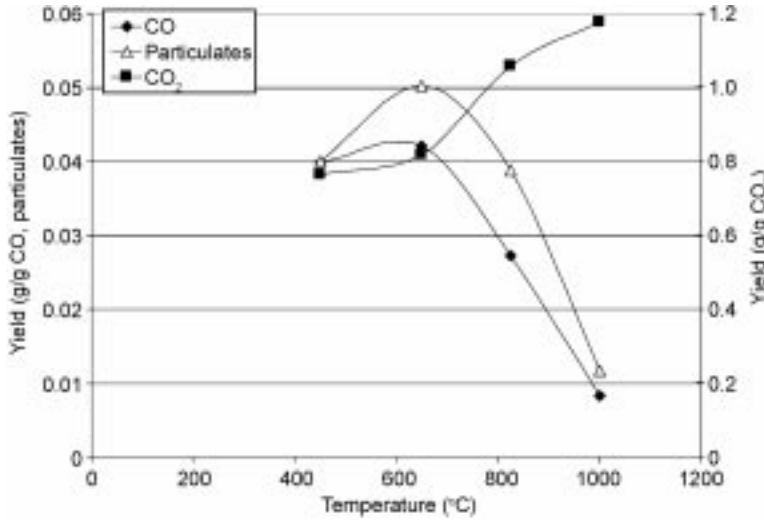


14.14 Main combustion products for PVC measured in the steady-state tube furnace.

PVC burns with a low heat release rate, because the halogen atoms in the structure release hydrogen chloride, almost 60% of its mass, which then inhibits the conversion of carbon monoxide to carbon dioxide. This is the major heat release step in polymer combustion. When hydrogen chloride gas comes off on heating, this causes a double bond to form between alternate carbons, strengthening the chain. As this residue gets hotter, the chain either cross-links as double bonds open and attachments to neighbouring chains occur, eventually leading to char formation or they break down and cyclise to form volatile aromatic hydrocarbons. If these only contain a few rings, they will give lots of black smoke, if they are large or cross-linked the residue may form a stable protective char layer.[27]

The results shown in Fig. 14.14 are for near 100% ('rigid' or unplasticised) PVC. Theoretically this contains 38.4% carbon and 56.7% chlorine, but in practice the actual chorine content is usually lower at around 52%. The yield pattern is very different from that of all the other polymers described, in that the yields of all products are relatively similar across the whole ϕ range from 0.5 to 2.5. Combustion is very inefficient across the range, with relatively low carbon dioxide yields and high yields of carbon monoxide, particulates and organics, and a significant residue, even under well-ventilated combustion conditions. At a ϕ of 2.3 the yields of carbon dioxide and carbon monoxide are approximately half those under well-ventilated combustion conditions, while the char residue increases by approximately 50%.

In contrast to the trend for polyethylene and polyamide 6.6 described in the previous paragraphs, the carbon monoxide yield for PVC appears to be independent of equivalence ratio. PVC forms more carbon monoxide than simple hydrocarbon polymers because hydrogen chloride interferes with the radical chain mechanism:[28]



14.15 Effect of temperature on yields under well-ventilated flaming conditions for PVC ($\phi < 1$).

$$HCl + H\cdot \rightarrow H_2 + Cl\cdot$$

$$HCl + OH\cdot \rightarrow H_2O + Cl\cdot$$

The high energy H· and OH· radicals are removed by reaction with hydrogen chloride and replaced with lower energy Cl· radicals, which are able to leave the flame without further reaction, or be regenerated by reaction with a hydrocarbon:

$$Cl\cdot + RH \rightarrow R\cdot + HCl$$

Crucially, removal of OH· (and also H·) prevents the conversion of carbon monoxide to carbon dioxide:

$$CO + OH\cdot \rightarrow CO_2 + H\cdot$$

Thus inhibition of flame reactions leads to a higher proportion of products of incomplete combustion, particularly carbon monoxide.

For halogenated materials such as PVC, combustion is inefficient even under well-ventilated combustion conditions, as shown in Fig. 14.14, but as temperature is increased there is a tendency for combustion efficiency to increase as shown in Fig. 14.15 for a plasticised PVC (28% chlorine).[11]

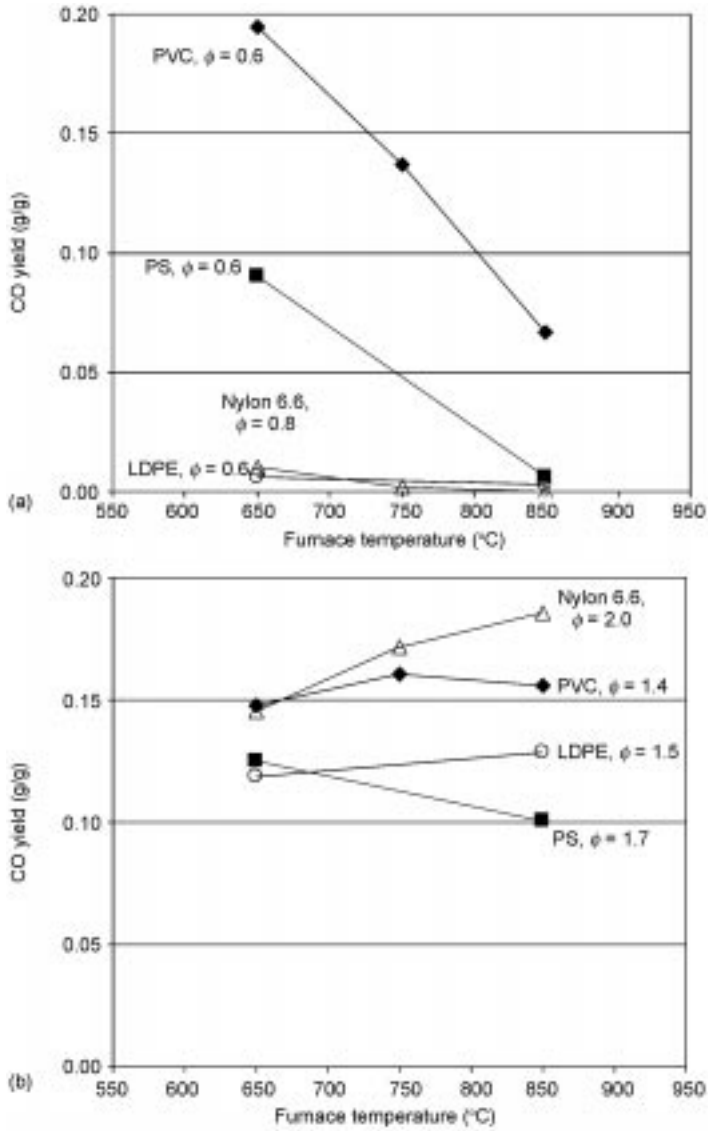
14.5 Effects of temperature on product yields

The average temperature of flames is around 1000 ºC, although regions of much higher and lower temperatures coexist in flame zones and are considered in

detailed chemical fuel combustion models. In compartment fires, fuel and air pass through turbulent flames, experiencing various mixture fractions containing different ratios of fuel, air and combustion products (see Chapter 2). These gases have a relatively short period of exposure to these extremely reactive conditions as they pass through and are carried up into the upper layer under the compartment ceiling. The temperature of this upper layer can vary from room temperature during the early stages of well-ventilated fires up to around 1000 ºC in under-ventilated post-flashover fires. The residence time of fire gases in this upper layer is somewhat longer than that in the flame zone, depending upon the fire dynamics. In well-ventilated fires, the combustion process runs to near completion in an excess of air as the products leave the flame zone and cool rapidly in the excess mass of entrained air, so that the reaction chemistry can be considered to have effectively ceased at this point. In under-ventilated fires the situation is rather different. The gas mixture emerging from the flame zone of under-ventilated fires is fuel rich and oxygen depleted. The mass of air entrained is relatively low and the upper layer temperature is likely to be around 300–600 ºC in pre-flashover under-ventilated fires and >600 ºC up to 1000 ºC in under-ventilated post-flashover fires. Also, in both pre- and post-flashover under-ventilated fires the flames penetrate the fuel-rich upper layer, so that partially combusted, fuel-rich upper layer gases are continually re-circulated through the upper flame zone.

Thus although the temperature profile of the flames may not be much different in well-ventilated and under-ventilated fires (and may be somewhat cooler in under-ventilated fires), the temperature environment and history of the fuel gases can be significantly different, involving primary combustion as the fuel passes through the flame for the first time, followed by secondary chemical reactions in the upper layer. Based upon the results of a small number of post-flashover large-scale fire tests, for which samples have been taken from the upper layer in compartment fires, it does appear that some differences in product yields and ratios may occur at higher upper layer temperatures.

The majority of small-scale test methods may involve flaming decomposition of the fuel specimen, but do not achieve high temperature upper layers, although several closed box methods may involve some degree of re-circulated products through the flame zone. The ISO 19700 tube furnace does not have an ‘upper layer’ region as such, but the products of combustion from the flame zone do pass through the length of the heated furnace tube before being expelled into the mixing chamber where they are rapidly cooled to near room temperature. By running the furnace at different temperatures it is therefore possible to expose a specimen to flaming combustion in under-ventilated or well-ventilated conditions, and then expose the primary combustion products to different ‘upper layer’ temperatures as they pass through the furnace tube set at different temperatures. The data presented in Fig. 14.16 show carbon monoxide yields obtained for various materials at three temperatures and at both low 0.6–0.8 and high 1.4–2.0 equivalence ratios.

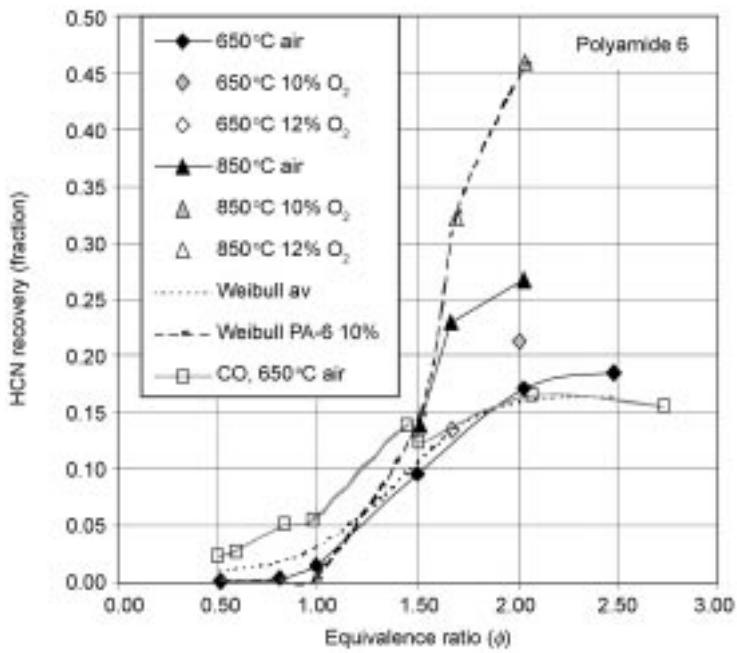


14.16 Influence of temperature on yields of carbon monoxide for LDPE, polyamide-6.6, PS and PVC[29] at (a) well-ventilated and (b) under-ventilated conditions.

The effects of changing the furnace temperature during flaming combustion depend on the material type and the equivalence ratio. The general picture is that for most materials the yields do not change very much as the furnace temperature is increased under either well-ventilated or under-ventilated combustion conditions. Under well-ventilated combustion conditions, where effi-

cient combustion results in high yields of carbon dioxide, water and heat, the effect of temperature increases are minimal on flaming decomposition of most polymers, but at ϕ values of 1 and above, there can be some changes in product yields. Figure 14.16(a) shows that, at low ϕ, temperature had a small influence on both LDPE and polyamide-6.6, but had a dramatic effect on PS and PVC, resulting in much decreased carbon monoxide yields at the higher temperatures. In under-ventilated combustion conditions on the other hand, Fig. 14.16(b) shows an opposite trend, such that three of the materials (LDPE, polyamide-6.6 and PVC) experienced an increase in carbon monoxide yield, albeit only marginal, and the fourth material (PS) had a reduced carbon monoxide yield at the higher temperature.

Figure 14.3 showed that for LDPE at ϕ values of 1.64, there was a significant increase in carbon monoxide, carbon dioxide and particulates with temperature, with the organic effluent fraction at first increasing, and then decreasing above 800 °C. For char-forming materials under stoichiometric conditions, combustion efficiency increases with temperature, producing increased carbon dioxide and decreased char, carbon monoxide and particulates. Polyamide-6 is an example of a polymer for which the yields of both carbon monoxide and hydrogen cyanide are sensitive to furnace temperature. As illustrated in Fig. 14.17, increasing the furnace temperature from 650 to 850 °C increased the conversion of fuel



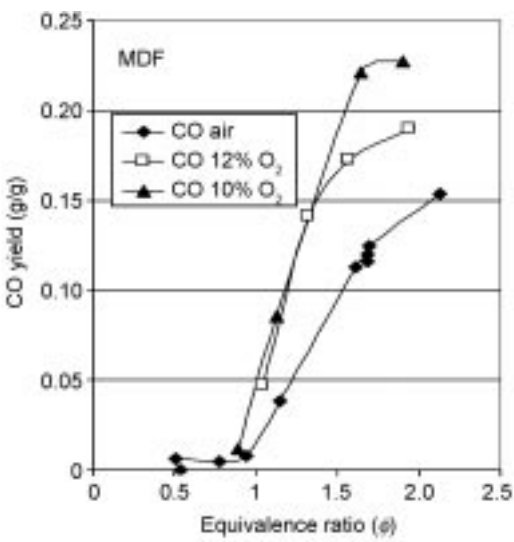
14.17 Effect on relationship between ϕ and hydrogen cyanide recovery for flaming combustion in air, 10% and 12% oxygen at 650 and 850 °C.

nitrogen to hydrogen cyanide (and hence also the hydrogen cyanide yields) by a factor of 1.5 in air (and 2.2 in 10% oxygen at a phi value of 2, as discussed in the following section) but had no effect on yields under well-ventilated combustion conditions.[7]

14.6 Effects of lowered oxygen concentration

A variable found to have a significant effect on product yields from some materials (but not others), is the oxygen concentration in the air supplying the combustion zone. All the results described in the previous section were obtained by passing air over the specimen. In addition, a number of experiments have been performed in which air–nitrogen mixtures were used, containing either 12% or 10% oxygen. It was found impossible to maintain flaming at oxygen supply concentrations of less than 10%. Two of the materials found to be sensitive to oxygen concentration were MDF and PA-6.

Figure 14.18 shows the relationship between ϕ and carbon monoxide yield for MDF under flaming combustion conditions in the tube furnace when supplied with air, 12% or 10% oxygen.[12] While this has no effect on carbon monoxide yield at equivalence ratios below 1, in under-ventilated conditions there is a progressive increase in carbon monoxide yield for a given equivalence ratios, so that in 10% oxygen the carbon monoxide yield is approximately 50% greater than that in air. PA-6 (Fig. 14.17)[7] was also found to be sensitive to oxygen concentration, so that both carbon monoxide and hydrogen cyanide yields were higher under 10% oxygen than in air at 650 ºC and the difference



14.18 Effect on relationship between ϕ and carbon monoxide yields of combustion in air, 10% and 12% oxygen at 650 ºC.

was even greater at 850 ºC. This effect was very much polymer dependent, showing little or no effect on some materials. Somewhat similar effects have been observed in compartment fires.[10]

14.7 Conclusions

Fire gases contain a mixture of fully oxidised products, such as carbon dioxide, partially oxidised products, such as carbon monoxide or aldehydes, fuel or fuel degradation products, including aliphatic or aromatic hydrocarbons, and other stable gas molecules, such as nitrogen and hydrogen halides. The yields of most of these species will depend on the material, the decomposition conditions (non-flaming or flaming) and for flaming, the ventilation conditions. For the most important asphyxiant gases (carbon monoxide and hydrogen cyanide) the yields may vary by up to a factor of 50 or more between well-ventilated and under-ventilated combustion conditions, which has important implications for the determination of toxic hazards during full-scale fires. Under combustion conditions temperature generally has a modest effect on toxic product yields, but can be significant for some materials, while for any given ϕ value, oxygen concentration can also have a significant effect on carbon monoxide and hydrogen cyanide yields in under-ventilated fires for some materials. The tube furnace provides an excellent method for exploring the relationship between combustion conditions and product yields. The relationships between equivalence ratio and yields of carbon oxides have been reported previously,[4,30] but this work shows how for several fire gases (notably carbon monoxide, hydrocarbons and hydrogen cyanide) yields tend to increase with increase in fuel–air ratio from fuel-lean ($\phi = 0.5$) to fuel-rich ($\phi = 1.5$) conditions, while NO_x, which is favoured by more oxygen rich conditions, shows a decreasing yield with ventilation in the tube furnace.

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15

Estimation of toxicity during burning of common materials

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Abstract: Fire toxicity varies with both material and fire condition. Most fuels in unwanted fires are organic polymer based, and for a particular material in a fire, it is possible to estimate the impact on lethality or incapacitation from knowledge of composition of the fire effluent produced under different fire conditions. The yields presented elsewhere have been translated into their predicted toxic effects. The materials include LDPE, PMMA, polystyrene, PVC, nylon, used alone, and in the presence of fire retardants and nanofillers.

Key words: fire, FED, FEC, toxicity, polymer, incapacitation.

15.1 Introduction

The hazards of fire effluents as irritants and asphyxiants have been described in Chapter 3 and 4 respectively. These hazards are clearly dependent on the fire conditions (Chapter 2). In the 1970s and 1980s the combustion toxicity of different materials was assessed by exposing quite large numbers of animals to fire effluents or their component gases in order to obtain statistically significant data. Since then, various models have been proposed to predict the toxicity of fire effluents on humans, based on existing animal exposure data. In many cases yield data have been published as a function of material and fire condition (for example Chapter 14). Given the ethical objections to unnecessary animal exposure tests, and the difficulty of relating data across different species, these models have now become the accepted methods for assessment of the fire toxicity of particular materials under different fire stages, for purposes ranging from performance-based design for fire safety in buildings and mass transport applications, through to forensic fire investigations.

In many cases it is important to know the most significant toxicants under particular fire conditions. Questions such as 'how does the fire toxicity of different materials compare?' or 'which component gives material X its high fire toxicity?' still need to be answered.

This chapter takes data which have been previously published and applies a simple rat lethality model to obtain the contribution of individual species to the

overall fire toxicity. The effects of concentration, dose and incapacitation versus lethality, are important and have already been discussed, but to provide a comprehensive estimation of the fire toxicity using each end point and calculation method would require a separate book in itself. Instead, an overview is presented here, to highlight the effects of the most common toxicant from certain materials and fire conditions. The data should not be used as a direct input to fire hazard analysis without considering all the aspects of fire toxicity, presented elsewhere in this book.

The toxicity of fire effluents is dependent on three factors:

- The rate of burning of the fuel.
- The material(s) being burnt (often the presence of elements such as nitrogen or halogens will increase the fire toxicity).
- The fire conditions.

The rate of burning of the fuel has not been addressed in this book since there is a wealth of published materials describing methods for prediction and estimation of mass loss rates, etc. The elemental composition of the material (fuel) provides a first idea of the fire toxicity.

Typical products from burning common materials are presented in Table 15.1.[1,2] Almost all fire effluents will contain carbon dioxide (CO_2) and carbon monoxide (CO), although not all at toxicologically significant concentrations.

Table 15.1 Major toxic gases from combustion

Toxic gas	Sources
CO (carbon monoxide) CO_2 (carbon dioxide)	Most combustible materials
CH_2=CHCHO (acrolein)	Cellulosic materials, polyethylene (PE), polypropylene (PP), wood, cotton, paper, acrylonitrile butadiene styrene (ABS), polystyrenes
HCHO (formaldehyde)	Polyoxymethylene, polypropylenes
HCN (hydrogen cyanide) NO_2 (nitrogen dioxide) NH_3 (ammonia)	Nitrogen-containing polymers, wool, silk, polyacrylonitrile (PAN), ABS, nylons, melamine urea/formaldehyde, polyurethanes
HCl (hydrogen chloride) HBr (hydrogen bromide)	Poly(vinyl chloride) (PVC) and materials with halogenated flame retardants
HF (hydrogen fluoride)	Polytetrafluoroethylene (PTFE), polyvinyl fluoride (PVF) and other fluorinated compounds and additives
SO_2 (sulphur dioxide) H_2S (hydrogen sulphide)	Sulphur-containing materials, wool, vulcanised rubbers, poly(phenylone sulphide)
$C_6H_5CH=CH_2$ (styrene)	Polystyrenes, ABS

Hydrogen cyanide (HCN) is more potent toxicant than carbon monoxide, but is only evolved from fuels containing nitrogen. Hydrogen chloride (HCl) and hydrogen bromide (HBr) exacerbate the irritating and choking effects of the smoke, but are only present when organic chlorine or bromine are present in the fuel. Salts such as sodium chloride have not been shown to yield hydrogen chloride in fire gases. Hydrogen chloride also readily combines with water to produce a dense white smoke capable of reducing visibility to zero before much heat, carbon monoxide, hydrogen cyanide, etc., are present.[3] Smoke will also be oxygen depleted, however, provided the concentration is greater than the 7% that causes incapacitation and it usually is, more toxicologically significant species will be present. For a particular toxicant, the human body always has one or more detoxication processes, either mechanical (mucociliar system) or biochemical; thus a dose absorbed over a long period may be less harmful than the same dose over a shorter period. In addition, the absorption rate of toxicants can differ widely; benzene is only absorbed at a few per cent and most can be found in the exhaled air, while hydrogen chloride is absorbed readily.

Most fire smoke toxicity assessments are based on relatively short list of fire gases. ISO documents[4,5] and other guidance identify the major toxic products, presented in Table 15.2. Sometimes the analysis is conditional on their presence in the effluent being suspected from knowledge of the material concerned.[6] However, for the purposes of this chapter, the published data are limited to only a subset of the ISO gases, namely carbon monoxide, hydrogen cyanide, nitrogen dioxide, hydrogen chloride, hydrogen bromide.

Table 15.2 Main combustion products and other irritants determined in a toxicity assessment[6]

Fire gases included in ISO documents	Other gases included in some fire smoke toxicity tests	Other gases considered hazardous while have been identified in large fire tests
Carbon dioxide, carbon monoxide, hydrogen cyanide, hydrogen fluoride, hydrogen chloride, hydrogen bromide, nitrogen oxides, sulphur dioxide, formaldehyde, acrolein	Hydrogen sulphide, carbon disulphide, acetaldehyde, formic acid, acrylonitrile, ammonia, phenol, benzene, toluene, styrene	Acetonitrile, butenenitrile, benzonitrile, propanaldehyde, butanaldehyde, pentanaldehyde, crotonaldehyde, benzaldehyde, mono and dichlorbenzenes, chloro-aliphatics and aromatics, benzene isocyanate, naphthalene, isocyanates, substituted phenols, polycyclic aromatic hydrocarbons (PAH)
Possibly, other irritants from the known composition of material		

15.2 Fractional effective dose (FED)

The effect of fire effluents on a human population may be estimated from the effect on animals either directly, using animal exposure, or indirectly from tables of concentrations leading to a particular effect (such as the limit below that causing irreparable damage, death or incapacitation of 50% of the population, etc.). From a regulatory perspective, the use of animals for routine product testing is not permitted in Europe,[7] so fire toxicity testing here must rely on chemical analysis which can involve many different techniques.[8]

The methodology in ISO 13344 (Equation 15.1) is based on the general approach of assuming additive behaviour of individual toxicants, and to express the concentration of each as its fraction of lethal concentration for 50% of the population (LC_{50}); it is based on rat lethality data. A FED equal to 1 indicates that the sum of concentrations of individual species will be lethal to 50% of the population over a 30 min exposure.[4,9] In the Purser model presented in ISO 13344,[4] Equation 15.1, a multiplication factor, V_{CO_2}, is used for carbon dioxide-driven hyperventilation, to account for the increased respiration rate resulting from inhalation of carbon dioxide on the increased uptake of harmful effect of the other toxic species, therefore increasing the FED contribution from all the toxic species. It also incorporates an acidosis factor A, to account for the toxicity of carbon dioxide in its own right.

$$\mathrm{FED} = \left\{ \frac{[\mathrm{CO}]}{\mathrm{LC}_{50,\mathrm{CO}}} + \frac{[\mathrm{HCN}]}{\mathrm{LC}_{50,\mathrm{HCN}}} + \frac{[\mathrm{HCl}]}{\mathrm{LC}_{50,\mathrm{HCl}}} + \ldots \right\} + V_{\mathrm{CO}_2} + A + \frac{21 - [\mathrm{O}_2]}{21 - 5.4} \quad 15.1$$

$$V_{\mathrm{CO}_2} = 1 + \frac{\exp(0.14[\mathrm{CO}_2]) - 1}{2}$$

where A is an acidosis factor equal to $[CO_2] \times 0.05$.

The data have been normalised to an arbitrary 1 g fuel decomposed in 200 l of fire effluent, on a mass charge basis, based on an established standard.[10] While this is a fairly high fuel-fire effluent volume loading, it illustrates the significant differences in contribution to FED of most of the fire gas components with change in material burnt, and with fire conditions.

15.3 Fire toxicity of common polymers with fire condition

Using previously published yield data, from the steady-state tube furnace[11–15] estimates of the toxicity (as 30 min rat lethality) have been calculated for a number of common polymers (low density polyethylene (LDPE), poly(methyl-methacrylate) (PMMA), polystyrene (PS), polyamide-6,6 (PA-6.6), poly(vinyl chloride) (PVC)) as a function of furnace temperature, which only occasionally makes a significant difference, and ventilation condition expressed as the

equivalence ratio, ϕ, on which the toxicity is highly dependent. The toxicity estimates have been made using the Purser model based[16] on rat lethality data.

15.3.1 LDPE

The variation of fire effluent toxicity from burning LDPE under different ventilation conditions, defined by the equivalence ratio, was used for calculation of the FED and is presented in Fig. 15.1. The condition at 650 ºC with equivalence ratio around $\phi = 0.7$ corresponds to well-ventilated flaming (stage 2 in Table 2.3), around $\phi = 2.0$ corresponds to the small ventilation controlled fire stage 3a, and that at $\phi = 2.0$ 850 ºC relates to a large post-flashover fire (stage 3b).

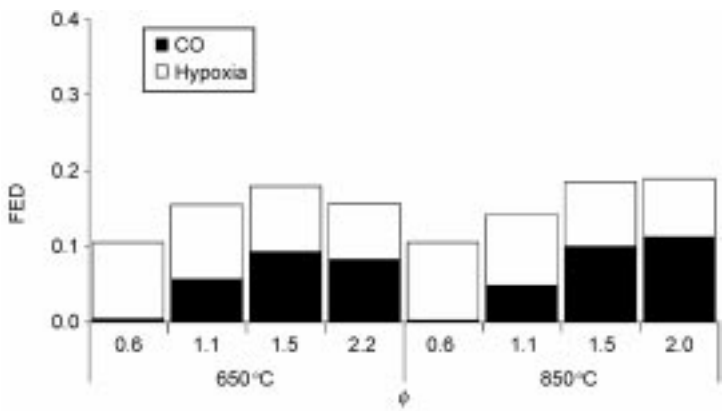
The contribution from carbon monoxide under fuel-rich conditions is considerably greater than under fuel-lean conditions. The total value of the FED is bigger when the experiments are carried out under small and large under-ventilated conditions.

15.3.2 PMMA

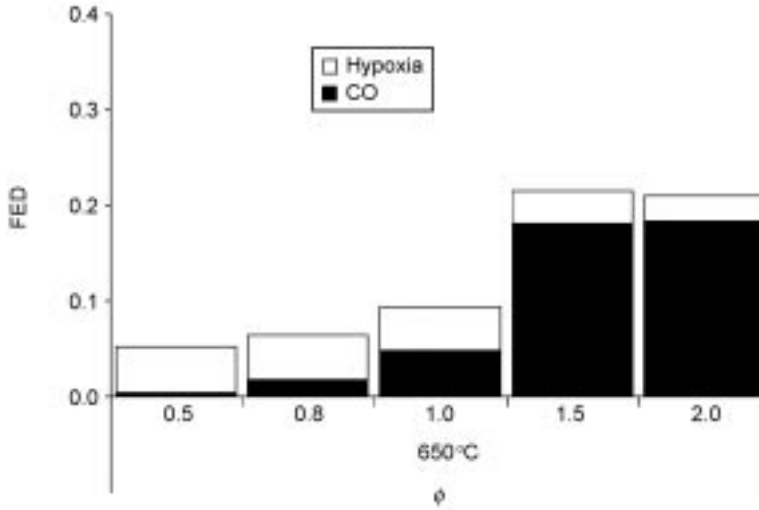
A similar trend is observed from burning PMMA as a function of equivalence ratio (Fig. 15.2). Unfortunately only data sets at 650 ºC were available. In common with most non-aromatic polymers containing C, H and O there is a significant increase in the contribution of carbon monoxide to toxicity with equivalence ratio.

15.3.3 Polystyrene

The toxic contribution of carbon monoxide at a temperature of 650 ºC, under fuel-rich conditions is remarkably similar to those generated under fuel-lean

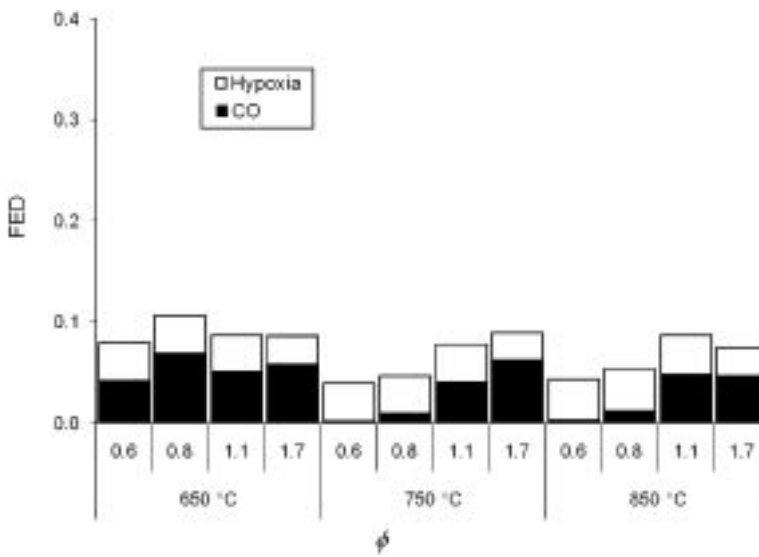


15.1 Contribution of each component to toxicity at different temperatures and ventilation conditions for LDPE.



15.2 Contribution of each component to toxicity at different temperatures and ventilation conditions for PMMA.

conditions, as shown in Fig. 15.3. An unchanged relationship between the carbon monoxide and hypoxia contributions when fuel-lean flaming occurred is observed. However, it is changed when vitiated experiments at $\phi > 1.5$, are carried out. A decreased correspondence between oxygen depletion, expressed by hypoxia, and carbon monoxide is observed.



15.3 Contribution of each component to toxicity at different temperatures and ventilation conditions for polystyrene.

The total value of the FED is similar at different stages of fire at 650 ºC. There are two factors with similar influence on the FED. Around half the contribution is from CO and half from oxygen depletion under fuel-lean and fuel-rich conditions ($\phi < 0.70$) at 650 ºC. For vitiated tests ($\phi > 1.50$) carbon monoxide makes more than half the contribution to the FED value. In conclusion, it can be stated that when the equivalence ratio is smaller than 1.50, significant contributions to the toxicity come equally from carbon monoxide and hypoxia. When the equivalence ratio is bigger than 1.50 the major contribution to the FED value is carbon monoxide. This is thought to result from the enhanced stability of the aromatic structure in a flame, resulting only in carbon monoxide in well-ventilated conditions, and failing even to break down to carbon monoxide in under-ventilated conditions.[17]

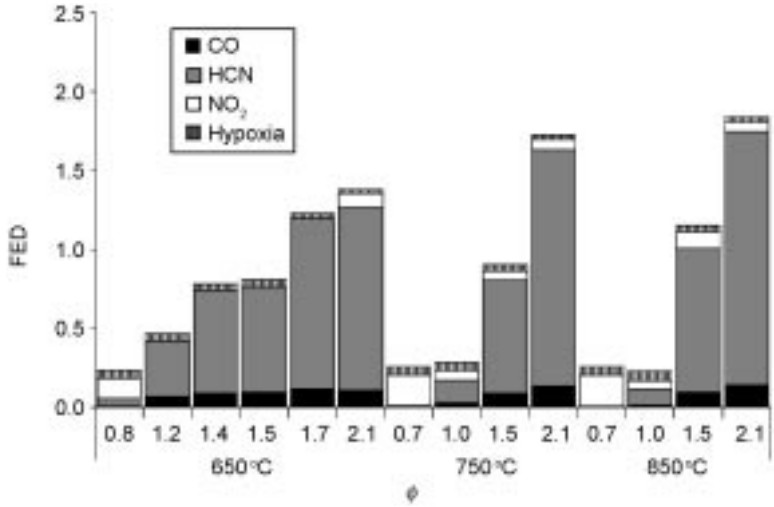
The most significant differences arise as the fire develops. Results obtained at higher temperatures than 650 ºC show greater differences of behaviour within different ventilation conditions. The changes between different stages of fire are more complex for temperatures of 750 and 850 ºC than for the tests carried out at 650 ºC. The hypoxia contribution under fuel-lean conditions is considerably greater than that of any other combustion products when the equivalence ratio is lower than 1. As the fire develops and the equivalence ratio increases, the contribution of carbon monoxide also starts to increase, at 750 and 850 ºC. It appears that the enhanced stability of the aromatic ring has less effect at these higher temperatures.

15.3.4 PA-6.6

The contribution of different toxic species to the FED values at different temperatures and different ventilation conditions from PA-6.6 is presented in Fig. 15.4. Nitrogen dioxide data for some tests carried out at 650 ºC were not available. In a developed fire, modelled in the tube furnace at 750 or 850 ºC, with high ventilation, where $\phi < 1.0$, the total value of the FED is lower than 1, the only significant contribution to the toxicity comes from nitrogen dioxide (~80%).

For stoichiometric combustion, $\phi = 1.0$, the total value of the FED is higher than 1 for experiments carried out at 650 and 750 ºC, and is estimated to cause death in 50% of the population over a 30 min exposure time for the mass loss rates per unit volume used in this study. The most toxic product at this stage is hydrogen cyanide, contributing approximately 60% to the FED value. Other combustion products contribute around 40% (hypoxia and nitrogen dioxide around 30%, and carbon monoxide 10%). However, the FED values for 850 ºC are lower than 1, and the main influence is caused by hydrogen cyanide and oxygen which make similar contribution (hydrogen cyanide 55%, nitrogen dioxide 40%) to the toxicity.

As the ventilation becomes limited, both the carbon monoxide and hydrogen cyanide contribution increase while the oxygen depletion, because of increased dilution of the fire effluent, decreases. The increase of hydrogen cyanide



15.4 Contribution of each component to toxicity at different temperatures and ventilation conditions for PA-6.6.

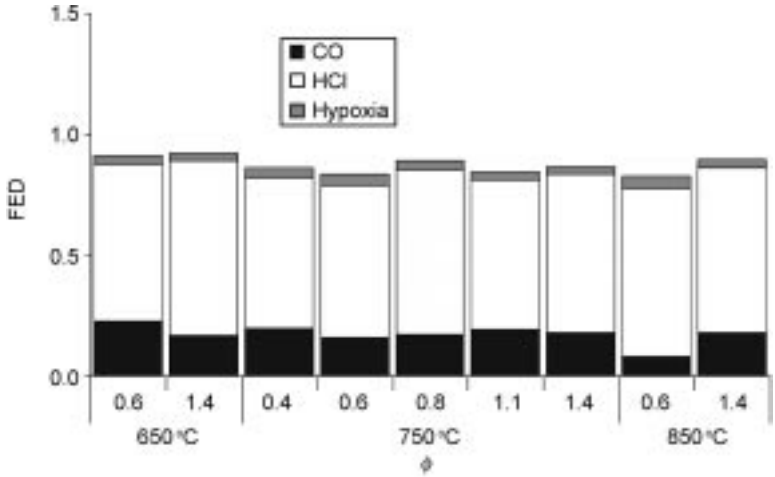
concentration, carbon monoxide, and oxygen depletion are independent of the temperature of the furnace, but increase in importance with higher ϕ.

For under-ventilated conditions, $\phi > 1.0$, carried out at 650 and 750 ºC, the FED value is higher than 1. The most significant contribution to the toxicity under those conditions was hydrogen cyanide, approximately 70% of the FED. Other combustion products have around 30% contribution, of which carbon monoxide is around 15%, and hypoxia 15%.

15.3.5 Unplasticised PVC

Figure 15.5 shows that hydrogen chloride generated during combustion of PVC makes the most significant contribution to the toxicity under all conditions. In addition, as an irritant gas hydrogen chloride will have bigger psychological and behavioural effects in terms of incapacitation, than the rat lethality shown here.[15] Even so, its contribution is greater than carbon monoxide or organic species, as shown by the FED components in Fig. 15.5.

For the mass feed rate and dilution factor used here, the total value of the FED is slightly lower than 1, indicating that the summed contribution of the individual species will cause death of 50% of the exposed rat population over a 30 min exposure. The biggest contribution, from hydrogen chloride, accounts for around 70% of the FED value. It should be noted that the lethal concentrations of hydrogen chloride are very large (~3500 ppm) compared with those causing incapacitation (200–1000 ppm) as discussed in Chapter 3. Other combustion products contribute around 30% to the FED value, for carbon monoxide 20% and hypoxia 10%.

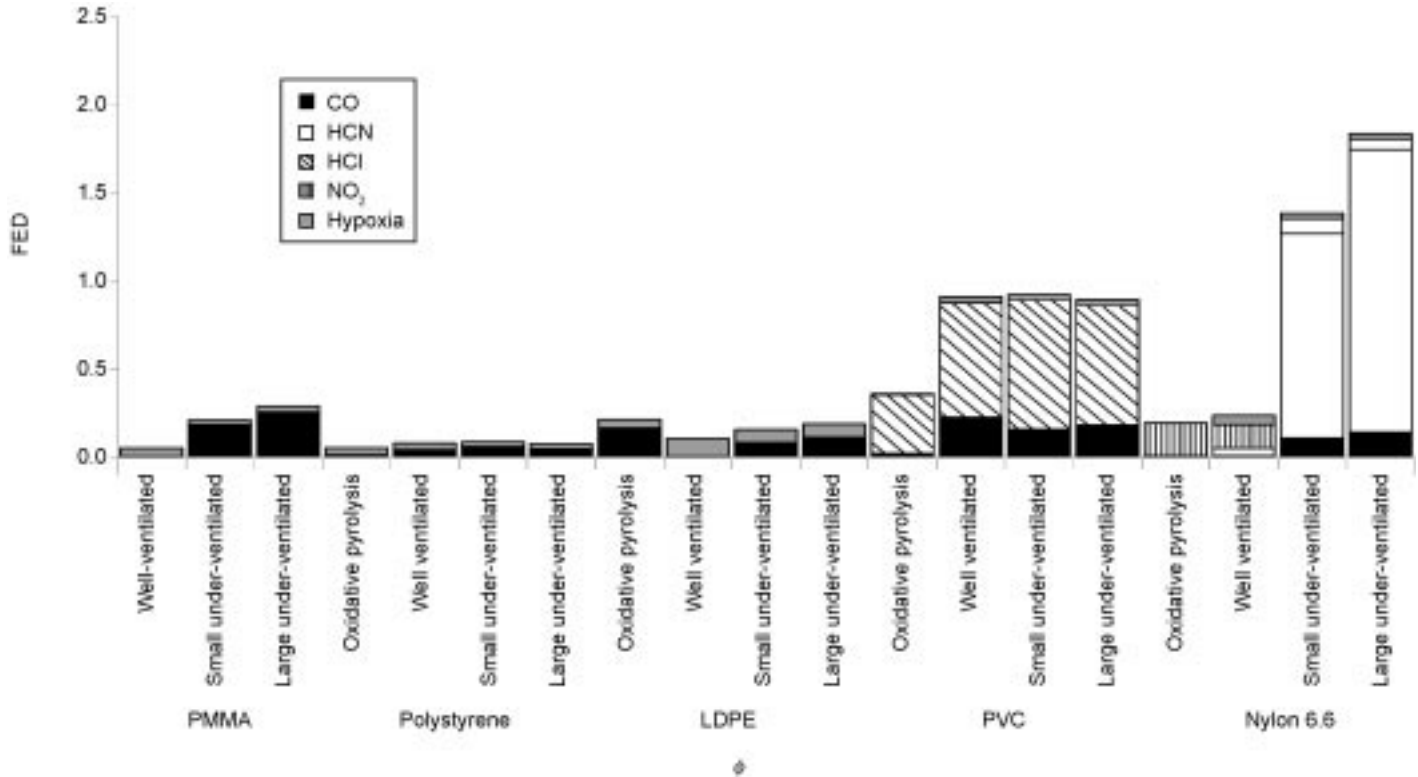


15.5 Contribution of each component to toxicity at different temperatures and ventilation conditions for PVC.

15.4 Summary of FED for various polymers

Most polymers and cellulosic materials (wood, paper, etc.) follow the trend shown by LDPE and PMMA of fire toxicity increasing from a very low value in well-ventilated conditions, to a much higher value in under-ventilated. As can be seen from Fig. 15.6, there is large variation in FED values for the other materials which could be considered as exceptions. For well-ventilated tests (650 ºC, $\phi < 0.75$) PA-6.6 and then PVC have the highest FEDs. For PA-6.6 where the presence of hydrogen cyanide in under-ventilated conditions has a very significant impact, there is a high dependency on scenario. Small under-ventilated tests (650 ºC, $\phi > 2.0$) gave overall higher FED values. It can be stated that hydrogen cyanide generated during small under-ventilated tests and post-flashover tests makes the most significant contribution to the toxicity. Hydrogen chloride has the biggest impact on the fire toxicity of unplasticised PVC, despite the significant increase in carbon monoxide yield, even in well-ventilated conditions, resulting from flame quenching by hydrogen chloride.

The contribution of carbon monoxide to the toxicity of burning polystyrene also shows characteristically low dependence on fire conditions. The predicted toxicities show variation of up to two orders of magnitude with change in fire scenario. They also show change of at least one order of magnitude for different materials in the same fire scenario. Finally, they show that in many cases carbon monoxide, which is often assumed to be the most, or even the only toxicologically significant fire gas, is of less importance than either hydrogen chloride, or hydrogen cyanide, when present.



15.6 Contribution of each component to toxicity at different temperatures and ventilation conditions for various polymers.

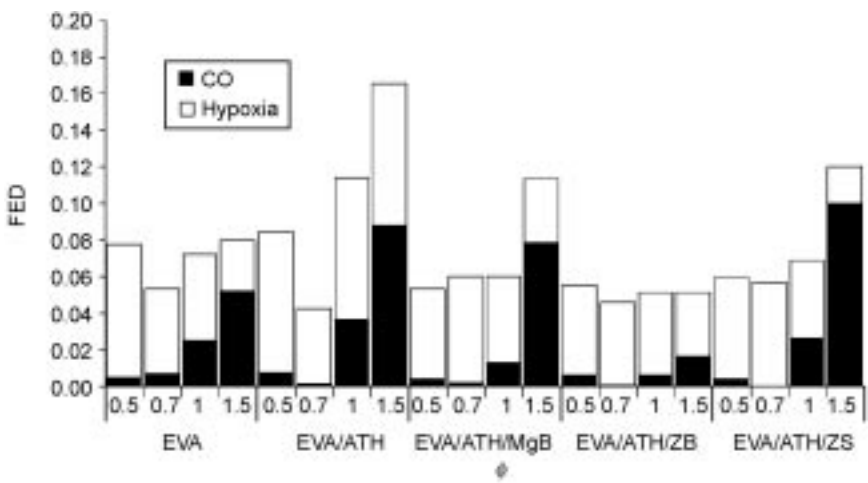
15.5 FED fire retarded materials

15.5.1 Flame retarded materials: ethylene vinyl acetate (EVA) + hydrated aluminium oxide (ATH)

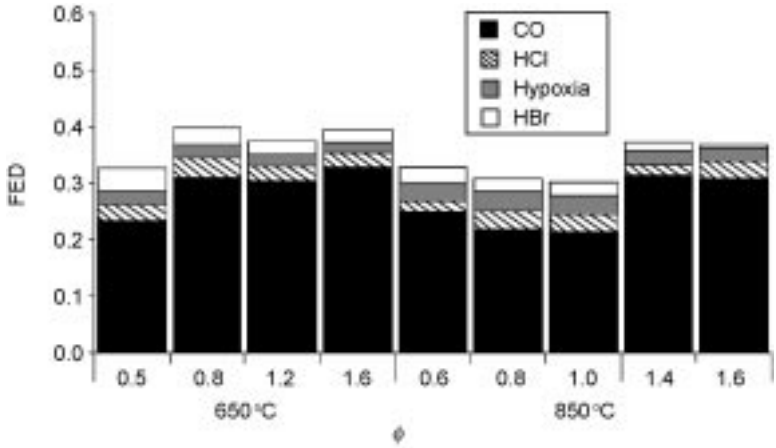
The materials were all based on ethylene vinyl acetate copolymer (EVA), containing 27% vinyl acetate. Fire retarded composites of the same copolymer EVA were formulated with 30% by weight of the EVA copolymer and 70% hydrated aluminium oxide (ATH), or 65% ATH and 5% zinc hydroxystannate (ZS) ($ZnSn(OH)_6$), or 5% magnesium borate (MgB) ($MgO\ (B_2O_3)_2\ H_2O$); or 5% zinc borate (ZB) ($2ZnO{\cdot}3B_2O_3{\cdot}3.5H_2O$).[18]

In order to compare the effect of filler on the combustion chemistry of the composite EVA materials, the same mass of EVA copolymer was used for each experiment, corresponding to a stoichiometric oxygen requirement of a constant $2.65\,l\,min^{-1}$. In the case of the filled composites containing 30% polymer and 70% fire retardant filler the sample mass was 3.33 times greater than the mass of pure EVA in order to keep the mass of polymer constant.

The results in Fig. 15.7 show that except as a diluent filler, ATH and ATH with MgB or ZS have only an effect on the fire toxicity increasing the carbon monoxide contribution during under-ventilated burning compared with EVA alone. This is believed[18] to result from catalytic oxidation of char (after-glow) by the freshly formed alumina surface. In contrast ATH with zinc borate has a dramatic effect on reducing the carbon monoxide contribution to fire toxicity especially in under-ventilated conditions. It is thought that zinc borate forms a glass which destroys the char-oxidising catalytic properties of the freshly formed alumina, leaving more carbonaceous residue in the condensed phase.



15.7 Contribution of each component to toxicity at different ventilation condition for EVA fire retarded composites.



15.8 Contribution of each component at different temperatures for GRP.

15.5.2 Glass reinforced polyester (GRP)

Fire retarded glass reinforced polyester (GRP) rooflight material, a translucent flat sheet had been formulated to achieve a 'class 1' rating to BS476 Part 7.[19] The major effect on the fire toxicity of the presence of hydrogen chloride and hydrogen bromide, was to increase the contribution of carbon monoxide, especially in well-ventilated combustion (Fig. 15.8). This makes the most significant contribution to the toxicity under all conditions, contributing around 80% of the FED. The carbon monoxide contribution to the FED is hardly changed at different furnace temperatures and ventilation conditions, resulting in FED with a remarkably low sensitivity to fire conditions.

15.6 FED nanocomposite materials: impact of fire retardants and nanofillers on toxicity

Polymer nanocomposites have been championed as the new solution to halogen-free fire retardant formulations because their presence is not detrimental to the physical properties. The materials used for the preparation of nanocomposites were commercial polypropylene (PP) with 5% polypropylene-graft maleic anhydride (PPgMA) fire retarded with 30% ammonium polyphosphate (APP) and compounded with Cloisite 20A nanoclays; polyamide-6 (PA-6) with an organic aluminum phosphinate combined with melamine polyphosphate and with 18% Cloisite 30B; polybutylene terephtalate (PBT) fire retarded with OP1240 18%, a non-melting metal phosphinate also used in combination with Cloisite 30B or nanoparticulate sepiolite amine; and ethylene-vinyl acetate (a polymer blend of EVA and LDPE) at 68% loading without clay or 63% with high aspect ratio nanoclay and used with two different fire retardants (FR),

aluminium hydroxide $Al(OH)_3$ (ATH) and magnesium hydroxide $Mg(OH)_2$ (MH). The preparation and characterisation of these materials have been reported elsewhere.[20–22]

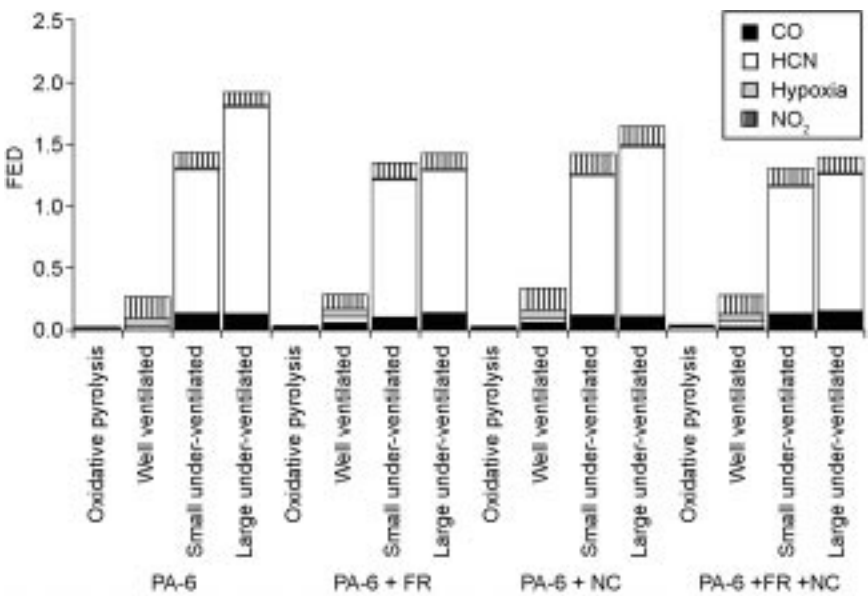
In each case the nanoclays (NC) were used at 5% loading, while the fire retardants followed industry standard practice. Four fire conditions were studied, corresponding to stages 1b, 2, 3 and 3b in Table 2.3.

15.6.1 PA-6 nanocomposites

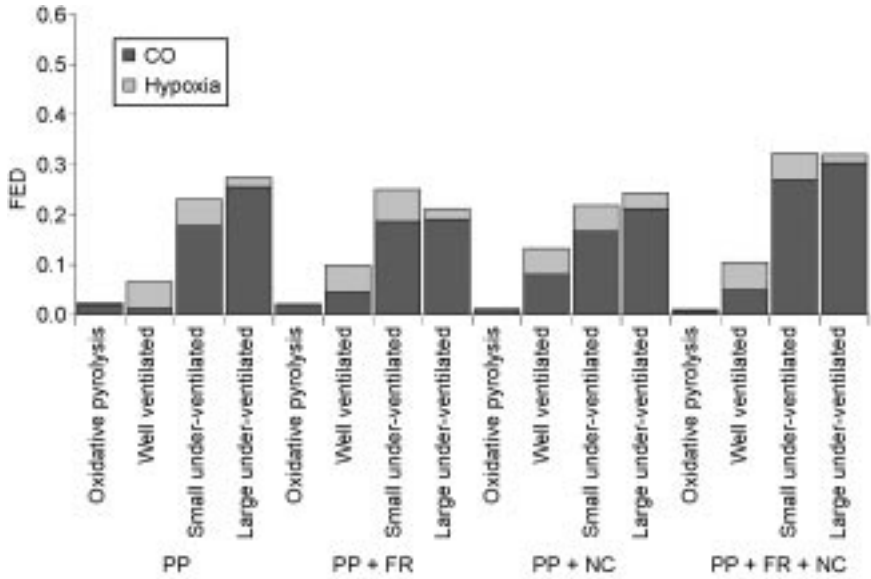
These PA-6 materials show very similar trends in contribution to fire toxicity as a result of the dominating effect of hydrogen cyanide on the toxicity for small and large under-ventilated flaming.[23,24] These are illustrated in Fig. 15.9. For developed fires, the FED is greater; the most toxic product at this stage is hydrogen cyanide, contributing approximately 80% to the FED.

15.6.2 PP nanocomposites

The relative toxicity is much lower than that for the polyamide samples in under-ventilated conditions which produced hydrogen cyanide (Fig. 15.10). Unlike hydrogen cyanide under well-ventilated conditions, it is clear that both NC and FR increase the toxicity of the effluent, by increasing the carbon monoxide yield.[24,25] Again there is a progressive increase in toxicity from small



15.9 Contribution of individual gases to toxicity from burning PA-6 nanocomposite materials under different fire stages.



15.10 Contribution of individual gases to toxicity from burning PP nanocomposite materials under different fire stages.

under-ventilated to large under-ventilated which is shown consistently across the samples. There is also a decrease in carbon monoxide for all the materials under the most dangerous under-ventilated conditions on incorporation of either NC or FR, and only a slight increase when both are present.

15.6.3 PBT nanocomposites

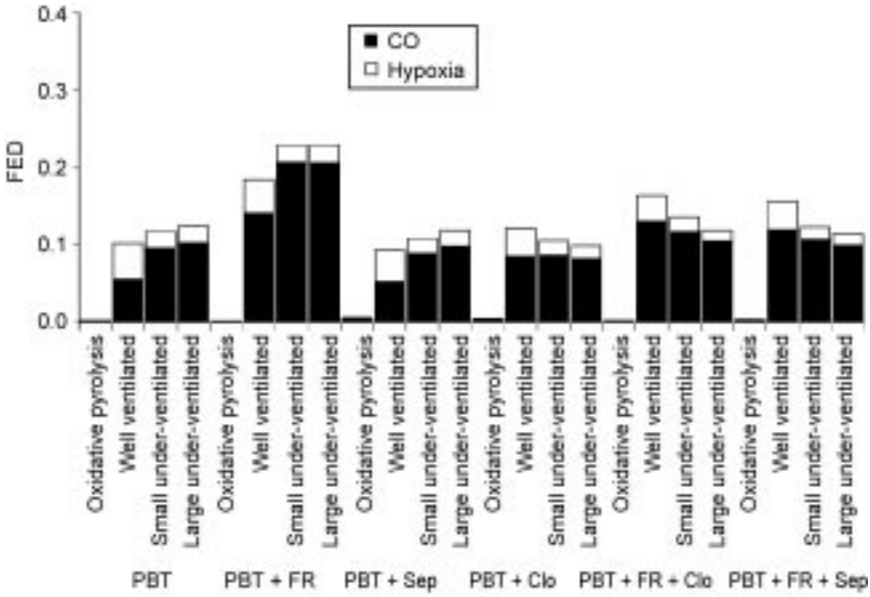
Figure 15.11 shows the consistently higher toxicity from burning PBT under different fire conditions and the additional increase in toxicity resulting from the use of the fire retardant. It is interesting to see the fire retardant effect on carbon monoxide yields disappear on incorporation of either of the nanoclays.[25]

15.6.4 Nanocomposites summary

Overall the presence of fire retardants and the incorporation of NC reduce the flammability, but this work has shown that there is no general adverse effect of these additives on the toxicity even under the most lethal under-ventilated fire conditions.

15.7 Fractional effective dose (FED) of whole cables

Ten commercial cables were investigated for fire toxicity using the condition specified in the International Electrotechnical Commission (IEC) standard, IEC



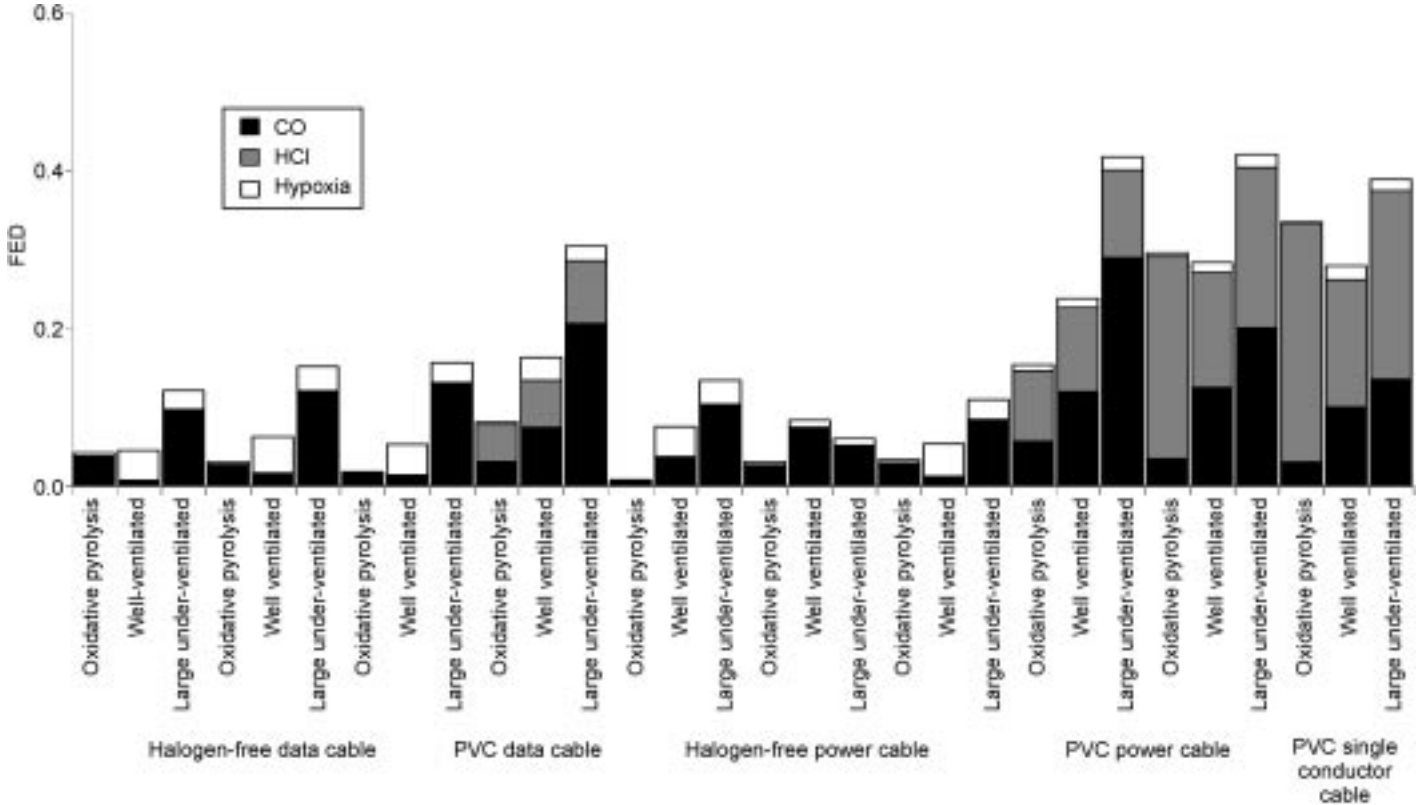
15.11 Contribution of individual gases to toxicity from burning PBT nanocomposite materials under different fire stages.

60695-7-50[26] which uses the steady-state tube furnace, but slight differences in the instruction for setting up the tube furnace ventilation condition to obtain a particular fire condition.

For each cable, the FED is shown for each of the three fire stages. In most cases (8/10) oxidative pyrolysis is the least toxic, presumably due to the low mass loss of the polyolefin polymers at 350 °C.[27] However, this temperature is high enough to release hydrogen chloride from PVC in two cases. In general the FED, based on the limited range of gases analysed, increases from oxidative pyrolysis, to well ventilated, to developed flaming. This is in line with expectations.

The two major toxicants are seen in Fig. 15.12 to be carbon monoxide and hydrogen chloride. However, it is notable that the carbon monoxide yield in the PVC fires is greater than that in the halogen-free fires and it is also noted that carbon monoxide yield in the PVC fires increase with vitiation. For hydrogen chloride the yield is almost independent of ventilation.

- The most hazardous fire condition is confirmed to be the under-ventilated fully developed fire.
- For the samples tested, the carbon monoxide yield for the PVC cables was greater than that measured for the low smoke zero halogen (LSZH) cables, and also increased with reduced ventilation. In comparison the hydrogen chloride yield was more or less independent of ventilation.



15.12 Contribution of individual gases to toxicity from burning cables.

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16

Prescriptive regulations and tests considering the toxicity of fire effluents

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Abstract: The toxicity of fire effluents is mainly prescribed in transportation, because besides road vehicles, there are only limited or no possibilities for escape in high speed trains, ships and airplanes. In buildings, only a few countries across the world such as France, Germany, Poland, Russia, China and Japan have toxicity requirements. The trend is towards a holistic fire performance approach including toxicity allowing the development of fire scenarios and modelling.

Key words: prescriptive regulations and tests, toxicity of fire effluents, building, rail vehicles, ships, aircraft, fire performance approach.

16.1 Introduction

Historically, statutory regulations and provisions relating to fire protection were developed to cover buildings. Later, with the advent of mass transportation, fire safety requirements were introduced for ships, railways and aircraft. For all these fields, fire protection is aimed at minimising the risk of a fire in order to protect life and property. The modern world of high rise buildings, skyscrapers, and huge warehouses, together with an unprecedented development in the size and means of transport has led to new challenges in the field of fire safety.

In the past, the focus of regulations and tests was on preventing the start and the development of a fire in a building. Nowadays the importance of fire parameters such as smoke development and the toxicity of fire effluents has been recognised. This is particularly true in transportation, where the possibilities for escape are limited, as is the case for aircraft, ships and railways – particularly underground and high speed trains. More details can be found in comprehensive reviews of fire safety regulations[1] and toxicity tests[2] in these fields.

Prescriptive fire protection requirements in buildings were mainly driven by classification systems and empirical tests based on parameters such as combustibility, ignitability, flammability and flame propagation. In some cases, smoke development and dripping were considered, and in a very few cases, toxicity requirements were added.

For many years the important role of heat release as a basic fire parameter has been recognised; it allows prediction of the size of a fire, and its growth rate, whilst at the same time providing information on other fire parameters such as smoke development and toxic fire effluent generation rates; both depend on the heat release rate in the course of a fire. Contrary to the prescriptive and empirical tests used in the past, the current trend is to fire performance criteria allowing the development of fire scenarios and modelling.

These new developments are also increasingly applied to fire toxicity testing, where the measurement of limit values for single components in fire gases is being superseded by a holistic approach which includes the use of data for modelling various fire scenarios. In building regulations, for the few existing national requirements, the approach is still based on prescriptive tests with limit values for single fire gas components. In transportation, particularly rail vehicles and now ships, effective dose and concentration are used to provide an indication of lethality and incapacitation, from the cumulative effect of the most noxious fire effluents, expressed as fractional effective dose or concentration (FED or FEC).

16.2 Mandatory toxicity requirements, classification and tests for products used in transportation and building

In transportation, toxicity testing is mandatory for ships under the control of the International Maritime Organisation, IMO. In aircraft, the Federal Aviation Administration (FAA), which has assumed a global position of overseeing aircraft safety, does not specify limits on fire toxicity. However, as major manufacturers of aircraft, both Boeing and Airbus Industrie have voluntarily imposed fire toxicity standards on all aircraft components. For example, Airbus Industrie specifies an additional test for smoke density and toxicity of combustion products for materials used in all Airbus models. In railways, the current national toxicity tests and specifications of European countries will be superseded by a harmonised European classification and testing system.

In building regulations, toxicity requirements for fire effluents from materials and products are only mandatory in a limited number of countries. The European harmonisation of the classification (Euroclasses) and testing of the reaction to fire of construction products does not address toxicity requirements.

16.3 Transportation

Flammability and fire toxicity requirements apply to all forms of mass transport, with the exception of passenger cars and coaches. On a national basis, France and the UK have developed toxicity requirements for their rolling stock, which

were adopted by some other countries such as Spain, Portugal, Italy, Benelux and the Nordic countries. The French and British tests are also required in the Channel Tunnel specifications for rolling stock. Russia has adopted toxicity requirements for thermal insulation of building products and foams for seating in rail vehicles. With the approval of the European standard EN 45545 'Fire protection on rail vehicles' in 2010, toxicity requirements will be mandatory in all European member states.

The toxicity requirements for materials and products used in ships are international and specified in the Fire Test Procedures (FTP) Code of the IMO. In aircraft, since 2006, the US FAA Technical Center has developed a laboratory-scale test ('Steel Cube Box') for evaluating toxic gas decomposition products generated during burn-through of a fuselage in a post-crash fire. However, the test was an isolated study, and is not likely to be introduced on a mandatory basis.

16.3.1 Rail vehicles

Technical legal provisions for rail vehicles vary from country to country. Generally the type of vehicle or the operational mode is taken into account. In addition, train operators frequently stipulate that various specifications laid down for train manufacturers in the conditions for delivery must be met.

The most important national fire protection requirements and tests for rail vehicles in Europe come from France, Germany and the UK. In France, requirements and fire tests in use for railways are described in standards for the choice of materials, electrotechnical equipment, and seats. Besides various fire tests, smoke density is determined and the toxicity of pyrolytic gases analytically evaluated. In Germany, the standard DIN 5510 deals with fire precautions in railways. Part 2 describes classification, requirements and test methods for the fire behaviour and fire side effects of materials and parts; toxicity requirements have recently been introduced in an annex of this standard. In the UK, fire tests are defined in the BS 6853 guidelines on rolling stock including the determination of the toxicity of fire gases. The French, German and UK national toxicity requirements and tests for rolling stock, as well as the European ones in CEN/TS 45545-2 are described below.

France

Requirements on materials and parts used in French railway vehicles are laid down in the standards NF F16-101[3] (Choice of materials), NF F16-102 (Electrotechnical equipment) and NF F16-201 (Fire behaviour of seats). NF F16-101 defines criteria for the fire behaviour, smoke development and toxicity of fire gases for different vehicles categories.

Fire behaviour

Different systems for the determination of the fire behaviour of materials are defined. The majority of materials are classified using the 'M-Classification' used in building codes according to NF P92-507.[4] Class M0 is non-combustible, while M4 is the most flammable. Small parts are tested using the oxygen index test (formerly NF T51-701) and the glow wire test (formerly NF C20-455), cables have to satisfy NF C32-070.[5] Details are shown in Table 16.1.

Table 16.1 Fire performance classes and test methods

Classification	Classes					Test and classification methods	Application
M	M0	M1	M2	M3	M4	NF P92-507 (using test methods NF P92-501, 503, 504 and 505)	Every material with dimensions sufficient for taking specimens
I	I0	I1	I2	I3	I4	NF T51-701 Oxygen index NF C20-455 Glow wire test	Small parts
–	–	A	B	C	D	NF C32-070	Cables

Seats have to be tested additionally as complete assembly according to NF F 16-201 with a paper cushion of 100 g as ignition source and a maximum flame duration time of 10 min.

Smoke development and toxicity of fire gases

The smoke development of materials is determined using NF X10-702-1.[6] This apparatus corresponds to the NBS Smoke Chamber ASTM E662, using vertically oriented samples. Square specimens of 76 mm × 76 mm are tested either in the flaming mode or the non-flaming mode with a radiant source of 25 kW/m^2, the values measured are the maximum smoke density D_m and the VOF_4 value with

$$VOF_4 = \tfrac{1}{2}(D_0 + 2D_1 + 2D_2 + 2D_3 + D_4)$$

The results of that test mode resulting in a higher VOF_4 value are used for classification.

For evaluation of fire gas toxicity, the material is tested and analysed to NF X70-100-1[7] and NF X70-100-2.[8] The gas concentrations t_i in mg/g are divided by 'critical concentrations' (CC) in mg/m^3, which cause no irreversible harm within 15 min. These are actually the immediately dangerous to life and health (IDLH) values published by NIOSH in 1987[9] and the results are summed up to get the toxicity index ITC (also referred to as the conventional index of toxicity, CIT):

$$ITC = 100\,\Sigma\,(t_i/CC_i)$$

Both smoke development and toxicity evaluation are combined to a smoke index IF:

$$IF = D_m/100 + VOF_4/30 + ITC/2$$

and classified in smoke classes F:

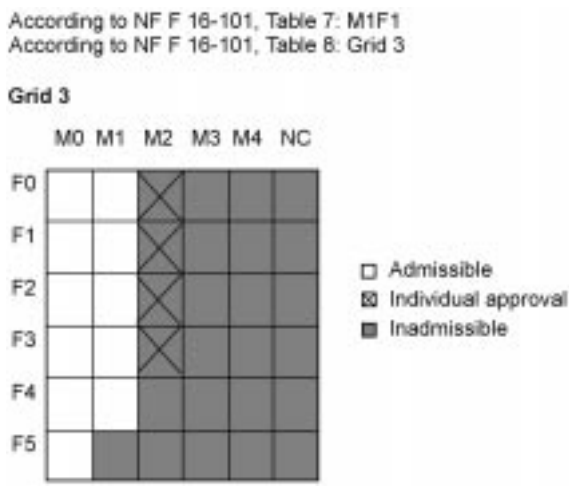
Smoke class	F0	F1	F2	F3	F4	F5
Smoke index IF	≤ 5	≤ 20	≤ 40	≤ 80	≤ 120	≤ 120

Requirements

The requirements for rolling stock materials are listed as a combination of M- and F-classes and depending on the operation classes. Because many of these requirements cannot be covered by actual materials, grids have been defined with admissible and inadmissible combinations of M- and F-classes and combinations that require an individual approval by the authority. An example is shown in Fig. 16.1.

Germany

In Germany, requirements regarding the fire performance, smoke development and dripping apply for materials and components used in rolling stock. To date, there are no German toxicity requirements. However, for allowing German rolling stock to be used immediately in other European countries with toxicity requirements, the new CEN/TS 45545-2 smoke and toxicity requirements and tests foreseen for rail vehicles have been nationally introduced in an annex of



16.1 Example for requirements for wall covering materials in category A vehicles.

DIN 5510-2[10] in 2008. They will remain valid until EN 45545 is implemented and the national standard DIN 5510 withdrawn.

United Kingdom

In the UK, guidelines on the design and construction of railway passenger rolling stock relating to fire are given in BS 6853.[11] This code of practice for fire precautions in the design and construction of passenger carrying trains covers new vehicles and changes to existing vehicles. Test compliance criteria regarding flame spread, smoke development and toxicity of fire gases for products used in passenger vehicles are laid down in BS 6853.

The assessment of the toxic potency of fire gases is carried out by determination of a weighted summation index R. Concentrations of eight gas components are measured using the mass-based French test method NF X70-100 by preference. The concentrations c_x for the different gases are weighted with reference values f_x and summed up to the index R:

$$R = \Sigma(c_x/f_x)$$

If the index does not meet the requirements, an alternative time-based analysis may be used to provide a sound technical hazard assessment.

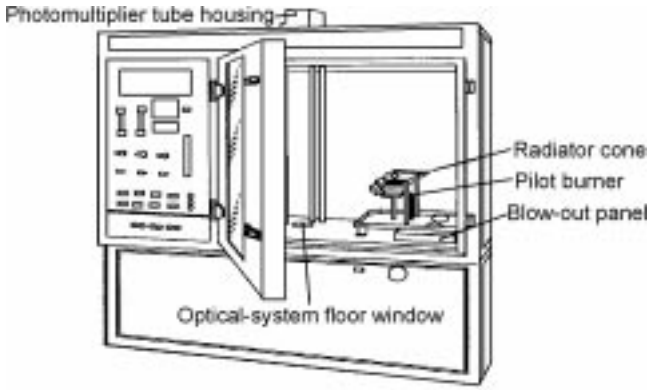
European Union

Fire safety requirements are part of the European Directive on the interoperability of the trans-European high-speed rail system. A Joint Working Group compiled from members of CEN/TC 256 and CENELEC 9X has been working in the formulation of a seven part standard EN 45545 'Railway applications – Fire protection on railway vehicles' since 1991. In 1998, the EU Commission and industry financed the Firestarr Project to develop suitable fire tests and a classification system for materials and components in EN 45545-2. The project was completed in 2001 and the results used to inform the development of the EN standard. However, there have been difficulties with the progress of the seven parts of the new standard. In order to speed up the standardisation procedure, it was decided to first publish the standard as a Technical Specification in 2008, before releasing the final EN 45545 in 2010.

In CEN/TS 45545-2: Requirements for fire behaviour of materials and components,[12] the determination of toxic gases from railway products is described in Annex C. There are two methods used for determining the composition of gases and fumes generated by the combustion of specified railway products.

Method 1: smoke chamber to EN ISO 5659-2[13]

The smoke chamber test (described in Section 12.3.2) is used for large area products (>0.25 m or >100 g) such as walls and ceilings, which are exposed to a



16.2 Smoke chamber to EN ISO 5659-2.

heat flux of 50 kW/m^2 without pilot flame. For floor coverings, that generally receive lower levels of radiant heat during a fire, the test specimens are exposed to a radiant heat flux of 25 kW/m^2 with pilot flame (Fig. 16.2).

Method 2: tube furnace to NF X 70-100-2

This method (described in Section 12.4.1) is used for cables and smaller parts (<0.25 m or <100 g) and based on the exposure of a small mass of test specimen (1 g). The test apparatus consists of a quartz tube and a fixed tubular furnace. Railway products are tested at 600 ºC.

The CIT is determined by using either method one or two. The method to be used is shown in Table 16.2. The CIT is determined and calculated from the eight selected fire gas components carbon monoxide, carbon dioxide, hydrogen

Table 16.2 Test method to be used for determination of CIT

Product	Method 1 EN ISO 5659-2 Smoke chamber area-based test	Method 2 NFX 70-100-2 Small mass-based test
Products with large areas or significant surface areas, e.g. interior walls, floor coverings, seat backs and coverings	Yes	No
Non-listed products, e.g. minor mechanical components, small electrotechnical products	No	Yes
Cables	No	Yes

Table 16.3 Reference concentrations of fire gas components for determination of CIT

Gas components	Reference concentration (mg/m^3)	Approximate equivalent (ppm)
CO_2	72 000	68 000
CO	1 380	2 000
HF	25	52
HCl	75	86
HBr	99	51
HCN	55	85
NO_2	38	34
SO_2	262	170

fluoride, hydrogen chloride, hydrogen bromide, hydrogen cyanide, sulphur dioxide and NO_x either by Fourier transform infrared (FTIR) spectroscopy or other analytical methods by measuring the concentrations of these components and relating them to their reference concentrations.[14] The reference concentrations are shown in Table 16.3; for comparison, approximated concentrations in parts per million (ppm) are also shown.

16.3.2 Ships

The International Maritime Organization (IMO) develops international regulations and standards to improve the safety of sea vessels. In 1996, the IMO developed the Fire Tests Procedure (FTP) Code.[15] This contains fire testing methods for flammability, smoke and toxicity to meet fire safety requirements for materials and components used on ships. The FTP Code fire tests are shown in Table 16.4.

FTP Code Part 2 is the smoke and toxicity test which is identical to the smoke chamber to ISO 5659-2 already mentioned above. The smoke and toxicity requirements measured in ISO 5659-2 are shown in Table 16.5. Here, seven gas components are measured and none must exceed the limit values indicated. Measurement techniques for the gas concentrations are not specified. Recognising that the evaluation of toxicity using this test is prescriptive and not based on fire performance, the criteria have been adopted as an interim solution until the revision of the FTP Code.

Revision of the FTP Code

The revision of the FTP Code started in 2006 with the target of completion in 2008. The objective is to update the existing tests in the FTP Code and to add new fire test methods. It was expected that Part 2 Smoke and toxicity testing

Table 16.4 FTP Code fire tests

FTP Code	Type of test	Referred test method	Similar test method
Part 1	Non-combustibility Test	ISO 1182:1990	–
Part 2	Smoke and Toxicity Test	ISO 5659-2	–
Part 3	Fire Resistance Test for Fire Resistant Divisions	IMO A.754(18)	ISO 834-1
Part 4	Fire Resistance Test for Fire Door Closing Mechanisms	–	–
Part 5	Surface Flammability Test	IMO A.653(16) IMO A.687(17)	ISO 5658-2
Part 6	Test for Primary Deck Coverings	IMO A.653(16)	ISO 5658-2
Part 7	Flammability Tests for Curtains and Vertically Suspended Textiles and Films	IMO A.471(XII) IMO A.563(14)	ISO 6940/41
Part 8	Test for Upholstered Furniture	IMO A.652(16)	BS 5852-1/-2
Part 9	Test for Bedding Components	IMO A.688(17)	EN 597-1/-2

Table 16.5 Smoke and toxicity requirements in the FTP smoke and toxicity test

Product application	Smoke generation	Toxicity	
	Average of max. optical density not to exceed D_s	Gas component	Max. acceptable concentration (ppm)
Surface of wall and ceiling	200	CO	1450
		HBr	600
Surface of floor	500	HCl	600
Primary deck covering (the first layer applied to the steel deck plate)	400	HCN	140
		HF	600
		SO_2	120
		NO_x	350

would extend to ISO 5659-2 by using the FED scenario described in ISO 13344,[16] using FTIR gas analysis. However, at the most recent meeting (May 2009) it was decided that individual gas concentrations would be retained.

16.3.3 Aircraft

Most countries in the world have adopted the US Federal Aviation Regulations (FAR) of the FAA as a basis for ensuring airworthiness.[17] The FAA is advised by experts from the US Aerospace Industries Association, the US Air Transport

Association, the International Civil Aviation Organization and the International Air Transport Association.

The methods used to test materials and components in the cabins and holds of transport aircraft are described in Appendix F of FAR Part 25 – Airworthiness standards: Transport category airplanes. The requirements for materials and parts used in crew and passenger compartments in transport aircraft are given in FAR §25.853. Bunsen burner flammability tests (horizontal, vertical, 45 and 60 degrees inclination) are used.

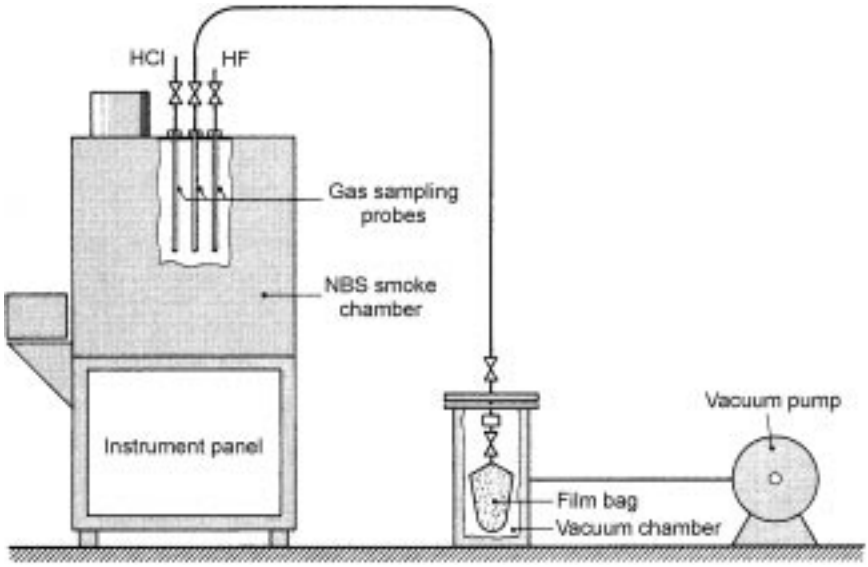
In 1986, the airworthiness standards were amended in the Federal Register with 'improved flammability standards for materials used in the interior of transport category airplanes cabins'. The test method is a modified version of the 'OSU-Chamber' from the Ohio State University to measure the rate of heat release of materials. Subsequent amendments to FAR Part 25 have imposed more stringent requirements on aircraft interiors, which concern crew and passenger seats and cargo or baggage compartments.

The burn-through resistance test has been developed by FAA after the Swissair 111 accident in 1998.[18] The test determines the fire performance of thermal/acoustic insulation materials in the lower half of fuselage with the kerosene burner and is passed if there is no flame penetration for 4 min. The test is compulsory for airplanes manufactured after 3 September 2009.

Additional requirements are often specified, or evidence from standard or modified tests is required, in order to evaluate secondary fire effects. Airbus Industrie, for example, specifies an additional test for smoke density and toxicity of combustion products for materials used in all Airbus models.[19] The basic layout of the test chamber used corresponds to the NBS smoke chamber, specified for example in ASTM E 662.[20]

The toxicity of all parts used in the pressurised area of the fuselage must be tested in the NBS smoke chamber equipped with three gas-sampling probes. These pass through the top of the chamber and reach half way down the smoke chamber as can be seen in Fig. 16.3. The samples required for determining toxicity should be taken at the same time as the smoke density is measured. 'Dräger Tubes' are used for analysis. Analysis for hydrogen chloride and hydrogen fluoride is done directly during the test and other toxic components are determined from a gas sample taken from a film bag filled with the help of a vacuum pump during the test. Analysis of thermal decomposition products resulting from flaming and non-flaming conditions is carried out. The measured values, for whatever thickness is used, must not exceed the concentrations summarised in Table 16.6.

In 2006, the US FAA Technical Center began to develop a laboratory-scale test for evaluating toxic gas decomposition products that could be generated inside the fuselage during a post-crash fire. The so-called 'Steel Cube Box' simulates an intact fuselage and serves as enclosure to collect emitted gases. A FTIR/total hydrocarbon gas analysis system is used to collect and measure toxic



16.3 Airbus Industrie material test specification: analytical measurement of toxicity with the NBS smoke chamber.

and flammable gases yielded during tests. Additional analysers measure the concentration of total hydrocarbons (THC) as propane, carbon monoxide, carbon dioxide and oxygen.

This test method has been developed to evaluate the potential toxicity of insulation constructions meeting the new burn-through test requirements, in order to ensure that no toxic components are formed inside the fuselage. However, the test will probably not be introduced on a mandatory basis.

Table 16.6 Limiting values of toxic smoke gas components within the test duration (16 min for electrical wires and cables, 4 min for all other materials) as specified in Airbus Industrie material test specification

Smoke gas components	Maximum concentration (ppm)
Hydrogen fluoride (HF)	100
Hydrogen chloride (HCl)	150
Hydrogen cyanide (HCN)	150
Sulphur dioxide (SO_2/H_2S)	100
Carbon monoxide (CO)	1000
Nitrous gases (NO/NO_2)	100

16.4 Buildings

In buildings, fire safety requirements concerning the toxicity of fire effluents exist in only a few countries across the world. In France, they are specific to building materials containing certain chemical elements, and in Germany they apply to building materials used in escape routes with a very low contribution to fire. In Poland and Russia, toxicity requirements are prescribed in certain cases for public buildings such as hospitals, schools, retirement homes and cinemas. In China, toxicity requirements apply in buildings, and particularly for thermal insulation products. In Japan, building materials have to meet fire gas toxicity requirements if certain fire performance requirements based on heat release are not met. In the following, the various toxicity requirements in these countries are dealt with in more detail.

16.4.1 France

In France, there are no general toxicity requirements for fire effluents from building products. However, following various spectacular fire incidents in discotheques in the 1970, official controls on the use of synthetic materials in buildings open to the public were introduced.

The regulations governing the use of such materials in buildings open to the public laid down in the Decree of 4 November 1975, its revision of 1 December 1976[21] and subsequent revision on 1 December 2002, specify that the total amounts of nitrogen and chlorine contained in synthetic materials which may be liberated as hydrogen cyanide or hydrogen chloride must not exceed 5 g and 25 g respectively per m^3 of enclosed space. Plastics, synthetic fibres and textiles, elastomers, paints, varnishes and adhesives are considered as synthetic materials. The 2002 revision extended this to insulating materials, and in 2007 fixed theatre seats were removed from the scope. Materials which achieve classes M0 or M1 with no or very limited contribution to fire need not be considered further. Certain materials, such as foams, and special applications are rated with other fire risk factors as shown in Table 16.7.

This decree remains in force, but is not very widely applied. Work is underway to consider the toxicity of fire effluents using performance-based methods from fire safety engineering. Studies have started to explore the options in this field.

16.4.2 Germany

In Germany, toxicity requirements apply to building materials used in high risk areas (escape ways), which have to meet non-combustibility Class A2 as can be seen from Table 16.8.

Table 16.7 Special provisions concerning chlorine and nitrogen levels

Building material classification	Application*		
	Ceiling	Floor	Miscellaneous
M0 or M1 (no or very low contribution to fire)	0	0	0
M2 or M3 (very limited or limited contribution to fire)			
Density $\geq 0.02\,g/cm^3$	$\frac{4bP}{3}$	0	bP
$< 0.02\,g/cm^3$	$\frac{16bP}{9}$	0	$\frac{4bP}{3}$
M4 (Acceptable contribution to fire)			
Density $\geq 0.02\,g/cm^3$	–	$\frac{bP}{5}$	bP
$< 0.02\,g/cm^3$	–	–	$\frac{4bP}{3}$

*P = weight in kg of the nitrogen- or chlorine-containing product.
b = nitrogen or chlorine content in % by weight.

Table 16.8 DIN 4102 classification and test methods for non-combustible building materials

Building material class	Building inspection designation	Test method
A	Non-combustible	
A1		Furnace test 750 °C
A2		'Brandschacht' test (a flammability test in vertical ducting) Smoke density Toxicity Calorific potential to DIN 51900-1 and heat release to DIN 4102-8 or furnace test 750 °C

The determination of the toxicity of fire gases is described in Annex C of DIN 4102-1. Quartz tube furnace, inhalation toxicity testing and calculation are specified in DIN 53 436.[22] The quartz tube test method, described in Section 16.4.5, and a precursor to the ISO steady-state tube furnace, is dynamic with an airflow of 100/l per hour. The animals (at least five rats) are exposed for a minimum of 5 min. The carboxyhaemoglobin level in the animals' blood is determined as well as the death rate (number of deaths per number of animals) observed within 14 days.

As the harmonised European classification and testing system currently does not require toxicity testing for construction products, and as the German toxicity test is related to DIN 4102, it is currently only used in exceptional cases at the instigation of the German authorities. The test will become obsolete with the withdrawal of DIN 4102, as to date, Germany has not notified the European Commission of its national toxicity requirements.

16.4.3 Poland

Toxicity requirements exist in Polish building regulations for high risk areas such as schools, hospitals and cinemas. They will be maintained in Polish building regulations, which are planned to be based on performance rather than on prescriptive requirements in 2010.

Poland has notified the European Commission of amendments in their national building regulations concerning fire safety, which became effective in August 2008. This includes the existing toxicity requirements, which remain as they were in the past. With notification Number 2008/185/PL, on 08 May 2008, Poland has notified the European Commission with some amendments in their building regulations as follows:

- Introduce fire safety adjustments resulting from Poland's membership of the EU, namely European fire classification; the provisions should facilitate the application in Poland of building products which are legally traded on the single European market and which bear CE marking; an Annex is introduced which permits simultaneous application (during the interim period) of the two products and materials fire classification systems – the hitherto national system used in the Regulation and the European classification.
- Take into account the evolution of the set of Polish Norms supplemented by European Norms, approved by the European Committee for Standardization (CEN), the European Electrotechnical Committee for Standardization (CENELEC) and the International Organization for Standardization (ISO).

This also includes the national toxicity requirements valid in Poland and described in the national Polish standard PN-88/B-02855 of 1988.[23]

In Poland, toxicity requirements are prescribed in building regulations, but only for wall coverings and ceilings in public buildings such as hospitals, schools, retirement homes and cinemas; easily combustible products may be used provided they are of low toxicity. Finishing materials such as curtains and blinds in public buildings must not be easily ignitable, have high fire toxicity or cause intensive smoke. In addition, toxicity requirements apply for seats in public buildings with more than 200 adults or 100 children; here the seats should not be easily combustible, and be of low fire toxicity when tested according to the Polish standard PN-88/B-02855 of 1988.

The national fire tests used in Poland and referred to in the national building regulations classification system will be replaced by the European Euroclasses and fire tests. What is left is the national Polish toxicity test to PN-88/B-02855 'Protection of Buildings from Fire: Assessment method for toxic products from pyrolysing and burning materials'. Use of this test for prescribed building materials has been mandatory in Poland since 2001. The test is based on the German quartz tube test to DIN 53436 (see Section 16.4.2), while the evaluation and classification of toxicity is made according to the Russian combustion gases toxicity test GOST 12.1.044-89 Part 4.20 (see Section 16.4.4). Both tests are described in Chapter 12.

Gas chromatography is used for analysis of carbon monoxide and carbondioxide, and other methods for the analysis of nitrogen dioxide, hydrogen cyanide and hydrogen chloride. The tests are conducted in a quartz tube heated by a short tubular furnace. The test conditions are:

- furnace velocity: 20 mm/min;
- air flux (counter-current to the direction of furnace motion): 100 dm^3/h = 1.66 l/min;
- temperatures of decomposition: 450, 550, 750 ºC;
- quartz tube length: 1000 mm;
- quartz tube diameter: 30 or 40 mm;
- sample mass: 5.4 g.

According to GOST 12.1.044-89 Part 4.20, the analysed toxic components are quantified as the mass of combustion product generated from the mass unit of the sample. The toxicity of the gaseous components is estimated using critical concentrations for each component, called W_{LC50}.

Lethal concentrations of various toxic components after 30 min exposure are:

- CO: 3.75 g/m^3
- NO_2: 0.205 g/m^3
- CO_2: 196 g/m^3
- HCN: 0.16 g/m^3
- HCl: 1.0 g/m^3

Toxic hazard is assessed on the basis of the arithmetic mean of factors W_{LC50M} for the temperatures 500, 550 and 750 ºC (W_{LC50SM}). This factor enables dominant toxic combustion products for each material to be determined, and materials to be classified into groups according to their toxic products.

On the basis of the W_{LC50SM} values, materials are divided into three groups: very toxic, toxic, and moderately toxic, as can be seen in Table 16.9. In addition, the test is used to characterise smoke production, classifying materials in terms of visual obscuration (as low obscuration, intermediate, intense and lachrymatory). The Polish toxicity requirements for public buildings are not likely to change in the near future. However, a set of new building regulations is

Table 16.9 Categories of toxic hazard in fire

W_{LC50SM} (g/m^3)	Category of toxic hazard in fire
0–15	Very toxic
15–40	Toxic
>40	Moderately toxic

currently worked out and will probably be introduced in the future. It is expected that the regulations will not be prescriptive, but rather performance-based and cover the whole planning of a building.

16.4.4 Russia

The classification of the fire behaviour of building products and the related standards are described in NPB 244-97: Decorative finishing and facing materials, fire hazard parameters.[24] The toxicity test apparatus and toxicity determination are described in Part 4.20, the classification criteria in Part 2.16.2 of GOST 12.1.044-89.

In the combustion gas toxicity test to GOST 12.1.044-89 Part 4.20,[25] the toxicity is determined by tests with live animals (mice) (Fig. 16.4). The decomposition device is described in Chapter 12, and can be run under smouldering and flaming conditions.

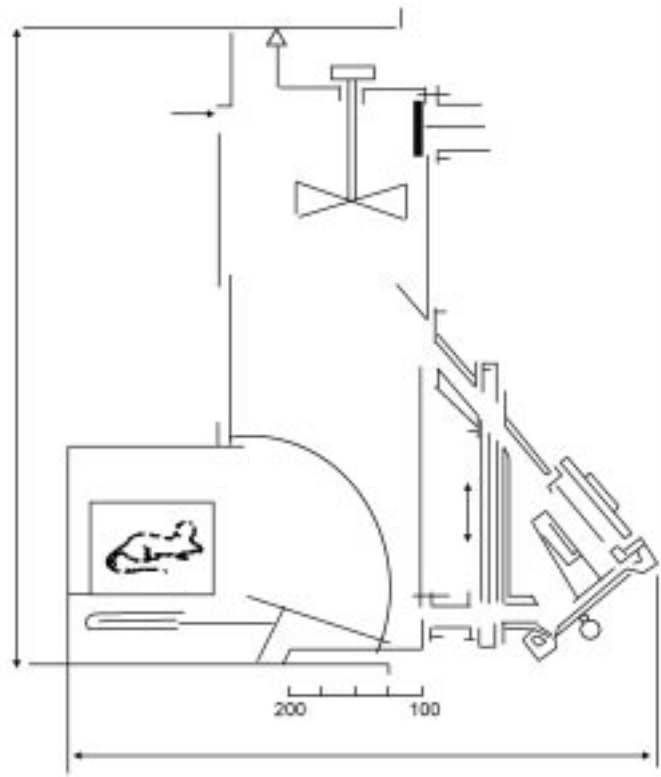
The test chamber consists of three parts:

- Combustion chamber with the decomposition device: volume 0.003 m^3;
- Prechamber containing the test animal: volume 0.015 m^3;
- Variable exposure chamber: minimum volume 0.1 m^3; maximum volume 0.2 m^3.

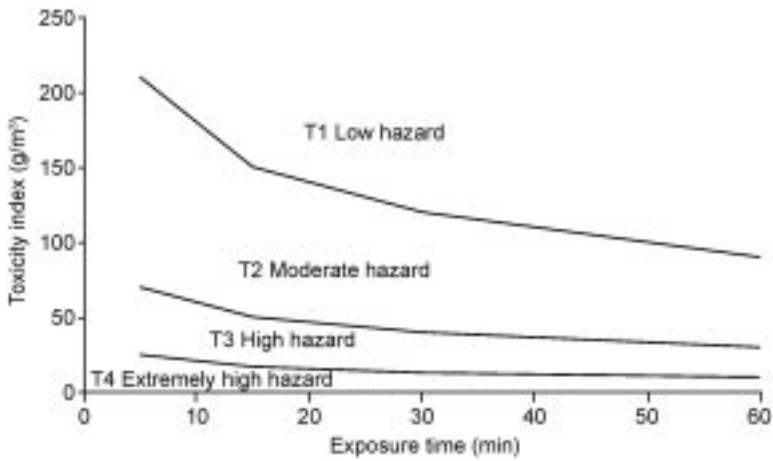
The toxicity of building materials is subdivided into four classes with the requirements prescribed in Part 2.16.2 of GOST 12.1.044-89 shown in Fig. 16.5.

The toxicity index $^{H}CL_{50}$ is based on the mass concentrations in the fire effluents (g/m^3) measured in the chamber leading to the death of 50% of the animals (lethal concentration LC_{50}, or here CL_{50}) within the time of exposure in the chamber (5–60 min). The LC_{50} values used are derived from the amount of carbon monoxide formed per sample mass unit (g/g), and their amount bound as carboxyhaemoglobin in the blood of the animals.

Analytical determination of fire gas components like carbon monoxide, carbon dioxide, hydrogen cyanide, NO_x, aldehydes and other substances is also carried out (although halogen acids such as hydrogen chloride, hydrogen bromide and hydrogen fluoride are not mentioned). However, the main effect is seen from the toxic action of carbon monoxide, also quantified as carboxyhaemoglobin, and referred to for toxicity index determination in this test method.



16.4 Toxicity test chamber to GOST 12.1.044-89 Part 4.20.



16.5 Toxicity index to GOST 12.1.044-89 Part 2.16.

16.4.5 China

The use of building materials in China basically conforms to the Fire Law of the People's Republic of China (issued and implemented in 1984). In practical applications, the performance requirements and the application fields for materials are specified in more detail in relevant laws and regulations, such as the

- fire protection code for building design;
- fire protection code for civil high rise building design;
- fire protection code for building internal decorations and others.

In order to define the fire performance of building materials, the China State Bureau of Quality and Technical Supervision has issued a standard on the classification and burning behaviour of building materials,[26] in which the classification of fire properties of building materials is specified, and the technical parameters and test methods that determine whether the materials reach the relevant class are described.

Particularly for fire retarded products and sub-assemblies in public places, fire safety requirements including toxicity apply. GB/T 20286-2006 requires the burning behaviour to be tested and marked on such products.[27] The toxicity requirements for Class 1 and 2 products and sub-assemblies are shown in Table 16.10. Classification and testing of the toxicity of fire effluents are described in the standard GB/T 20285-2006,[28] which supersedes GA 132-1996. The new standard became effective in November 2006. The test method is derived from the German quartz tube furnace test to DIN 53436, and the rotating cages for mice from the Japanese Notification JIS A 1321. The acute inhalation toxicity of fire effluents (incapacitation, irritancy, lethality) is determined in a biological assay on 10 mice. The test duration is 30 min.

The toxicity classification of fire effluents hazard for materials is shown in Table 16.11. There are three main classes for safe materials (AQ), materials of moderate safety (ZA) and hazardous materials (WX). For fire retarded products and sub-assemblies, classes ZA2 or ZA3 have to be met.

Table 16.10 Classification of the toxicity of fire effluents to GB/T 20286-2006

Fire retardant level	Standard	Requirements
Class 1	GB/T 20285-2006	Toxicity of fire effluents $\leq$ ZA2
Class 2	GB/T 20285-2006	Toxicity of fire effluents $\leq$ ZA3

Table 16.11 Toxicity classification of fire effluents hazard for materials

Level	Safety level AQ		Sub-safety level ZA			Hazard level (WX)
	AQ1	AQ2	ZA1	ZA2	ZA3	
Loading limit of material per unit volume (mg/l)	≥ 100	≥ 50	≥ 25	≥ 12.4	≥ 6.15	< 6.15
Requirements	Anaesthesia (incapacitation)		Laboratory rat died within inhalation toxicity period of 30 min (including the period within 1 h after inhalation toxicity test)			
	Irritancy		Average weight of laboratory rat recovered within 3 days after inhalation toxicity test			

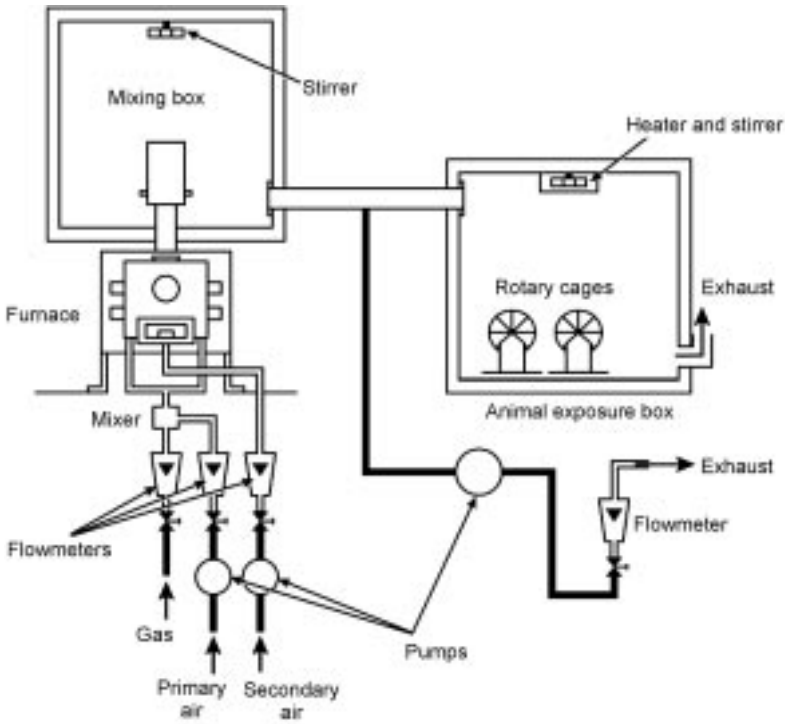
16.4.6 Japan

The Japanese Building Standards Law (BSL) aims at 'protecting the lives, health, and wealth of citizens, and thus contribute to the prosperity of the community, by laying down guidelines and standards for plots of land, building design, furnishing and use'. A revision of the main parts of the BSL, including the fire safety design systems, came into force on 1 June 2000.[29] This revision has started a process of change from a specification-based to a performance-oriented design.

Under the BSL, the Ministry of Land, Infrastructure, Transport and Tourism (MLIT) gives mandates to organisations to develop and evaluate classification systems and test methods for building materials and products in relation to fire safety. Eventually, such systems will be approved by MLIT. Currently, Notification No. 1231 of 1976[30] is still valid and used to evaluate the toxicity of fire effluents from building products. However, if a building product shows low heat release values in the cone calorimeter test, it may be exempted from toxicity testing.

Notification No. 1231 determines the incapacitation point of test animals. The test apparatus consists of a furnace based on the UK fire propagation test to BS 476 Part 6 where the test materials are decomposed; the decomposition products pass via a mixing chamber into the exposure chamber with the test animals placed in cages with running wheels (Fig. 16.6). The testing device is described in Chapter 12.

The specimen in the furnace is decomposed over an area of 180 mm by 180 mm for 6 min. During the first 3 min it is exposed to the gas pilot flame (partial heat load) and subsequently to the additional electric heater (full heat load). Eight cages each contain a running wheel and a 5-week-old female mouse, weighing between 18 and 22 g. The running wheels are made from aluminium



16.6 Toxicological inhalation apparatus according to Notification No. 1231.

and weigh about 75 g. The time from the start of heating until incapacitation of the mice is registered automatically up to a total time of 15 min.

The mean standard incapacitation time for standard specimens of red lauan wood (Philippine mahogany) is determined. The mean incapacitation time is also determined for the material under investigation. Two separate investigations are carried out for each material. If the mean incapacitation time is longer than that of the standard specimen, the material is permitted.

The mean incapacitation time X_s is obtained from

$$X_s = X - \sigma$$

where X is the arithmetic mean and σ the standard deviation of the incapacitation times for the eight mice. If no incapacitation occurs the time is reckoned as 15 min.

16.5 Future trends

In fire safety regulations, the trend is towards fire performance tests allowing the development of fire scenarios and modelling. These new developments are also increasingly applied for toxicity testing in transportation and building.

In transportation, toxicity requirements apply on an international basis. For railways, the new European toxicity requirements will be used instead of the existing national ones and apply for all European member states. The tests are analytic and the evaluation is based on fire scenarios. For ships, this system will be taken over in the frame of the revised FTP Code. For aircraft, Airbus Industrie may also introduce the new evaluation procedures and discontinue the use of Dräger tubes. In the USA too, the trend is toward such evaluation procedures at least in the toxicity tests under development.

In building, toxicity requirements only apply for a limited number of countries so far. In France, the toxicity of fire effluents may be considered in future performance-based requirements for building. Studies have started to explore the options in this field. The Polish prescriptive toxicity requirements for public buildings are not likely to change in the near future. However, new, performance-based building regulations are currently being considered. Russia will take over the European Union reaction to fire classification and testing systems for building, and the existing national fire tests may become obsolete. It is unclear what will happen with the Russian toxicity requirements and tests. In China, toxicity requirements apply for construction products and particularly thermal insulation foams. In Japan, the toxicity testing of building products is required for materials exceeding certain heat release values. In all these countries, in principle, the toxicity tests are conducted with animals. However, in the light of the efforts to limit the use of animals in toxicity testing and of the introduction of fire performance requirements and related fire scenarios, the trend is to analytical tests, and this is already the case in the transportation sector.

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17

An international standardised framework for prediction of fire gas toxicity

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Abstract: Most of the recent developments in estimating and quantifying fire effluent toxicity have been channeled through one of the ISO technical committees, 'ISO TC92 SC3 Fire Threat to People and the Environment'. This international group of experts has produced a suite of standards allowing the quantification of fire effluent toxicity to be estimated so that fire safety engineers, fire investigators and other professionals have a robust framework around which to base their judgment. The current and future work, and content of key standards and groups are outlined.

Key words: ISO, fire, effluent, toxicity, people, environment, standards, fire safety engineering.

17.1 Introduction

The development of national and industry-specific standards as described in Chapter 16 has largely been piecemeal, often with standards and regulations developed in response to events such as fire disasters, or the perception of their likelihood. Development of standards, on a national or industry-specific level, is a simpler process than development of international standards; it requires less harmonisation in the cultures, practices and approaches, but results in different strategies for dealing with common problems. In the European Union, for example, the desire to remove trade barriers across Europe has eventually led to the harmonisation of classification of building products, following the Construction Products Directive.[1] This has been a slow process in which individual countries withdrew their existing classification criteria in exchange for new, and usually different, test methods and criteria. In contrast, in the area of fire effluent toxicity, a high proportion of the leading work developing a coherent set of standards and guidance for the assessment of the fire threat to people, and more recently also to the environment, has been undertaken on an international level by the International Organization for Standardization (ISO). In the longer term, this has clear advantages, since industries and regulators do not have the breadth of different standards to contend with, and with the progressive globalisation of

trade, represents the only practicable solution to the problem of regulating fire toxicity. These documents are then available for adoption by national organisations (such as the British Standards Institution (BSI), the American National Standards Institute (ANSI) or the Deutsches Institut für Normung (DIN)) or specific communities (such as CEN, the European Committee for Standardization, or IMO, the International Maritime Organisation).

The main objectives[2] of ISO/TC92 are to develop standards and other documents to cover:

- fire safety engineering – design and evaluation methods used to verify that appropriate fire safety objectives have been achieved;
- the fire performance of materials, products, elements of structure, structures and systems and their contents, where appropriate, in end use conditions;
- the application of fire safety management;
- characterisation of occupant performance and behaviour when subjected to fire conditions and fire like emergency situations.

TC92 has a long of tradition of work in the area of fire safety in buildings, but in 1995 its scope was extended to fire safety in general, and TC92 became a 'horizontal committee', with responsibility for coordination of all fire activities in ISO. The possibility of TC92 moving into areas such as transportation, tunnel safety and forest fires is being explored. Fire investigation is a growing discipline and TC92 could also become involved in this area. TC92 holds meetings once every two years as a whole, with the timing and location of SC1, 2, 3 and 4 coinciding with the plenary meeting of TC92.

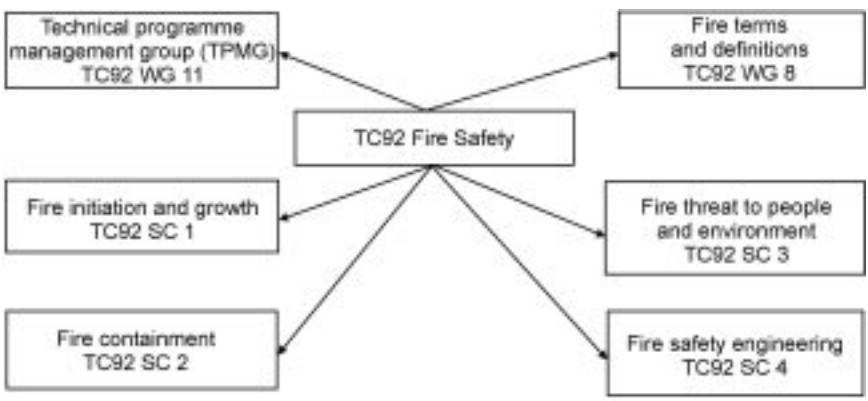
17.2 The workings of the International Organization for Standardization (ISO) Technical Committee on Fire Safety (TC92)

ISO standards are written by members of their technical committees (TCs), or more often by the respective subcommittees (SCs) and their working groups (WGs). ISO technical committees comprise experts designated by national standards organisations which have opted to be members of that particular ISO committee. The aim is to develop documents by consensus, which have the support of the national experts, and who will hopefully convey that support to their individual countries. The current membership of the Fire Safety Committee TC92 is shown in Table 17.1.

Most of the work within ISO TC92 (Fire Safety) is undertaken by one of its four subcommittees, shown in Fig. 17.1: SC 1 Fire initiation and growth; SC 2 Fire containment; SC 3 Fire threat to people and environment; and SC 4 Fire safety engineering. In addition it has two of its own working groups: one dealing with vocabulary, for all the fire standards, WG 8 Fire terms and definitions, producing just one standard (ISO 13493);[3] the other, WG 11, the technical

Table 17.1 Membership of ISO TC92 (Fire Safety)

Participating countries: 26	Observing countries: 44	
UK (BSI) **Secretariat**		
Australia (SA)	Argentina (IRAM)	Moldova, Republic of (INSM)
Belarus (BELST)	Austria (ON)	Mongolia (MASM)
Belgium (NBN)	Azerbaijan (AZSTAND)	Montenegro (ISME)
Brazil (ABNT)	Barbados (BNSI)	Morocco (SNIMA)
Canada (SCC)	Botswana (BOBS)	Pakistan (PSQCA)
China (SAC)	Bulgaria (BDS)	Philippines (BPS)
Czech Republic (UNMZ)	Colombia (ICONTEC)	Poland (PKN)
Denmark (DS)	Croatia (HZN)	Portugal (IPQ)
France (AFNOR)	Cuba (NC)	Romania (ASRO)
Germany (DIN)	Ecuador (INEN)	Saudi Arabia (SASO)
Greece (ELOT)	Egypt (EOS)	Singapore (SPRING SG)
Hungary (MSZT)	Estonia (EVS)	Slovakia (SUTN)
Italy (UNI)	Fiji (FTSQCO)	Slovenia (SIST)
Japan (JISC)	Finland (SFS)	Sri Lanka (SLSI)
Kenya (KEBS)	Hong Kong, China (ITCHKSAR)	Switzerland (SNV)
Korea, Republic of (KATS)	India (BIS)	Tanzania (TBS)
Netherlands (NEN)	Indonesia (BSN)	Thailand (TISI)
New Zealand (SNZ)	Iran, Islamic Republic of (ISIRI)	Trinidad and Tobago (TTBS)
Norway (SN)	Ireland (NSAI)	Tunisia (INNORPI)
Russian Federation (GOST R)	Israel (SII)	Turkey (TSE)
Serbia (ISS)	Jamaica (BSJ)	Ukraine (DSSU)
South Africa (SABS)	Malaysia (DSM)	Venezuela (FONDONORMA)
Spain (AENOR)		
Sweden (SIS)		
USA (ANSI)		



17.1 Structure of ISO TC92 (Fire Safety).

programme management group (TPMG), which advises on the work on the TC's programme.

17.2.1 Sub-committees of ISO TC92 (Fire Safety)

Most of the work on fire toxicity is covered in subcommittee 3 (SC3), but the responsibility of SC1 for test protocols has recently been used to justify the development of Fourier transform infrared (FTIR) analysis of fire effluents for the ISO room (ISO 9705) and the smoke density chamber (ISO 5659) in conjunction with SC3. These could be used to quantify toxic product yields, although the fire conditions may be poorly defined, and they do not meet the requirements specified for such tests by SC3.

The objectives of **SC 1 – Fire initiation and growth** are summarised below.

1. Test protocols, measuring techniques and fire scenarios in support of fire safety engineering.
   a) Test protocols, measuring techniques and procedures for securing data of fundamental fire properties.
   b) Test protocols, measuring techniques and procedures for input data to FSE models.
   c) Standards relating to fire scenarios and characteristic fire growth of products.
2. Performance codes.
   a) Test protocols for reference scenarios.
   b) Test protocols, measuring techniques and procedures for fire calorimetry.
3. Maintain and improve existing SC 1 standards.
   a) Updating tests already in use.
4. Test validation.
   a) Protocols to determine the precision of fire test procedures.
   b) Test protocols for validation of fire growth predictions.
5. Instrumentation protocols for measurement technologies used in fire test procedures.

The objectives of **SC 2 – Fire containment** are shown for completeness. This subcommittee is concerned with 'fire resistance', the maintenance of structural integrity in fire. However, developments in the use of composite materials, such as fibreglass and more recently carbon fibre epoxy composites used to construct aircraft fuselages, could be flammable, and release toxic products, in addition to their core requirement of maintaining structural integrity, even in a fire.

1. Maintain and improve existing ISO standards.
   a) Improve current measurement techniques and review their application in all appropriate standards. Review the acceptance criteria and data

output formats for all fire resistance standards with the intent of applying them uniformly across all assembly types.
   b) Improve conditioning of test articles.
   c) Improve reproducibility of test results. This must be done by considering specimen construction, restraint details, conditioning and test exposure conditions.
   d) Characterise laboratory ambient conditions and measurement of unexposed surface temperatures.
2. Develop new fire standards where need is identified. Integrate outputs from fire resistance tests and calculations with fire safety engineering.
   a) Generate data which allow prediction of the fire performance of the material, product, or assembly, in the orientation in which it might be installed in practice.
   b) Specify the exposure conditions corresponding to the material, product or assembly might most likely be exposed in practice.
   c) Provide numerical output suitable for electronic data storage and retrieval.
   d) Define, in measurable units, any external force, restraint, stress or pressure applied to the sample.
   e) Account for special testing conditions (for example, edge effects), or justify the corresponding lack thereof, to enable the data to be applied to actual installation conditions.
   f) Describe in the appendix or scope of each standard that fire safety engineering is a potential use of the standard.

The work of **SC 3 – Fire threat to people and environment** has been focused on the proper understanding and assessment of the toxicity of fire effluents, although recent work has also included the environmental effects of fire effluents. Two objectives are listed in the business plan,[2] followed by a rather fanciful list of projects covering the work over the next 4 years. The first objective covers most of the existing standards, and those under development, the second focuses on the application to fire safety engineering.

1. Provide appropriate guides and calculation methods, along with instrumentation, measurement and validation procedures for analysis and assessment of the impact of fire and its effluents on people and the environment.
2. Develop guidance on the use of such procedures in fire safety engineering, including the compilation of criteria for human exposure. Data on the harmful effects are only to be used in the context of fire safety engineering, rather than being the basis for pass/fail tests.

Projects for the coming 4 years (where appropriate standard numbers have been shown in brackets, and are described in the following sections) are:

1. Chemical species produced in fires (includes both gases and smoke).
   a) Standards for instrumentation and procedures for the analysis of fire-generated gases and aerosols (19700, 19701, 19702, 29903).
   b) Documentation of chemical yields and formation rates relative to fire types and stages, including stability, transport and decay rates.
   c) Standards for measuring the concentrations of COHb and HCN in blood and guidance for relation to exposure (27368).
2. Generation of data on yields of chemical species in fires.
   a) Criteria for appraising bench-scale test apparatus for this purpose (16312-1).
   b) Assessment of currently used devices and procedures (16312-2).
3. Acute toxic effects – incapacitation (inability to effect one's own escape).
   a) Quantification of the impact of asphyxiant and irritant fire gases on people (13571).
   b) Procedures and guidance for establishing exposure criteria.
4. Chronic toxic effects (later, following pre-normative work).
   a) Quantification of the effects of soot containing PCDD (polychlorinated dibenzodioxins), PCDF (polychlorinated dibenzofurans), PAH (polycylic aromatic hydrocarbons) on people and the environment.
   b) Procedures and guidance for establishing exposure criteria.
5. Heat effects.
   a) Quantification of the effects of both radiant and convective heat in causing thermal burns, hyperthermia and respiratory distress of people (13571).
   b) Procedures and guidance for establishing exposure criteria.
6. Smoke effects.
   a) Guidance for establishing visibility criteria for people.
7. Environmental effects of fires.
   a) Guidance on environmental effects for which international standardisation is appropriate (26367-1).
   b) Identification (definition) gas, liquid, solid contaminants (26367-2).
   c) Effect of combustion conditions on yields.
   d) Assessment of harm from multiple contaminants.
   e) Bioimpact of contaminants.
   f) Containment of runoff of fire suppression water (26368).

The importance of relating fire toxicity to fire conditions is recognised in the clear links between SC3 and the fire safety engineering of SC4, rather than with the pass/fail tests of SC1, which are better suited to simple ignitability, flame spread and heat release tests. The objectives of **SC 4 – Fire safety engineering** are as follows:

1. Provide the necessary fire safety engineering (FSE) documents called for in

the TC92 framework document supporting performance-based design and assessment.
2. Develop and maintain a set of ISO documents on the use of fire safety engineering.
3. Develop engineering design and evaluation methods to be used for verifying that appropriate fire safety objectives are achieved.
4. Standardise, when not handled by another SC or TC, the necessary calculation or other assessment methods, including determination of their accuracy and limitations.
5. Provide the full range of standards required for performance-based fire safety design and assessment.
6. Develop rules and/or standards for validation procedures.
7. Develop guidance documents for best engineering practice.
8. Set up links with regional standardisation bodies involved in FSE.

Among the planned projects over the next 4 years are several relating to fire toxicity, including the following:

1. Develop documents for the overall process of fire safety engineering considering interaction among components of fire safety, possible tools to be used for analysis and all foreseen fire safety objectives such as:
   a) life and health safety;
   b) property safety;
   c) prevention of business interruption;
   d) prevention of environmental contamination;
   e) conservation of heritage.
2. Input to FSE methods, including development of evacuation data.

17.3 Fire threat to people and the environment TC92 SC3

SC3 meets twice per year, normally coinciding with SC4's meetings. Its structure is dictated by its workload – individual working groups are disbanded when the work is completed. Currently there are four working groups:

- TC92/SC 3/WG 1 Physical fire models
- TC92/SC 3/WG 2 Fire chemistry
- TC92/SC 3/WG 5 Prediction of toxic effects of fire effluents
- TC92/SC 3/WG 6 Fire threat to the environment

Within the working groups, experts develop standards, taking the views of the national member bodies (as represented by the experts) into account, in order to maximise the likelihood of a positive vote in the ballots at each stage of standard development. Thus, although the subcommittee takes votes and makes decisions at their plenary meetings, these are primarily procedural – the role of the

committee is to produce documents which will be supported by an international consensus.

Although individual working groups have their own designated experts, in most cases experts contribute to more than one or all of the working groups, largely independent of their designations. WG 1 is primarily concerned with the generation of fire effluents; the techniques used to relate these to particular fire conditions; the relationships between different generation methods; and the validity of individual results and methods. WG 2 is primarily focused on the chemical analysis of fire effluents from physical fire models; from real fires; and in the blood of fire victims. These effluents include both the gaseous, aerosol and (particularly in the case of environmental work in conjunction with WG 6) non-volatile fire residues. WG 5 relates the composition of fire effluents to the toxic effects. The most recently established group, WG 6, deals with the fire threat to the environment, increasingly seen as a major concern, as fire fighting protocols have been broadened from protection of life and property, to include protection of the environment.

17.4 Overview of assessment of hazards to life

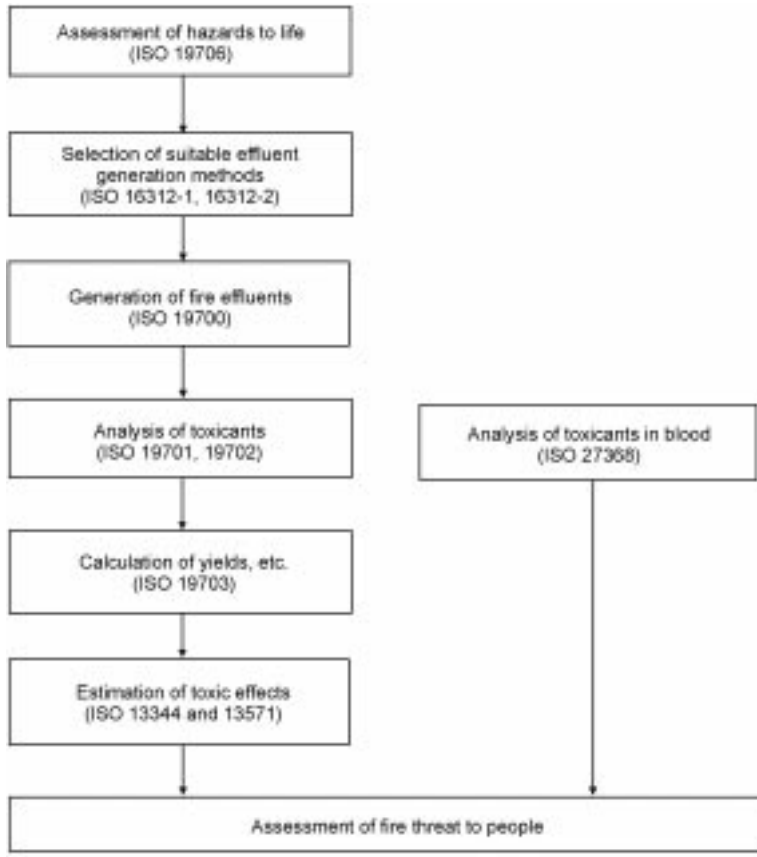
The contribution of individual components and the existing standards towards the overall assessment of hazards to life from fire is shown in Fig. 17.2.

17.5 Current International Organization for Standardization (ISO) standards covering fire threat to people and the environment

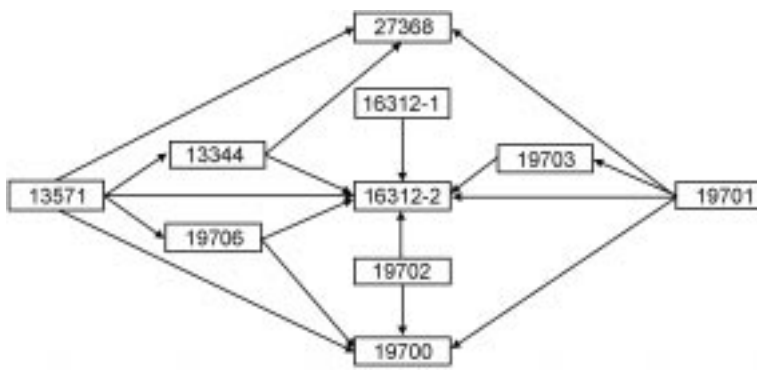
Figure 17.3 shows a 'hierarchy of standards', indicating which SC3 standards are considered essential for use of others (for example ISO 13571, 13344 and 19701 are considered essential for use of ISO27368). Using the same logical progression as in Fig. 17.2, a brief description of each of the standards is provided.

17.5.1 ISO 19706:2007 Guidelines for assessing the fire threat to people

This standard provides the introductory framework for assessment of the fire threat to people. Its purpose is to provide general guidance to the fire threat to people and to the development of quantitative information on effluent potency for use in fire hazard and risk assessment. It considers the consequences of a single acute human exposure to fire effluent. It covers the development, evaluation and use of relevant quantitative information for use in fire hazard and risk assessment, from fire incidence investigation, fire statistics, real-scale fire tests and from physical fire models. It addresses the uncertainty in the



17.2 Overview of processes and standards leading to the assessment of the hazards to life from fire (relevant standard numbers are shown in brackets).



17.3 'Hierarchy of standards'.

characterisation of fire effluent, the measurement of effluent effects, and the accuracy of the measurements. The data can be used with computational models for analysis of the initiation and development of fire, fire spread, smoke formation and movement, chemical species generation, transport and decay and people movement, as well as fire detection and suppression.

17.5.2 ISO 16312-1 Guidance for assessing the validity of physical fire models for obtaining fire effluent toxicity data for fire hazard and risk assessment – Part 1: Criteria

Ensuring life safety often involves an explicit fire hazard or risk assessment, which includes the potential for harm due to the effluent produced in the fire. A bench-scale test apparatus or 'physical fire model' is generally the most practical and economic choice for generating accurate data on the composition of toxic effluent, but it is essential to recreate the environments of full-scale fires. This standard describes the technical criteria for evaluating physical fire models used in effluent toxicity studies for obtaining data on the effluent from products and materials under fire conditions relevant to life safety. Bench-scale methods are discussed in more detail in Chapter 12.

17.5.3 ISO TR16312-2 Guidance for assessing the validity of physical fire models for obtaining fire effluent toxicity data for fire hazard and risk assessment – Part 2: Evaluation of individual physical fire models

The role of a physical fire model, or bench-scale method, is to generate accurate toxic effluent composition. This must be capable of simulating the essential features of the complex thermal and reactive chemical environment in full-scale fires, which vary with the physical characteristics of the fire scenario and with time during the course of the fire. This technical report comprises assessment of the criteria in ISO 16312-1 to test methods in current use for generating data on smoke effluent from burning materials and commercial products. Twelve physical fire models are discussed in the current version: the first five are closed systems; the remainder open, or with air continuously flowing past the combusting sample. Additional apparatus may be added as it is developed or adapted for generating information regarding the toxic potency of smoke. It assesses the utility of physical fire models for generating fire effluent toxicity data of known accuracy. Using the criteria established in ISO 16312-1 and the guidelines established in ISO 19706, the aspects of the models that are considered are:

- the intended application of the model;
- the combustion principles it manifests;

- the fire stage(s) that the model attempts to replicate;
- the types of data generated;
- the nature and appropriateness of the combustion conditions to which test specimens are exposed; and
- the degree of validity established for the model.

Concern over the emphasis in this chapter led to publication of a critical review of bench-scale test methods.[4]

17.5.4 ISO 13344:2004 Estimation of lethal toxic potency of fire effluents

The pyrolysis or combustion of combustible material produces a fire effluent atmosphere, which, in sufficiently high concentration, is toxic. Since it is necessary to quantify such toxicity, ideally without involving the exposure of animals in standard tests, this standard refers to existing animal exposure data, and calculations to express test results as they would have been obtained had animals actually been exposed.

The two parameters calculated using this standard are the FED (Fractional Effective Dose) and the LC_{50} of the material in $g\,m^{-3}$. The lethal toxic potency values (LC_{50}) are specific to the fire model selected, the exposure scenario and the material under test. Lethal toxic potency values associated with 30 min exposures of rats can be predicted using calculations which employ combustion atmosphere analytical data for carbon monoxide (CO), carbon dioxide (CO_2), oxygen (O_2) (oxygen depletion) and, if present, hydrogen cyanide (HCN), hydrogen chloride (HCl), hydrogen bromide (HBr), and other toxicants which have been demonstrated to be appropriate. If the fire effluent toxic potency cannot be attributed to the toxicants analysed, this is an indication that other toxicants or factors must be considered (see Chapters 3–8).

17.5.5 ISO 13571:2007 Life-threatening components of fire: Guidelines for the estimation of time available for escape using fire data

The crucial criterion for life safety in fires is that the time available for escape be greater than the time required for escape. The methodology described in this standard provides a framework for estimating the time available for escape – the interval between the time of ignition and the time after which conditions become untenable, such that occupants can no longer take effective action to accomplish their own escape. The standard considers four effects which make conditions untenable during fires: exposure to radiant and convected heat; inhalation of asphyxiant gases; exposure to sensory/upper-respiratory irritants; and visual obscuration due to smoke.

The nature of both the fire (e.g. heat release rate, quantity and types of combustibles, fuel chemistry) and of the enclosure (e.g. dimensions, ventilation) determines the toxic gas concentrations, the gas and wall temperatures and the density of smoke throughout the enclosure as a function of time. The characteristics of the occupants (e.g. age, state of health, location relative to the fire, activity at the time of exposure) also affect the impact of their exposure to the heat and smoke. The interrelationship of all these factors is described in Annex A, which also describes the context and mechanisms of the fire-effluent toxicity component of life threat. The toxic effects of aerosols and particulates and their interactions with gaseous fire-effluent components are not considered, nor are the longer-term adverse health effects following exposure to fire atmospheres.

Equations are presented to enable estimation of the conditions which prevent occupants from being able to escape, in order to predict the time for which escape is feasible. It is intended to be used with models of fire, fire spread, smoke formation and movement, chemical species generation, transport and decay and people movement, as well as fire detection and suppression. Two methods are presented for assessment of fire-effluent toxicity: the toxic gas model and the mass-loss model (see also Chapters 3, 4, 7 and 8).

17.5.6 ISO 19700:2007 Controlled equivalence ratio method for the determination of hazardous components of fire effluents

This technical specification describes the steady-state tube furnace (Purser furnace) and a methodology for using it to determine the equivalence ratio corresponding to the toxic product yields obtained. The document has been developed as a precursor to a full international standard to encourage wider deployment of the apparatus. As a bench-scale physical fire model, it is used to measure toxic product yields from materials and products over a range of decomposition conditions in fires. The decomposition conditions are defined in terms of the fuel/air equivalence ratio ϕ, temperature and flaming behaviour.

Performance-based assessment of the toxic hazard in a fire needs the yield of toxic products under specified fire conditions as input data. For a particular material or product, the effluent yields in fires depend upon the thermal decomposition conditions, particularly non-flaming or flaming, and for flaming decomposition the fuel/oxygen ratio. The technique described provides data on the range of toxic product yields likely to occur in different types and stages of full-scale fires. For more extreme conditions product yields can be obtained by using a wider range of apparatus settings, as described in an annex. The apparatus uses a moving test specimen and a static tube furnace at different temperatures and air flow rates as the physical fire model. The method can be used for individual materials, and products that are layered providing the

layering will not significantly alter the product yields compared to real fires. For a fuller description of the apparatus, see Chapter 12.

Other annexes describe the application of data from the tube furnace to the calculation of lethal toxic potency according to ISO 13344, and the assessment of toxic hazards in fires according to ISO 13571.

17.5.7 ISO 19701:2005 Methods for sampling and analysis of fire effluents

The analysis of fire gases for use in toxic hazard and life threat assessment is challenging for the analyst. Fire atmospheres are by nature hostile environments, temperatures in excess of 1000 ºC are common, the atmosphere may be laden with solid and liquid particulates, and the gas phase itself may contain many corrosive, toxic and irritant species together with relatively large quantities of condensable water. These properties are largely incompatible with most instrumental analytical methods where a 'clean' sample is required. This poses many problems both for the qualification and quantification of the chemical species and particulates in fire atmospheres. It may be necessary to filter particulates and remove interferences, and take into account losses in the sampling train. This standard presents a range of chemical analytical methods, suitable for the analysis of individual chemical species in fire atmospheres. Analysis methods for the following components of fire effluent are described:

- narcotic (asphyxiant) gases – carbon monoxide, hydrogen cyanide, oxygen and carbon dioxide.
- irritant gases and vapours in the fire atmosphere – hydrogen chloride, hydrogen bromide, hydrogen fluoride, NO_x, acrolein, formaldehyde, sulphur dioxide, ammonia, antimony and arsenic, phosphorus and phosphates.
- particulates – although more detailed methodologies for quantifying particle mass number density and particle size in a new standard under development. These topics are also addressed in Chapter 11.

The annexes provide brief guidance for the analysis of several other species of interest in fire atmospheres; methods which use aspirated chemical colour change tubes; the general principles of sampling; and the main instrumental methods available for fire gas analysis.

17.5.8 ISO 19702:2006 Toxicity testing of fire effluents: Guidance for analysis of gases and vapours in fire effluents using FTIR gas analysis

The standard describes the application of FTIR spectroscopy as a single method to determine nearly all of the important toxic gases. The standard includes specific recommendations for sampling systems for use in small-scale and large-

scale measurements, for spectral resolution, and for collection and use of calibration spectra. Quantitative analysis methods are discussed and their applicability outlined.

17.5.9 ISO 19703:2005 Generation and analysis of toxic gases in fire: Calculation of species yields, equivalence ratios and combustion efficiency in experimental fires

This standard provides definitions and equations for the calculation of toxic product yields and the fire conditions under which they have been derived in terms of equivalence ratio and combustion efficiency. Sample calculations for practical cases are provided. The methods can be used to produce either instantaneous or averaged values for those experimental fires in which time-resolved data are available. It is intended to provide guidance to fire researchers for appropriate experimental fire data to be recorded, calculating average yields of gases and smoke in fire effluents in fire tests and fire-like combustion in reduced scale apparatus, characterising burning behaviour in experimental fires in terms of equivalence ratio and combustion efficiency using oxygen consumption and product generation data.

17.5.10 ISO 27368 Analysis of blood for asphyxiant toxicants: Carbon monoxide and hydrogen cyanide

Carbon monoxide and hydrogen cyanide are the two primary toxic combustion gases present in fire atmospheres. The toxic insult to exposed victims must be assessed by the analysis of their blood for carbon monoxide as carboxyhaemoglobin (COHb) and hydrogen cyanide as cyanide ion (CN^-). Current practice tends to be very consistent for carboxyhaemoglobin determination, but very variable in the more problematic analysis of hydrogen cyanide. Both are necessary for:

- estimating life-threatening characteristics of fire atmospheres;
- evaluating the degree of toxicity caused by smoke inhalation in fire victims;
- determining the cause and manner of death of fire victims;
- improving understanding of direct causes of fire injury and death;
- enhancing understanding of acute and delayed adverse effects of smoke on fire casualties;
- administering immediate treatment for smoke poisoning and monitoring delayed adverse effects of smoke;
- choosing appropriate emergency, long-term and/or follow-up treatments for surviving fire casualties;
- setting priorities for emergency treatment of multiple fire casualties;
- establishing relationships between fire atmosphere carbon monoxide and hydrogen cyanide concentrations, blood carboxyhaemoglobin and CN^-

levels, and the degree of toxicity and performance impairment;
- achieving correlations between concentrations of the two gases in fire atmospheres and of carboxyhaemoglobin and CN^- in blood in order to improve tenability models;
- identifying deficiencies with materials, products, assemblies, structures and escape routes; and
- improving forensic toxicology analytical processes and procedures.

Various different methods are currently used for obtaining blood analysis data for these two fire toxicants and a lack of standardised procedures may result in a wide variation of interpretation. This standard sets out best-practice standardised procedures for blood sample collection, sample storage, sample processing/preparation, sample treatment and transfer to analytical instrumentation, analytical instrumentation and techniques, and data presentation, reporting and interpretation. The analytical methods are based upon their suitability to perform analysis on ante-mortem and post-mortem blood samples from fire victims and are commonly used in forensic toxicology analytical operations.

The analytical principle, analysis time, repeatability, reproducibility, robustness, effectiveness and instruments used are considered for those methods. Some of the methods described may not be suitable for analysing putrid or clotted blood; burned (solid) blood may be analysed after homogenisation.

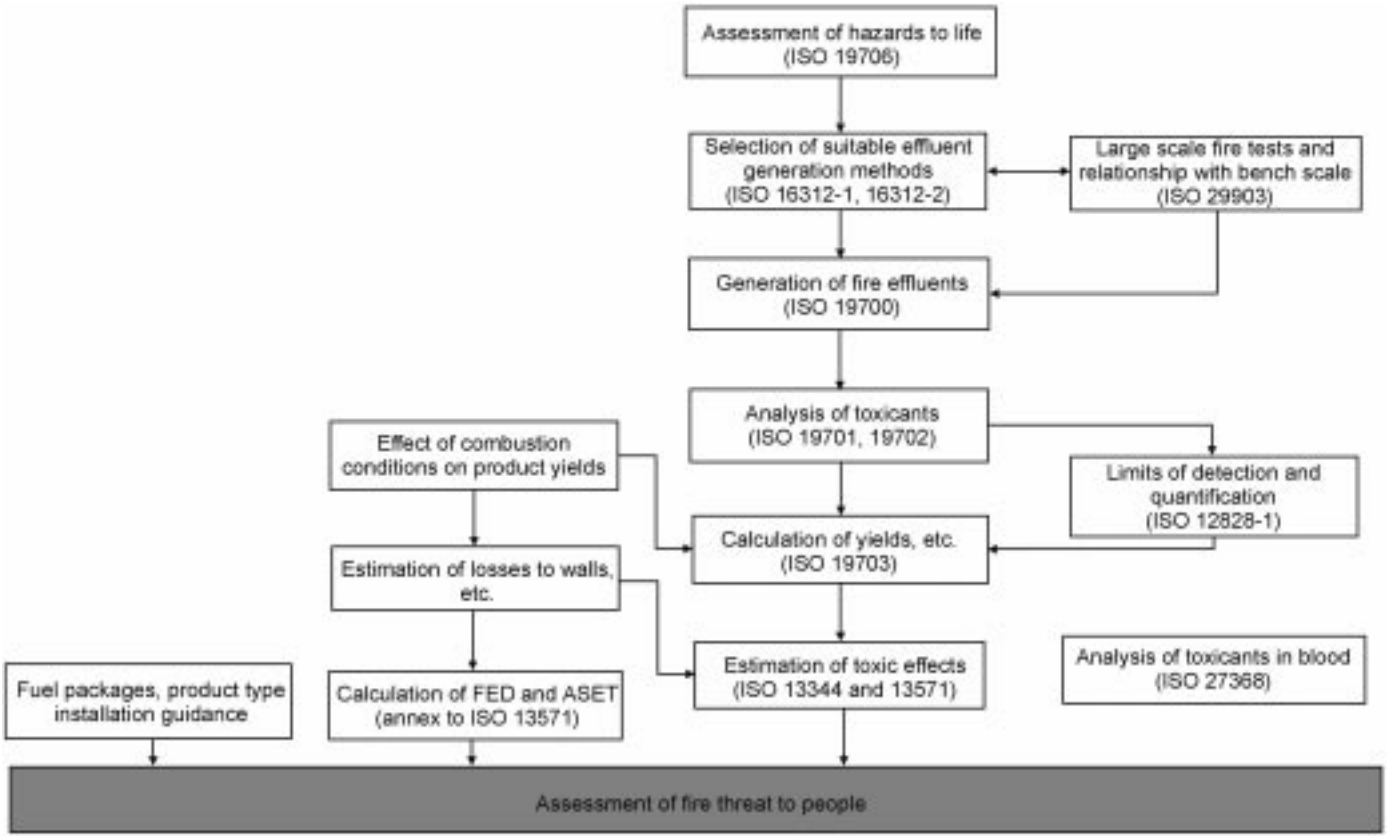
17.6 Proposed International Organization for Standardization (ISO) standards for fire toxicity

Standards in fire toxicity are in a state of constant development within ISO TC92 SC3 (Fig. 17.4). Those with a number, allocated when they have been declared as a new work item, are generally at a more advanced stage of development than those without an ISO number. The number will generally remain unchanged as the documents progress to published standards.

17.6.1 ISO 29903 Guidance for the comparison of toxic gas data between physical fire models of different scales

This International Standard will provide principles for characterising the yields of toxic gases from a laboratory fire test and provides bases for comparing the results among different types and scales of such tests. It uses the uncertainties in the gas yield determinations to establish similarity or difference between test results. It is intended to serve as a tool for:

- definition of the relevance and significance of toxic gas data from fire tests;
- the comparison of toxic gas data from fire tests of different scales and characteristics; and
- extrapolation of toxic gas data between different fire tests.



17.4 Overview of proposed standards on assessment of hazards to life from fire within the ISO TC92 SC3 Framework.

17.6.2 Guidance on requirements for large-scale test methods to represent toxic gas and smoke hazards in different full-scale fire scenarios

The standard will provide guidance on large-scale test strategies for the evaluation of toxic and environmental fire hazards. The work will also extend (and provide reference scenarios) for the small-scale tests such as ISO TS 19700. It will provide a process for determining the requirements for full-scale physical fire models to represent the hazards from smoke and toxic gases in a range of full-scale fire scenarios. This will facilitate the evaluation of fire threat to people and the environment, a major requirement for life-safety design. Although there appears to be some overlap with the previous proposed standard, it has been agreed that they will be developed in parallel, to minimise any duplication.

17.6.3 ISO DIS 21489 Controlled atmosphere cone calorimeter for toxicity assessment

A joint development with TC92 SC1 has been proposed to investigate the standardisation of these ad hoc apparatuses and to evaluate the suitability of the controlled atmosphere cone to toxicity measurement. From the published data currently available it is apparent that this method will not meet the criteria set out in ISO 16312-1, so could not be suitable for the assessment of fire toxicity for anything other than well-ventilated flaming. The limitations of this approach have been discussed in Chapter 12.

17.6.4 ISO 12828-1 Validation method for fire gas analyses – Part 1: Limits of detection and quantification

This proposal addresses the significant differences in analytical capabilities between different laboratories and techniques. Given the wide range of species present in fire effluents, and the potential for harm at limits below normal levels of detection, guidance is provided for quantifying the limitations inherent within any set of laboratory data. For consistency in the interpretation of results from different toxicity assessment methods comparison must be made in terms of:

- the lower concentrations of particular species which are able to be detected adequately (limits of detection), LoD; and
- the lower concentrations of particular species which are able to be quantified adequately (limits of quantification), LoQ.

LoD and LoQ are defined and justified. The standard provides methods for determining suitable values for these two parameters for a specific analytical procedure, and for a specific chemical species. These can be applied to method

validation, classifications based on toxicity indexes and interlaboratory reproducibility exercises.

17.6.5 Obtaining measurements during accidental or arson-initiated fires

This document provides a template for the ideal quantification of the components of fire effluent, with sufficient personnel, and access to the active fire scene, for which appropriate sampling devices are available. It also provides options for obtaining useful, but less comprehensive, data with more limited resources. It is applicable to the sampling and analysis of effluents being produced during 'real' fires, i.e. 'unwanted accidental or arson initiated fires which have the potential to harm people'. It provides general principles for the collection of data:

- the choice of personnel to obtain these data;
- the important times and locations for taking effluent samples where life is at risk from the effluent;
- the technology and methodology needed to obtain and store samples, and a template for recording these data in a standard format, including fire scenario details and uncertainty values for the analytical results.

17.7 Future standard development in fire toxicity and fire safety engineering: 'the matrix'

In addition to the documents described above, which are currently under development, a matrix of current and proposed standards has been drawn up in conjunction with TC92 SC4 to highlight deficiencies in the current provision. The following new work items have also been proposed in the area of fire toxicity.

- Technical Report on the effect of combustion conditions on effluent components **(SC3 WG2)**:

  > This document will summarise and interpret the findings of research on the variation of the yields of toxic compounds, visible smoke, and heat with combustion conditions, notably equivalence ratio and possibly the chemical composition of the combustible effluents.

- International Standard on calculation of wall losses of gases and smoke **(SC3 WG2)**:

  > This document would include the published methods for assessing the decrease in gas and smoke concentrations as a function of distance from the fire. Non-normative annexes would compile the results of tests of wall losses.

- Technical Report on the sub-incapacitating effects of fire effluent **(SC3 WG5)**:

  This document would compile and interpret the published literature on the effects of toxic gases, visible smoke, and heat at levels below those that lead to incapacitation.

17.8 Proposed standards on the harmful effects of fire effluents on the environment

This is a relatively new area of work for the subcommittee, but clearly one of increasing importance. Although outside the immediate scope of this book, details have been included for completeness, and their relevance to the overall theme of fire toxicity.

17.8.1 ISO 26367-1 Guidelines for assessing the adverse environmental impact of fire effluents – Part 1: Fundamentals

Large fires present dramatic and persistent adverse effects on the environment. This has been accentuated by a number of high impact incidents over the past half century. Annex A contains a list of major fire incidents in recent years. This standard provides guidance on:

- the assessment of the hazards of fire effluent to the environment and to people through environmental exposure;
- the collection of relevant data for use in environmental fire hazard and risk assessments.

It is intended to serve as a tool for the development of standard protocols for:

- the assessment of local and remote adverse environmental impacts of fires, and the definition of appropriate preventative measures;
- post-fire analyses to identify the nature and extent of the adverse environmental impacts.

17.8.2 ISO 26367-2 Guidelines for assessing the adverse environmental impact of fire effluents – Part II: Quantification of impact

This proposed standard focuses on quantification and impact from fire products that are environmentally significant, both in terms of long-term effects (e.g. persistent organic pollutants, POPs) and short-term effects (in terms of plant damage and smog). The following major environmental pollutants are considered:

- POPs: polycyclic aromatic hydrocarbons (PAHs), brominated and chlorinated dibenzodioxins (e.g. TCDDs) and dibenzofurans (TCDFs), polychlorinated biphenyls (PCBs).
- Ecotoxicants with long-term effects: metals, particulates, perfluorooctane-sulphonates (PFOS) (used in firefighting foams).
- Ecotoxicants with acute effects: NO_x, SO_x, metals, halogenated acids.
- Hormonal disruptors and ecotoxicants with specific biological effect: nonylphenol and nonyphenol ethoxylates.

17.8.3 ISO 26368 Guidelines for mitigation and containment of fire-fighting water run-off

In industrial premises from which people have been evacuated, where there is no water run-off containment facility, in many European countries current fire fighting practice is leave the fire to burn out to avoid polluting local water courses. This standard provides guidance on the control of the run-off of fire-water and associated effluent that are capable of:

- exposing vulnerable aquatic and terrestrial environmental compartments to potentially serious direct chemical or biological threat;
- indirectly compromising the health and safety of both local and remote exposed human and animal populations.

This proposed standard gives information on the risks from firefighting water run-off, and provides a summary of current potential approaches for controlling and eliminating adverse environmental impact caused by firefighting water run-off. It addresses essentially post-fire industrial safety issues (warehouses, storage facilities, process plants handling and/or storing products of 'critical' pollution potency).

17.8.4 Sampling and analysis of fire effluents which can harm the environment

This proposed standard covers the sampling and analysis of effluents produced during accidental fires which have the potential to harm the environment. The principal requirement for the sampling and analysis of effluents from accidental and arson-initiated fires, which may harm the environment, is to provide information on:

- the nature and concentrations of airborne effluents over time and distance;
- the nature and concentrations of 'run-off' compounds and solid and liquid ground contaminants over time and distance.

Wildland fires

The outbreak of wildland fires across the globe has led to a realisation that society is ill-equipped to deal with such emergencies. Since the title of the subcommittee ('Fire threat to people and the environment') suggests that this would be the appropriate forum for development of suitable international guidance, several member countries have requested the subcommittee to give the matters more detailed consideration. However, the scope of this work is very broad; ranging from ignition and combustion behaviour, through fire spread, its effects on the environment, to fire suppression and management, and the urban–forest interface; so the current position (June 2009) is that the long list of potential standards have not yet been accepted even as future areas of work.

17.9 References

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18

Computer simulation of fire hazards and evacuation

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Abstract: The application of computer simulation to predict fire, smoke and evacuation conditions in full-scale fires is described. For safety and financial reasons, this is in great demand by building developers and owners. Significant improvements in computational power and methods now allow this challenging problem to be solved with good precision. Recent research concerns the consideration of toxic gas in numerical simulations, for building evacuation, and for fire investigation. The fundamental approaches of different types of models (zone models, field models – CFD, mixture fraction models) and their application on toxic hazard assessment are discussed. Further, methods and opportunities of evacuation simulation are summarised.

Key words: simulation, CFD, zone model, evacuation, FDS, toxicity.

18.1 Numerical fire analyses: history, motivation and types of application

Rapid and sustained improvements in computer power, the parallel development of effective computational methods and their scientific and technical bases have resulted in significant advancements in numerical simulation in all fields of engineering and computation for several years. Full-scale fires are some of the most demanding subjects for numerical simulation. Different complex non-linear problems need to be solved, while the coupling and interaction between combustion models, flame spread and fluid dynamics of turbulent flows are particularly challenging. Beyond that, building fires typically occur in very large geometrical spaces, where the local effects of smaller dimensions and turbulent flow can have significant effects on the results. Such cases need to be solved by the use of field models with a fine grid resolution. The combination of large spaces and the need for fine grids can lead to very complex models with long simulation times. To solve such problems, modern high-end computers with plenty of memory and multiple central processing units (CPUs) running in parallel must be used. Finally, the precicision and reliability of currently available material parameters for the description of physical and chemical

behaviour is often not sufficient. Therefore assumptions for material behaviour need to be made, the validity of which influences the precision of the results. With increased application of computer simulations, the availability of appropriate material data will gradually improve to meet the demands of the global research community. Owing to these constraints, computer simulation of full-scale fires is still a relatively new field, in comparison with other applications of numerical simulation.

For situations where existing fire simulation models have been accepted and are already in use, there are tremendous advantages of simulation over classical methods (such as prescriptive codes and analytical approaches to temperature and evacuation time). Study of the influence of different parameters (for instance exhaust conditions, heat release rate, control of fire extinguishing systems) allows a very detailed insight into the nature of fires. This knowledge, which can now be achieved non-destructively and at reasonable cost, can generally be used for the optimisation of fire safety technology for rescue, evacuation and extinction. Seen from an economical perspective, building owners can save considerable costs by applying fire simulation for evidence of fire safety. Mostly simulation can provide evidence for a substantially reduced number of fire protection measures in comparison to solutions which were dimensioned based on prescriptive regulations or analytically.

Typically the objective of fire hazard calculations is to prove, or improve the fire safety of buildings, including:

- safe evacuation of people from buildings;
- access for rescue and fire extinction measures;
- fire-resistant construction;
- prediction of toxicity for humans and environment (such as for forensic fire investigation);
- explosion protection.

For these objectives, different classes of models are applied:

- Models for calculation of fire spread, gas and wall temperatures, pressures, smoke obscuration, and toxic gas production (field models (computational fluid dynamics, CFD) or zone models).
- Models for the evacuation of people.
- Models for the evaluation of static fire resistance of the construction (preventing the collapse of structural steelwork, etc.).

18.2 Types of fire simulation models

18.2.1 General

There are three important types of simulation methods for fire protection engineering:

- Single zone fire models or post-flashover models (e.g. COMPF2 (USA)[1]).
- Zone models (multi-room/multi-zone-models, e.g. CFAST (USA),[2] MRFC (Germany),[3] ARGOS (Denmark),[4] Branzfire (New Zealand),[5] NAT (France),[6] Ozone (Belgium)[7]).
- Field models, CFD-Codes, e.g. Fire Dynamics Simulator (FDS), Fluent, CFX, Cobra3D.

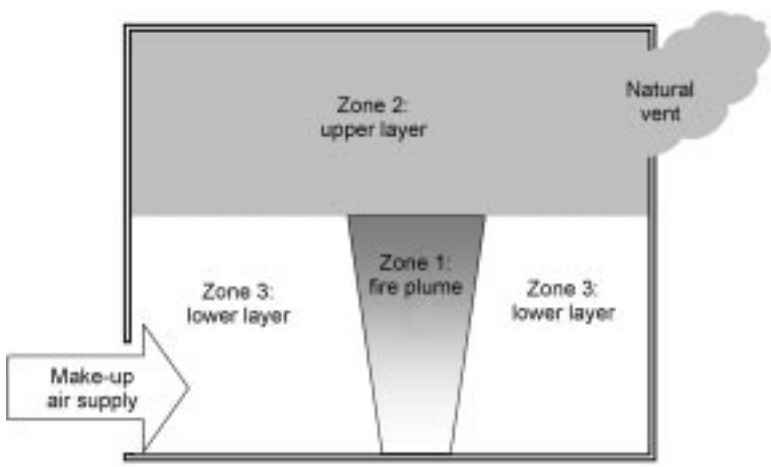
There is a compromise between accuracy and speed in the choice of tools that are used.

18.2.2 Post-flashover models

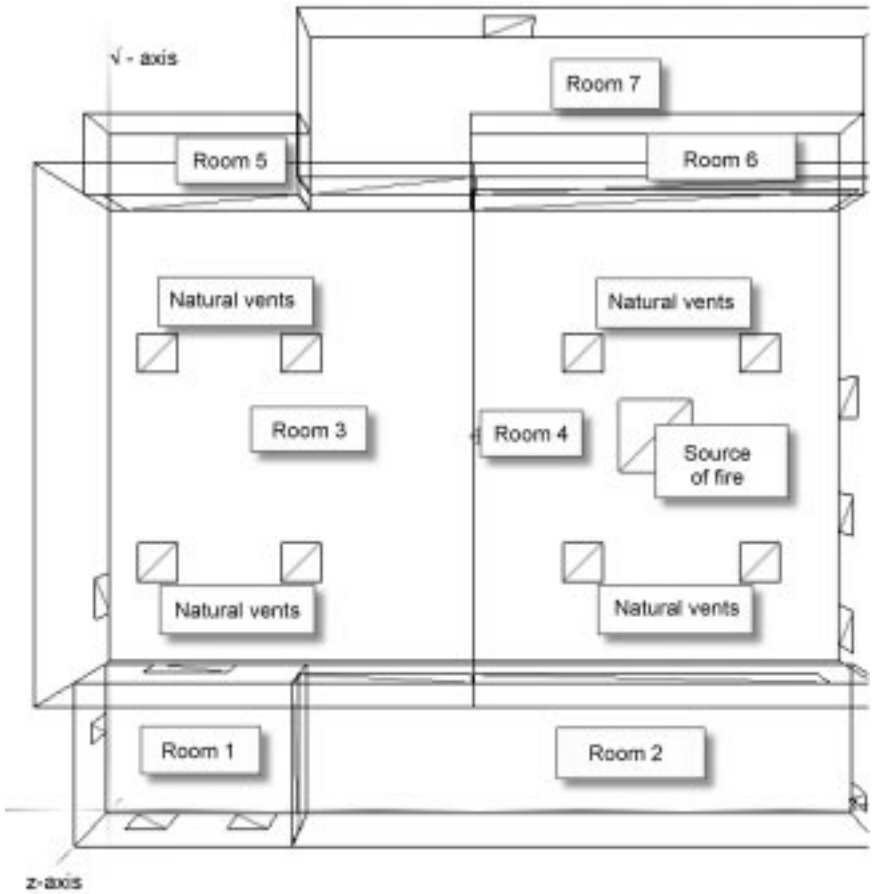
Post-flashover models are simple zone models for single compartments that are based on the assumption that gas temperature in the compartment is uniform. These models are used to determine the temperature–time curve in order to assess the load-bearing capacity of structural elements under the specific conditions set by the user.

18.2.3 Zone models

These types of models solve the fundamental equations of mass and energy transfer for fairly large regions or zones, within the room or compartment being modelled. Typically, these models divide the compartment or room into two or more discrete zones representing the fire plume, the hot smoke layer and the lower cooler layer (Fig. 18.1). Zone models are widely used in fire protection engineering because of their simplicity. To build up a simulation in a multi-room



18.1 Basic approach of a zone model, showing the separation into two 'homogeneous' layers.



18.2 Plan view of the geometry of a compartment in a zone model (MRFC).

zone model, the geometrical data of several compartments (Fig. 18.2) and the thermo-physical properties of the structure are needed, as well as the fire described by a rate of mass loss. The output is computed by conservation of mass, conservation of energy, ideal gas law and relations for density and internal energy as well as different plume equations.

For CFAST, the technical manual[8] reports that the production of different products is described by the species yields in relation to the mass of fuel burned. Hydrogen cyanide and hydrogen chloride are assumed to be products of pyrolysis as well as the consumption of oxygen that is treated as a negative yield.

Carbon dioxide, carbon monoxide, water and soot are products of combustion, dependent on a combustion chemistry scheme based on the carbon–hydrogen–oxygen balance. These species are carried in the effluent flow to the various compartments and accumulated in the upper layer.

The zone model divides each compartment into two distinct zones, with uniform characteristics to predict the thickness and temperature of, and the species concentration (carbon dioxide, carbon monoxide, hydrogen cyanide, soot, etc.) in, the hot, upper layer and the cold, lower layer in each compartment as a function of time. The concentration of carbon dioxide in the lower layer is used as a marker for irritants.

Even though the results of zone models are not as accurate as those of CFD models, in many cases they are still sufficient. The zone models have the advantage that a three-dimensional model is created within a short time, and that results are computed and post-processed within a few minutes. Therefore it is very easy to undertake parametric studies which can even be cost effective for competitively priced projects.

18.2.4 Field models, CFD

Field models are used to calculate the values of field functions under given boundary and loading conditions. Field functions are physical quantities which depend on their geometrical location, such as temperature (a scalar field) or velocity (a vector field). The prevailing numerical methods for the solution of field problems which are widely applied today are:

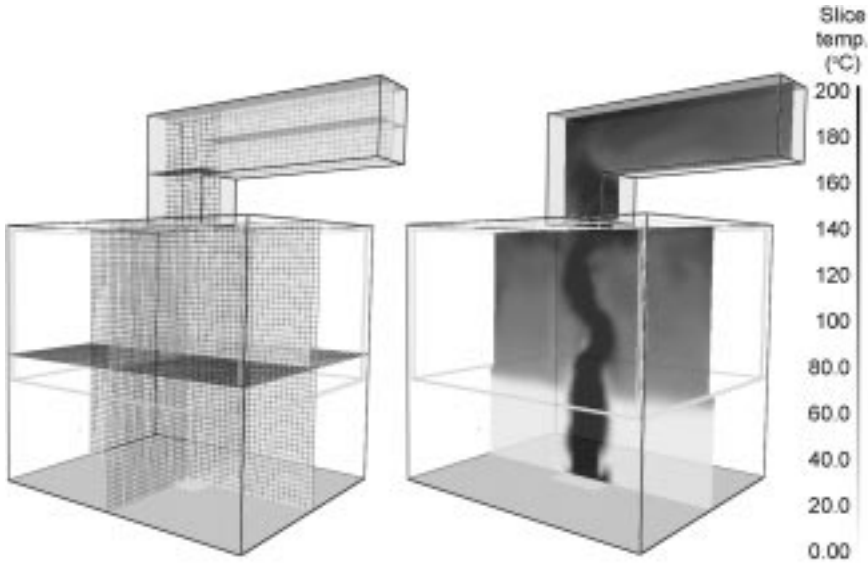
- FVM (finite volume method);
- FDM (finite differences method);
- FEM (finite element method).

All three methods require the geometrical discretisation of the computational domain into grid cells or elements with simple shapes. By application of the numerical approximation method on the partial differential equations for the grid cells, a system of algebraic equations for the complete model is created which can be solved numerically.

There are several commercial codes which have been designed to simulate real-scale fires. Many of them use an FDM which requires the volume of the fire enclosure to be divided into rectangular cells making up a three-dimensional grid (Fig. 18.3).

For some years, the FDS, developed by the American National Institute of Standards and Technology (NIST) in cooperation with VTT Technical Research Centre of Finland, has been the most-widely used CFD fire modelling software, both for academic and commercial simulation of fire-driven fluid dynamics. This is an open-source CFD software, which:

> solves numerically a form of the Navier–Stokes equations appropriate for low-speed, thermally-driven flow with an emphasis on smoke and heat transport from fires. The partial derivatives of the conservation equations of mass, momentum and energy are approximated as finite differences, and the solution is updated in time on a three-dimensional, rectilinear grid. Thermal



18.3 FDS model of a hood experiment with grid and temperature plot.

radiation is computed using a finite volume technique on the same grid as the flow solver. Lagrangian particles are used to simulate smoke movement, sprinkler discharge, and fuel sprays.[9]

The current version of this software is FDS 5, which offers some advantages in the mixture fraction model, important for the calculation of toxic combustion products, compared to the previous version, FDS 4.

18.2.5 Mixture fraction models in FDS 4 and FDS 5

In the earlier FDS (FDS 4) two types of combustion model were used. A global one-step model for direct numerical solution (DNS) calculation where the diffusion of fuel and oxygen can be modelled directly, and a mixture fraction-based combustion model for large eddy simulation (LES) calculation was included.[10]

The mixture fraction, a single variable $Z(x,t)$, is a non-dimensional quantity representing the mass fraction of a species, at a particular location, that was originally part of the fuel stream. The main assumptions are that the combustion is mixing-controlled and that the specific mass fraction of each species (fuel, nitrogen, oxygen and combustion products such as carbon dioxide, water, carbon monoxide and soot) are in 'state relation' to the mixture fraction. Additionally it is assumed that the chemical reactions occur so rapidly that fuel and oxidiser cannot exist at the same time in one cell. On that basis the local oxygen consumption rate at the flame surface is computed, together with the heat release

to which it is directly proportional. It does not include any information about the combustion efficiency. This has had two different effects on the results from FDS 4. For fires which become vitiated, there is no change in the carbon monoxide/carbon dioxide production ratio, and when the under-ventilated conditions lead to extinction, the combustion reaction does not stop even when the heat release is set to zero.

Although FDS 4 produced very reasonable results for simulation of well-ventilated compartment fires, Forell[11] showed that the one-step combustion model in FDS 4 was not capable of making accurate predictions of under-ventilated conditions. Under these conditions, the predicted temperatures were either far too high (too many reactions go to completion) or the heat release rate decreased and the temperatures were significantly underpredicted (too many reactions are stopped completely).

According to the global equivalence ratio (GER) concept,[12] carbon monoxide yields undergo an important change between $0.5 < \phi < 1.5$ (see Chapter 2). External combustion, away from the fire plume has been shown to occur over an extended range, where the equivalence ratio for external combustion ϕ_{EC} is between $\phi_{EC} \approx 0.3$ and $\phi_{EC} \approx 2.3$. Therefore in many cases the final CO yields are influenced considerably by the occurrence and efficiency of external combustion. According to Forell's work, the limitations of the FDS 4 combustion model can be solved by post-processing the properties of exhaust gases using an extension of Beyler's ignition criterion.[13] The mixture fraction $Z(x,t)$ must be related to the local equivalence ratio which is used as the ignition criterion, ϕ_{EC}. However, FDS 4 is only partly applicable to building fire simulations under conditions of increased equivalence ratios.

To overcome the limitations of the single parameter, a mixture fraction combustion model, based on a multiple parameter mixture fraction, has been implemented into FDS 5[9,10] (described in Chapter 20). It was developed to describe local extinction, incomplete combustion, and the formation and destruction of carbon monoxide. In order to validate the new model, Floyd[14] simulated three sets of experiments (a methane–air slot burner, a vitiated fire environment under a small hood, and a set of reduced-scale enclosure fires, at NIST).

The model successfully predicted the peak carbon monoxide concentration as a function of height within the flame. For the higher equivalence ratio experiments, the model under-predicts fuel and oxygen and over-predicts carbon monoxide yields. The simulation of the under-ventilated fires showed that the calculated carbon monoxide and carbon dioxide concentrations tended to be over-predicted. Floyd describes one reason for these over-prediction phenomena of carbon monoxide formation: the assumption that in FDS 5 the first step of the reaction is infinitely fast.

18.2.6 Limitations and advantages of fire models for toxic hazard assessment

A fundamental limitation of both zone and CFD fire models is that they are not yet capable of successfully modelling the fire itself (burning rate of the fuel). Thus for both CFAST and FDS, the fire, in terms of a heat release rate curve, is an input parameter supplied from theoretical fire growth expressions (t^2 fire curves) or experimental data (for example, calorimeter data for individual burning items). The heat release rate data provides two linked inputs for the models – the heat release rate from the burning fuel, and the mass loss rate ('pyrolysis rate') for the fuel. Although the models are capable of calculating the actual heat release from the fuel in any particular enclosure, or at any particular vent, based upon local oxygen consumption, they do not generally adjust for effects on fuel mass loss rate, which is an input parameter unaffected by the computation. Since most calorimeter data are obtained under open burning conditions, these data can provide a reasonable estimation of fire behaviour under well-ventilated combustion conditions. In under-ventilated combustion conditions the actual mass loss rate for the fuel is lower than that under well-ventilated conditions. This can result in an over-prediction of the fuel mass loss concentration in the fire enclosure. FDS does have an alternative method for specifying the fire, whereby the fuel mass loss rate is calculated from the heat of vaporisation of the fuel and the heat exposure of the fuel surface, calculated as part of the simulation. However, developing sub-models capable of accurately predicting the actual fire behaviour is a difficult area of continuing research.

In addition to difficulties in predicting fuel mass loss rate there remain significant limitations in the ability of the models to calculate the yields of toxic fire gases throughout a fire. As discussed, yields for different species may be set as input parameters calculated from experimentally derived input data as functions of mixture fraction or equivalence ratio. While the models do a reasonable job of calculating 'major species' such as carbon dioxide yields and oxygen consumption, an area of uncertainty and continuing development is their ability to calculate the yields of the 'minor species' important in calculating the hazards to occupants such as carbon monoxide, hydrogen cyanide, irritants and particulates. However, since these species (perhaps excepting soot) have relatively little influence on the fire development and interaction with the fire enclosures, they can be calculated by post-processing simulation data.

An advantage of using fire modelling combined with FED analysis to predict time to incapacitation in fires (available safe escape time – ASET) is that it is possible in separate simulations, to vary key parameters and examine the sensitivity of hazard predictions to the values input or predicted. As an example, a simple simulation was carried out of a single room fire using CFAST. The time to incapacitation from carbon monoxide exposure for a room occupant was

calculated using three different assumptions regarding carbon monoxide yield during the fire. Carbon monoxide yield was assumed to be one of:

- a constant low value measured under well-ventilated combustion conditions;
- a constant high value measured under vitiated combustion conditions; or
- a variable related to the duration and degree of vitiation of the simulated fire.

The results of the simulation indicated that use of the low value assumption considerably overestimated the time available for escape before incapacitation was predicted, while the constant high value and variable assumption produced almost identical predicted times to incapacitation. This showed that the calculated time to incapacitation was very sensitive to the carbon monoxide yield, but not particularly sensitive to the dose rate.[15]

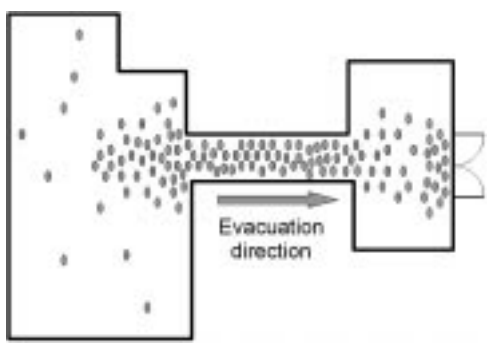
18.3 Evacuation simulation

18.3.1 Intention

For performance-based fire protection engineering, the calculation of evacuation is important to solve questions such as the following:

- How much time elapses between a fire alarm and occupants starting to move towards the exits?
- How much time does a crowd flow need to leave a building?
- Will a bottleneck in the escape way lead to a critical situation (Fig. 18.4)?
- Are there places in the building from which evacuation to exits is uncertain?
- After what time must personal injuries be considered?
- Which kind of harm to evacuees may be expected?

When evacuation simulations are combined with fire modelling and FED analysis it is possible to examine interactions between evacuating occupants and the developing fire conditions,[16] in particular:



18.4 Evacuation scheme.

- the times to incapacitation for occupants in each fire enclosure (ASET times);
- the effects of exposure to smoke, heat and toxic products on evacuation behaviour, exit choice and movement speeds (effects on required safe escape time, RSET).

18.3.2 Evacuation models

To answer questions like this and to prove safe evacuation, different approaches are possible:

- Capacity analysis (NFPA 130).
- Hydraulic models (Predtechenskii and Milinskii).[17]
- Flow-based simulation models (EVACNET4, EESCAPE and EGRESSPRO).
- Cellular automata (EGRESS, TIMTEX and Pathfinder).
- Agent-based modelling (SIMULEX, EXODUS, Gridflow and CRISP).

Capacity analysis

The NFPA 130 Standard (National Fire Protection Association, USA) addresses egress from railway carriages and establishes minimum requirements 'that will provide a reasonable degree of safety from fire and its related hazards'.[18]

Hydraulic model

In the model of Predtechenskii and Milinskii a crowd movement is considered like a fluid flow. The model of mathematical fundamentals laid down by Predtechenskii and Milinskii in the 1970s is an effective method to predict evacuation time (walking time and waiting time) for flows of people as a function of density. The movement depends on the situation (regular evacuation or emergency movement), the required space (e.g. summer/winter clothing, with luggage) and character of route (stairway up/down).

Flow-based modelling

In flow-based models simulation is based on nodes. The approach in flow-based evacuation models is similar to the principles of a potential flow, where the velocity field is defined as the gradient of a scalar velocity potential. The fluid flows from locations with high potential to locations with low potential. In order to transfer this theory to evacuation models, nodes are defined in the geometrical space which are assigned different values of potential, and which influence the behaviour of the evacuees in its environment. The values of the potential at a node depend on the distance to exits. The potential of nodes has its lowest values

at the exits and is raised with increasing distance from them. Consequently, people moving towards the exits are similar to the fluid in a potential flow.

The movement of people is further influenced by attributes of nodes which define the available escape space and the apparent density of people there. The limitation of flow models is that all human interactions and human responses to the hazards are missing.

Cellular automata modelling

In cellular automata evacuation models, the space between structural parts is divided into individual floor cells with evacuees modelled as individuals on the centre or the perimeter of a cell, movement is controlled by probabilistic choices.

Agent-based modelling

The distinguishing feature of agent-based models is the individualisation of evacuee groups. Each evacuee (agent) is assigned their own characteristics (e.g. walking speed, influence of gender and age) and gets their own optimal escape route, computed in time steps, depending on density of the other agents, but independently of them.

Complementary models

To take into account the influence of asphyxiants and irritants on the evacuees the output data of a fire simulation model must be post-processed by the evacuation scenario (e.g. FDS + Evac, NIST). With the FED methodology the capability of an evacuee to escape under the certain conditions of the fire will affect the evacuation.[19]

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19

Toxic hazard calculation models for use with fire effluent data

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Abstract: In fire safety engineering terms it is necessary to ensure that available safe escape time (ASET) is greater than required safe escape time (RSET) by an acceptable margin of safety. ASET depends upon the time–concentration curves for smoke, irritant and asphxyiant gases and heat and the effects of their concentrations or accumulating doses on occupant escape capability, and in particular time to incapacitation. Smoke and irritant gases also influence RSET, by affecting behaviour and movement speeds of escaping occupants.

This chapter presents the full suite of fractional effective concentration and fractional effective dose expressions developed in Chapters 3 and 4, and describes how they are used in combination and applied to time–concentration fire data obtained from full-scale fire experiments or computational fire dynamics models, in order to calculate time to escape impairment, incapacitation and lethality. A worked example of application to actual fire data is presented. The application of the method to fire safety engineering design and forensic fire investigation is discussed, with guidance on consideration of uncertainties and variations in human susceptibility.

Key words: fractional effective concentration, fractional effective dose, escape from fires, asphyxiants, irritants, smoke, heat, available safe escape time, required safe escape time.

19.1 Introduction

Life safety hazard from fires in buildings (or other enclosures) depends upon the performance of a dynamic system involving interactions between the building, the fire and the occupants. Since fire hazards are essentially time-based phenomena, the objective is to ensure as far as possible that should a fire occur, the occupants are warned and have time to escape before conditions become untenable. In fire safety engineering terms it is necessary to ensure that available safe escape time (ASET) is greater than required safe escape time (RSET) by an acceptable margin of safety.[1,2]

In order to determine the ASET time for any system it is necessary to determine the following:[3]

- The time–concentration (or time–intensity) curves for the major toxic products, smoke and heat in the fire at the breathing zone of the occupants, which in turn depend upon:
  - fire growth curve (mass loss rate of the burning fuel (kg/s) and its dispersal volume (kg/m^3) with time);
  - the yields of the major toxic products (kg/kg) and heat (kJ/kg) (for example kg carbon monoxide per kg of material burned).

  These terms can be measured directly in full-scale tests or calculated using appropriate fire dynamics computations as described in Chapters 18 and 20, with appropriate input data including reaction-to-fire properties and data on product yields under a range of fire conditions.
- The concentration/time/physiological effect relationships of these products in terms of the physiological/toxic potency of the products and heat (the exposure concentration (kg/m^3), or exposure dose ($kg\,m^{-3}$ min or ppm min)) causing toxic effects (and the equivalent effects for heat and smoke obscuration). The important end points are:
  - concentrations, doses (or heat intensity) likely to impair escape efficiency due to behavioural and/or physiological effects;
  - exposure concentrations or doses likely to cause incapacitation or prevent escape due to behavioural and/or physiological effects;
  - lethal exposure concentrations or doses.

  These terms can be calculated by the application of appropriate physiological methods (fractional effective dose (FED) methods) presented in Chapters 3 and 4.

The time required for occupants to escape depends upon a set of parameters related to fire detection and warning times, the behaviour of occupants in response to alarms in terms of starting (pre-movement) times and exit choice, and the time required to travel through escape routes and out of the building. In situations when evacuating occupants see or are exposed to smoke their exit choice and movement speed (and hence their travel time) can be affected. These effects need to be considered in evacuation calculations, and calculation methods for these parameters have also been presented in Chapters 3 and 4.

This chapter contains a listing of all the different FED calculation expressions developed in Chapters 3 and 4 and illustrates their use by application to a set of smoke and toxic gas data measured during a full-scale experimental fire.

19.2 A comprehensive hazard calculation model for time and dose to incapacitation and lethality

From the physiological effects of exposure to the different individual irritant and aspxhyiant gases described in Chapters 3 and 4 it has been possible to develop a comprehensive set of FED models for the assessment of human fire hazards.

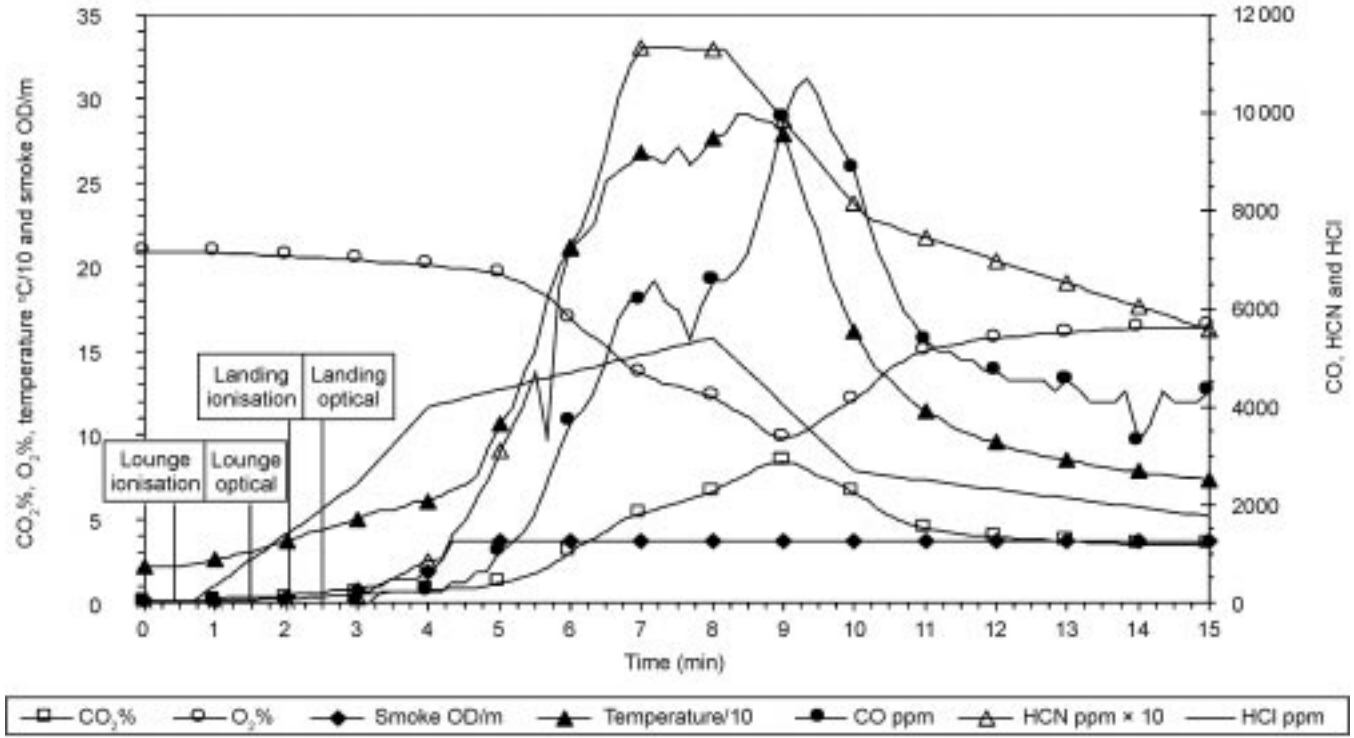
These models are designed to be applied to time–concentration curves for smoke and toxic gases in full-scale fires for which the data have been obtained either from full-scale fire experiments or from data derived using fire engineering zone or computational fluid dynamics (CFD) models. Complementary models have also been developed for calculating the effect of convected and radiant heat on exposed subjects.

Figure 19.1 shows an example of a typical data set of fire time–concentration curves to which the FED models can be applied. The models are used to calculate time and dose to incapacitation and lethality for human exposures to fire effluents. They may be used for fire engineering design or product evaluation purposes by calculating ASET, which is the time from ignition to that at which exposed subjects are predicted to become incapacitated to an extent to which they are no longer able to escape unaided. This time may then be compared with an absolute requirement or in a performance-based analysis with RSET, which is the time from ignition to that when all occupants are able to reach a place of safety. Toxic fire effluents are the main determinants of ASET, but they can also affect RSET in that exposure to fire effluent may affect escape behaviour, and movement speed is reduced in smoke, so that methods have also been developed to calculate these effects. In addition to effects on escape capability these methods can also be applied to determine the consequences in terms of long-term survival probability and health consequences for subjects surviving immediate exposure at the fire scene.

In a forensic context the models are used to establish causes of injury and death in fires in conjunction with full-scale incident re-creation experiments or calculations. In this context the application of FED modelling can be valuable as a validation of such re-creation experiments or calculations, in that predicted effects on occupants obtained using the models can be compared to estimates of the conditions to which the actual occupants were exposed, back-calculated from the carboxyhaemoglobin (COHb) and blood cyanide concentrations in decedents and survivors. If the results of the two approaches agree this is good evidence that the actual fire conditions were similar to those in the tests or simulations.

For a hazard analysis of a fire such as that shown in Fig. 19.1 it is possible to calculate a number of different end points in relation to ASET as follows:

- Time when optically obscure smoke and irritants are predicted to significantly impair the escape efficiency.
- Time when irritancy is predicted to be so severe as to effectively prevent escape.
- Time to incapacitation (loss of consciousness) from the effects of asphyxiant gases.
- Time to incapacitation due to heat exposure.
- Time at which a lethal exposure dose of asphyxiants has been inhaled.



19.1 Example of time–concentration curves for smoke, toxic gases and temperature at head height in the domestic lounge of a house during an armchair fire. The doorway to the hall is open but the house is otherwise enclosed. The time for triggering of smoke detectors is shown.

- Time at which heat exposure and burns are predicted to be lethal.
- Time at which an exposure dose of lung irritant sufficient to cause severe injury or death some hours after exposure has been inhaled.

The way the calculations for these different end points are applied may depend to some extent on the purpose of the analysis. For a deterministic design application it may be considered that the design has failed if occupants are predicted to be exposed to smoke at all, or to smoke of sufficient density to impair escape efficiency. For a probabilistic design, or for a forensic application, it may be important to consider the further consequences of different exposure scenarios, requiring calculation of time to incapacitation or to a lethal exposure.

In the following section a summary is presented of all the calculation models described in Chapters 3 and 4, with an example of an application. Full descriptions of the models with further application examples are presented in the *SFPE Handbook of Fire Protection Engineering*[3] while a simplified set is presented in ISO 13571.[4]

19.3 Fractional effective dose (FED) methodology for hazard analysis

As stated, some toxic or physical effects of exposure to combustion products occur almost immediately on exposure, and the severity of the effect is proportional to the concentration of the substance and its potency. This applies to visual smoke obscuration and to the painful effects of exposure to irritants. For example, irritant smoke in the eyes or nose immediately causes pain (sensory irritation), reflex closure of the eyes and breathing difficulties (see Chapter 3).

For other substances, such as asphyxiant gases, the effect depends upon the dose inhaled. The effects therefore take some time to develop and depend upon the concentration inhaled and the time over which it is inhaled (see Chapter 4). The effects tend to be more persistent than those of sensory irritation, since it takes some time for the toxic material inhaled to be detoxified (for example, hydrogen cyanide) or expelled (for example, carbon monoxide). An example of a dose-dependent effects is collapse from asphyxia resulting from exposure to carbon monoxide.

In practice, for irritants and asphyxiants (and to some extent also for heat) a distinct threshold concentration or exposure dose can be identified at which serious effects are predicted. This is known as the effective concentration or exposure dose for a given toxic or physiological end point (for example, the exposure dose of carbon monoxide required to cause loss of consciousness or the exposure dose of heat required to cause skin pain). For application to toxic hazard calculations the concept of fractional effective concentration (FEC), or dose, is used whereby the exposure concentration or dose at any point during a

fire is expressed as a fraction of the exposure concentration or dose predicted to produce a given effect. For example the concentration of smoke present at any time during a fire can be expressed as a fraction of the concentration required to seriously impair escape capability. Thus

$$\text{FEC}_{\text{smoke}} \text{ (fractional effective concentration of smoke)} = 1$$

represents a smoke concentration considered capable of seriously limiting escape capability where $\text{FEC}_{\text{smoke}}$ = concentration (of smoke) present in a fire at any time divided by the concentration considered to significantly affect escape efficiency.

The exposure dose of carbon monoxide can be expressed as a fraction of the exposure dose predicted to cause incapacitation. Thus F_{Ico} (fraction of an incapacitating dose of carbon monoxide) can be expressed as:

$$F_{\text{Ico}} = \frac{\text{conc. gas present} \times \text{time}}{\text{conc.} \times \text{time for incapacitation}} \tag{19.1}$$

e.g.

$$F_{\text{Ico}} = \frac{1000 \text{ pm CO} \times 20 \text{ min}}{35\,000 \text{ ppm min}} = 0.57 \tag{19.2}$$

Although the FED calculations for different asphyxiant gases are based upon this simple concept, they are in practice more complex for a variety of physiological reasons as described in Chapter 4, but the user is required to know only the concentration and exposure duration to perform the FED exposure dose calculation.

Another reason for expressing the concentration or dose as a fraction of an effective concentration or dose for each toxic product is that a fire atmosphere contains a mixture of toxic products of differing potencies. In order to sum the effects of the different effluent components it is necessary to normalise them in terms of the effective dose. Furthermore, the concentrations of toxic products change with time during a fire, so that for constituents whose effects are dose-related, it is necessary to calculate the effective doses received, based upon the concentrations averaged over short periods of time, and then integrate these over successive periods. The aim is to calculate the time at which the summed effective doses reach unity, at which point the end point (such as incapacitation) is predicted to occur. The general FED equation is therefore:

$$\text{FED} = \int_{t1}^{t2} \sum_{i=1}^{n} \frac{C_i}{(Ct)_i} \Delta t \tag{19.3}$$

where C_i is the average concentration, of an dose-related toxicant such as an asphyxiant gas 'i' over the chosen time increment; Δt is the chosen time increment, expressed in minutes; and $(Ct)_i$ is the specific exposure dose expressed as concentration $\times$ minutes, that would constitute an effective dose (i.e. an

exposure dose producing a defined endpoint such as preventing an occupant's safe escape).

Effective concentrations and exposure doses for defined end points for smoke, heat and toxic effluent mixtures are presented in the following sections.

19.3.1 Tenability calculations for smoke

For exposure to generic irritant smoke it is considered that escape efficiency is likely to be significantly impaired at the concentrations shown in Table 19.1. For application to ASET calculations different end points are recommended for small and large enclosures, since in large enclosures it is necessary to see greater distances to locate escape routes and exits. In this context the limiting concentration for smoke (FEC_{smoke}) at any time during a fire is as follows:

$$FEC_{smoke} = \frac{\text{smoke OD/m}}{0.2 \text{ or } 0.08} \tag{19.4}$$

For RSET calculations it is possible to calculate walking speed in generic smoke as follows:

$$\text{Walking speed in non-irritant smoke (m/s)} = 1.36 - 1.9 \times \text{smoke optical density (OD/m)} \tag{19.5}$$

$$\text{Walking speed in irritant smoke (m/s)} = 2.27 - 9 \times \text{smoke optical density (OD/m)} \tag{19.6}$$

Table 19.1 Smoke tenability limits

Smoke density and Irritancy OD/m (extinction coefficient)	Approximate visibility diffuse illumination	Reported effects
None	Unaffected	Walking speed 1.2 m/s
0.5 (1.15) non-irritant	2 m	Walking speed 0.3 m/s
0.2 (0.5) irritant	Reduced	Walking speed 0.3 m/s
0.33 (0.76) mixed	3 m approx.	30% people turn back rather than enter
Suggested tenability limits for buildings with:		
– small enclosures and travel distances		OD/m = 0.2 α_k 0.5 (visibility 5 m)
– large enclosures and travel distances		OD/m = 0.08 α_k 0.18 (visibility 10 m)

Where OD/m is $\log_{10}$ (I_0/I), the logarithm of the ratio of the intensities of light transmitted over a pathlength of 1 m from a light source to a receiver in the absence and presence of smoke, respectively. The light extinction coefficient α_k is ln (I_0/I).
For situations where smoke is expressed in terms of particulate mass concentration, these equate to approximately 0.7 and 0.3 g particulates/m^3 respectively (where particulates g/m^3 $\sim$ 0.356 $\times$ OD/m).

For smoke involving any particular irritant compound or mixture of specific irritants walking speed can be calculated for the combined fractional irritant concentration (FIC), according to Equation 19.7:

$$F_{\text{wvirr}} = \frac{(\text{e}^{-(1000x/b)^2}) + (-0.2x + 0.2)}{1.2} \tag{19.7}$$

where F_{wvirr} = fractional walking speed (1 = normal walking speed 1.2 m/s); $b = 160$ and x = FIC (calculated according to Equation 19.9 for incapacitation).

Using an additive model, the overall effect of exposure to an irritant smoke on fractional walking speed (F_{wv}) between 1 and 0 would then be given by:

$$F_{\text{wv}} = 1 - (1 - F_{\text{wvsmoke}}) - (1 - F_{\text{wvirr}}) \tag{19.8}$$

where F_{wv} = overall fractional walking speed; F_{wvsmoke} = fractional walking speed due to smoke effects on visibility (Equation 19.5 walking speed/1.2); and F_{wvirr} = fractional walking speed due to irritant effects for irritants compounds 1 to n.

19.3.2 Tenability limits and FICs for sensory irritants

For ASET calculations, two threshold concentration endpoints may be calculated for sensory irritants:

- A concentration capable of seriously impairing escape capability and movement speed.
- A concentration capable of causing incapacitation, such that the subject effectively cannot move.

The threshold concentrations shown in Table 19.2 are proposed for common fire irritants likely to severely affect escape capability in most humans. In order to allow for more sensitive individuals it is recommended that design limit threshold of 0.3× these levels might be used. Since fire effluents contain a mixture of irritants it is necessary to consider how they work in combination. It is currently recommended that they should be considered additive. The overall FIC for an irritant mixture is then as follows:

$$\begin{aligned}\text{FIC} = {} & \text{FIC}_{\text{HCl}} + \text{FIC}_{\text{HBr}} + \text{FIC}_{\text{HF}} + \text{FIC}_{\text{SO}_2} + \text{FIC}_{\text{NO}_2} \\ & + \text{FIC}_{\text{CH}_2\text{CHO}} + \text{FIC}_{\text{CH}_2\text{O}} + \Sigma\text{FIC}_x\end{aligned} \tag{19.9}$$

where ΣFIC_x = FICs for any other irritants present.

19.3.3 Post-exposure lung inflammation and survival

In addition to incapacitating effects of sensory irritation, affecting escape capability, a proportion of inhaled irritants penetrates to the deep lung, and when a sufficient exposure dose is accumulated this can lead to inflammatory

Table 19.2 Exposure concentrations and exposure doses for incapacitation and lethal lung damage

Gas	Concentration predicted to impair escape (ppm)	Concentration predicted to cause incapacitation (ppm)	Exposure doses predicted to be lethal to half the population (ppm min)
HCl	200	1000	114 000
HBr	200	1000	114 000
HF	200	500	87 000
SO_2	24	150	12 000
NO_2	70	250	1 900
NO	–	>1000	~30 000
CH_2CHO (acrolein)*	4	30	4 500
HCHO (formaldehyde)*	6	250	22 500

* Where the concentrations of acrolein and formaldehyde (or other important irritants) are unknown, a term derived from smoke density 0.5 OD/m may be used as an indication of irritancy likely to impair escape efficiency and 90 OD/m min may be used as an indication of lethal organic irritant exposure dose.

processes which can be fatal over periods of several hours to several days after exposure. A guide to concentrations and exposure doses of common irritant gases likely to cause incapacitation at the scene or death following exposure is given in Table 19.2.

The FED equation for the lethal effects of inhaled irritants (i.e. FLD or fractional lethal dose) is:

$$\begin{aligned} \mathrm{FLD_{irr}} = {} & \mathrm{FLD_{HCl}} + \mathrm{FLD_{HBr}} + \mathrm{FLD_{HF}} + \mathrm{FLD_{SO_2}} + \mathrm{FLD_{NO_2}} \\ & + \mathrm{FLD_{CH_2CHO}} + \mathrm{FLD_{HCHO}} + \Sigma \mathrm{FLD}_x \end{aligned} \qquad 19.10$$

19.3.4 Tenability limits and hazard calculations for asphyxiant gases

The main cause of incapacitation and death during and immediately after fires is exposure to asphyxiant gases. Incapacitation results from loss of consciousness due to the combined hypoxic effects of carbon monoxide, hydrogen cyanide and carbon dioxide, with some additional effects from low oxygen hypoxia, nitrogen oxides and inhaled irritants. Loss of consciousness prevents escape and further uptake of asphyxiants while comatose is likely to result in death within a further minute or so unless the occupant is rescued. The most useful tenability end point to work to is therefore considered to be loss of consciousness ($F_{\mathrm{IN}} = 1$), with design limits set to prevent this occurring. Since individual susceptibility varies in the population, this is predicted to represent the median of the distribution of exposure doses resulting in collapse.

Approximately 11.3% of the population is considered likely to be susceptible below an FED of 0.3 (see ISO 13571).[4] It will be necessary for the designer or regulatory authority to select an FED level suitable to protect vulnerable subpopulations in the chosen application (for example 0.3 or some other value depending upon the application).

The effects of combinations of asphyxiant gases causing incapacitation in fires are considered to be approximately additive, but a number of interactions need to be considered (see Chapter 4):

- The FED values for carbon monoxide and hydrogen cyanide are considered directly additive as has been demonstrated experimentally.
- Nitric oxide and nitrogen dioxide (designated as NO_x in mixtures) also act as asphyxiants, reducing oxygen carriage in the blood due to the conversion of haemoglobin to methaemoglobin. To this extent their asphyxiant effects can be considered additive with those of hydrogen cyanide and carbon monoxide. However, methaemoglobin combines with hydrogen cyanide in the blood, thereby reducing its asphyxiant effect. Nitrogen dioxide is also a potent lung irritant.
- The effects of irritants on lung function also cause some hypoxia and so an additive term is included consisting of the FLD_{irr}.
- The main effect of carbon dioxide is to increase the breathing rate and thus the rate of uptake of carbon monoxide and hydrogen cyanide. A multiplicatory term V_{CO_2} is used to calculate this effect.
- Low oxygen hypoxia will be additive with the overall hypoxic effects of carbon monoxide and hydrogen cyanide, but is not increased by V_{CO_2} (in fact hypoxia is lessened by carbon dioxide).
- The beneficial effects of increased carbon dioxide on the hypoxic effects of carbon monoxide and low oxygen hypoxia resulting from right shifting of the oxyhaemoglobin dissociation curve are ignored.
- The direct intoxicating effects of carbon dioxide are considered unlikely to occur before other effects so are normally ignored but exposure to 7% carbon dioxide or higher itself causes incapacitation within a few minutes.

On the basis of these considerations the overall FED equation for asphyxiants is:

$$F_{IN} = (F_{Ico} + F_{Icn} + F_{INOx} + FLD_{irr}) \times V_{CO_2} + FED_{Io} \qquad 19.11$$

where: F_{IN} = fractional effective dose for incapacitation (loss of consciousness) due to asphyxiants; F_{Ico} = fractional effective dose for incapacitation by carbon monoxide; F_{Icn} = fractional effective dose for incapacitation by hydrogen cyanide (note that if necessary this can be corrected for the presence of other nitriles besides hydrogen cyanide and for the protective effect on cyanide poisoning of nitric oxide and nitrogen dioxide. [CN] can then be calculated as: [CN] = [HCN] + [Total organics nitriles] − 0.67[NO + NO_2]); F_{INOx} =

fraction of an incapacitating dose of NO + NO_2 due to methaemoglobin formation = [NO_x ppm × t_{min}]/15000; FLD_{irr} = fractional lethal dose for irritants (note that where significant concentrations of acid gases are present this term is calculated according to Equation 19.10. Otherwise it may be expressed in terms of smoke optical density as OD/m × t(min)/90.); V_{CO_2} = multiplicatory effect of inhaled CO_2 and F_{Io} = fractional effective dose for incapacitation by low oxygen hypoxia.

For a simple analysis the direct asphyxiant effects of NO_x and those of NO_x on hydrogen cyanide asphyxia may be ignored without significant error.

For each of these gases it is necessary to obtain an expression for the fraction of a dose required to cause incapacitation. The derivation of these expressions has been detailed in the relevant sections of Chapters 3 and 4 and in the section on asphyxiation by fire gases in the *SFPE Handbook of Fire Protection Engineering*.[3] Basically, the exposure dose acquired over any period of time during a fire is expressed as a fraction of the dose required to cause incapacitation for each asphyxiant component. These are then summed and corrected for V_{CO_2} to provide an overall F_{IN} for each time period. The expressions for the different components of Equation 19.11 are as follows:

F_{INOx} – see below Equation 19.11
FLD_{irr} – see Equation 19.10
F_{Ico} – see Equation 19.12 in following paragraph
F_{Icn} – see Equation 19.13 in following paragraphs
F_{Io} – see Equation 19.14 in following paragraphs
V_{CO_2} – see Equation 19.15 in following paragraphs

For the effects of carbon monoxide the FED is expressed in terms of %COHb. The denominator is the %COHb predicted to cause loss of consciousness in an active (escaping) person = 30% COHb (or 40% COHb for a resting person). The numerator is the Stewart equation,[5] by which the %COHb in the subject is calculated from the inhaled carbon monoxide concentration in the fire, the exposure time and the volume of air breathed each minute:

$$F_{Ico} = 3.317 \times 10^{-5}[CO]^{1.036}(V)(t)/D \qquad 19.12$$

where: [CO] = carbon monoxide concentration (ppm v/v 20 ºC); V = volume of air breathed per minute (l/min); t = exposure time in minutes; and D = exposure dose (%COHb) for incapacitation.

The following values are taken for V and D:

Activity level of subject	V (l/min)	D %COHb
Resting or sleeping	8.5	40
Light work – walking to escape	25	30
Heavy work – slow running, walking up stairs	50	20

This expression (the Stewart equation) was obtained from young adult male human volunteers. It is suitable for adults in situations where the carbon monoxide concentration is high in relation to the blood carboxyhaemoglobin concentration (as for most flaming fires and short exposure durations). Where long exposures may lead to near equilibrium conditions, the Coburn Forster Kane (CFK) equation[6,7] should be used since significant deviations from the Stewart equation may then occur. The Stewart equation somewhat underestimates uptake rates for children. Where more precise carbon monoxide uptake calculations are required, differences in body size (including children) can be accommodated using the CFK equation. For a basic design, use of the Stewart equation is recommended. Differences in body size and other susceptibilities can be considered as allowed for in the overall safety margin chosen to accommodate more susceptible subpopulations (for example an FED 0.3 or other end point).

As an alternative to using this expression the FED_{Ico} may be expressed as a carbon monoxide exposure dose ratio. This method is used for ISO 13571.[4] For this method the FED_{Ico} is expressed as CO ppm $\times$ $t/35\,000$. This is approximately equivalent to a 'light work' case for a subject breathing approximately 20 l air/min.

Since occupants must at least walk in order to escape from a fire, the default case suggested is that for light work. However, this could be varied according to the case. For example a sleeping person escaping from a basement might start by being at rest, then awaken and walk to a stair (light work) then climb the stair (heavy work).

For the effects of hydrogen cyanide and low oxygen hypoxia, the expressions are more complex, because the denominators are not constants. Exponential expressions have been developed to fit the time to incapacitation versus exposure concentration curve from experimental exposures in non-human primates (hydrogen cyanide) and humans (hypoxia), so that the fractional incapacitating doses for hydrogen cyanide (F_{ICN}) and hypoxia (F_{IO}) as follows:

$$F_{ICN} = \left\{ \left(\frac{\exp\left([CN]/43\right)}{220} \right) - 0.0045 \right\} t \qquad 19.13$$

where [CN] = HCN concentration (ppm v/v at 20 °C) and t = exposure time in minutes.

$$F_{Io} = \frac{t}{\exp\left\{[8.13 - 0.54(20.9 - [\%O_2])]\right\}} \qquad 19.14$$

where $[\%O_2]$ = oxygen concentration (% v/v at 20 °C); t = exposure time in minutes; and I = exposure dose for incapacitation.

Similarly, a curve has been fitted to the effect of carbon dioxide on uptake rate due to ventilation (breathing volume per minute) based upon human experimental data.

$$\text{Ventilatory stimulation by } CO_2\ (V_{CO_2}) = \exp\left([CO_2]/5\right) \qquad 19.15$$

where $[CO_2]$ = carbon dioxide concentration (% v/v at 20 °C).

FEDs are calculated for successive short periods during the fire and then integrated with time in order to calculate the time when incapacitation is predicted (FED = 1). Owing to the rapid (t^2) rate of increase of asphyxiant gas concentrations in most flaming fires, variations in individual susceptibility and uncertainties in prediction of incapacitating doses tend to have relatively minor effects on predicted times to incapacitation.

19.4 Overall hazard analysis for a fire

The calculation method for applying the FED expressions to a fire hazard analysis for a fire data set is shown in Table 19.3 for set time–concentration gas, smoke and heat data. The fire data averaged over 1 min intervals are shown in the upper part of the table. The lower parts of the table show the results obtained by applying each of the FED expressions for the different fire effluent parameters. FEC_{smoke} is a concentration-related effect so it is necessary simply for determining the time at which the parameter reaches or exceeds unity. For the overall FIC it is necessary to sum the FICs of each individual gas during each time period. Since irritancy is also a concentration-related effect it is then necessary simply to determine the time at which the parameter reaches or exceeds unity. If the fire conditions were to improve the FEC_{smoke} and FIC may decrease below 1, in which case the occupants would no longer be regarded as being incapacitated. The fractional lethal effects of irritants are dose-related, so the fractional doses of each gas have been summed for each minute, and the totals for each minute are then added to calculate the accumulating dose with time. In this example the doses are so small that no significant accumulated dose is predicted. The fractional incapacitating effects of the asphyxiant gases are determined by calculating the fractional dose of carbon monoxide, hydrogen cyanide and low oxygen hypoxia, and the multiplicatory effect of carbon dioxide (V_{CO_2}) and then entering the results with the FLD value into the F_{IN} equation (Equation 19.11).

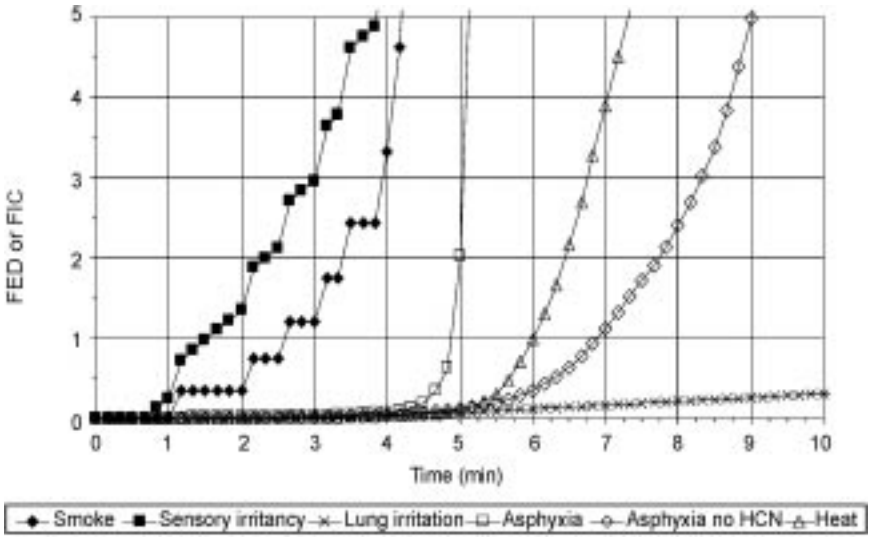
The results for each successive minute are then summed until the accumulated dose reaches or exceeds unity. The effects of radiant and convected heat are also dose-related and calculation expressions can be found in the *SFPE Handbook of Fire Protection Engineering*. In practice FED calculations are made over shorter averaged time periods during a fire, typically 5 or 10 second intervals.

Figure 19.2 shows an example of an overall hazard analysis for the furniture house fire illustrated in Fig. 19.1. The FEC or FED of each physiological effect is calculated throughout the fire, with the end point for each effect reached at an FIC or FED of 1.

Table 19.3 Example of FED calculation method for a fire data set

	1	2	3	4	5	6
Gas concentrations each minute						
Smoke (OD/m)	0.1	0.2	0.5	1.5	3.0	3.5
HCl (ppm)	10	50	150	200	250	200
Acrolein (ppm)	0.4	0.8	2.0	6.0	12.0	14.0
Formaldehyde (ppm)	0.6	1.2	3.0	9.0	18.0	21.0
CO (ppm)	0	0	500	2000	3500	6000
HCN (ppm)	0	0	50	150	250	300
CO_2 (%)	0	0	1.5	3.5	6.0	8.0
O_2 (%)	20.9	20.9	19.0	17.5	15.0	12.0
Temp. (°C)	20	65	125	220	405	405
Heat flux (kW/cm^2)	0	1.0	4.0	10.0	25.0	25.0
Fractional smoke concentration						
FEC_{smoke}	0.50	**1.00**	2.50	7.50	15.0	17.50
Fractional irritant concentration						
FIC_{HCl}	0.06	0.28	0.83	1.11	1.39	1.11
$FIC_{acrolein}$	0.10	0.20	0.50	1.50	3.00	3.50
FIC_{form}	0.10	0.20	0.50	1.50	3.00	3.50
ΣFIC	0.26	0.68	**1.83**	4.11	7.39	8.11
Fractional lethal dose (irritants)						
FLD_{HCl}	0.00	0.00	0.00	0.00	0.00	0.00
$FLD_{acrolein}$	0.00	0.00	0.00	0.00	0.00	0.00
FLD_{form}	0.00	0.00	0.00	0.00	0.00	0.00
ΣFEC_{irr}	0.00	0.00	0.00	0.00	0.00	0.00
Fractional asphyxiant dose						
F_{Ico}	0.00	0.00	0.02	0.07	0.13	0.23
F_{Icn}	0.00	0.00	0.01	0.15	1.52	4.87
FLD_{irr}	0.00	0.00	0.00	0.00	0.01	0.04
V_{CO_2}	1.00	1.00	1.35	2.01	3.32	4.95
F_{Io}	0.00	0.00	0.00	0.00	0.01	0.04
F_{IN} (asphyxiants)	0.00	0.00	0.04	0.45	5.50	25.29
ΣF_{IN}	0.00	0.00	0.04	0.50	**6.00**	31.29
Fractional heat doses						
FED_{rad}	0.00	0.00	0.00	0.00	2.54	2.54
FED_{conv}	0.00	0.03	0.27	1.84	14.67	14.67
FED_{heat}	0.00	0.03	0.27	1.84	17.21	17.21
ΣFED_{heat}	0.00	0.03	0.30	**2.14**	19.35	36.55

The end point, escape impairment (for smoke obscuration and irritancy) or incapacitation (for heat and asphyxiant gases) is reached when the FIC or FED value reaches 1.
Limiting values are emboldened. Lethal values are approximately 2–3 times incapacitating levels for dose-related parameters.
The actual figures for the different parameters in this table were calculated using earlier versions of the different FED expressions, so slightly different numbers may be obtained using the latest versions of the equations presented in the text.



19.2 FED analysis in terms of times to incapacitation for an occupant of a domestic house lounge during an armchair fire.

For the example shown the first hazard to exceed the tenability limit is impairment of escape capability due to the effects of irritant organics and acid gases in the smoke products at 1.5 min. This is followed 1 min later by the limit for optical obscuration by smoke particulates. The combined effect of these two hazards is to seriously impair or prevent escape. After 5 min it is predicted that an occupant would lose consciousness, primarily due to the asphyxiant effects of hydrogen cyanide, with death occurring within approximately a further 30 seconds. For this fire, escape impairment due to the effects of heat exposure is predicted after 6 min, although several minutes further exposure would be required for burns to occur. Also shown for comparison is the predicted time to incapacitation if there had been no hydrogen cyanide present (after 7 min). This would be due mainly to the asphyxiant effects of carbon monoxide and carbon dioxide. The analysis therefore illustrates that, for this fire, hydrogen cyanide is the main driver of incapacitation due to ashyxiant gases. Notice that just before 5 min the F_{IN} curve is increasing very rapidly to high off-scale values by 5 min. This means that the predicted time to incapacitation is very insensitive to errors or uncertainties in measuring or estimating the concentration of hydrogen cyanide during the fire, or in predicting the precise concentration–dose–effect relationship for hydrogen cyanide in humans. The exposure dose of irritants capable of causing potentially fatal deep lung inflammation some hours after exposure is only around 0.2 after 10 min, so this effect is predicted not to occur, although elderly subjects have been found to be particularly sensitive to potentially fatal infective bronchopneumonia following exposures of this kind in fires.

19.5 Application to escape calculations

The example illustrated in the previous section is for tenability time in a case where the occupant is in the room of fire origin, which is a small lounge in a domestic dwelling. In such situations it is possible also to consider the comparison of time available for escape with time required for escape. The main considerations for escape in such a scenario are related to the times required for detection of the fire and triggering of the smoke alarms (see Fig. 19.1), and the time required for occupants to become alerted and carry out a range of behaviours before attempting to leave the house. The actual time required to walk out of the room, and then out of the house is relatively small.

These aspects are described in a detailed study of occupant behaviour in domestic fires by Purser and Kuipers.[8] For an occupant upstairs in the same house other aspects related to their interaction with the fire conditions become important. One consideration is exit choice behaviour. If an occupant of an upstairs room became aware of increasing smoke obscuration on the upstairs landing, at what smoke density might they decide that it would be too dangerous to escape via the stairs, and decide to shut the bedroom door and stay where they were, or attempt escape via a window? Some guidance on this kind of issue is presented in Table 19.1. If occupants did decide to escape via the stairs, what effect would exposure to irritant smoke have on their ability to descend the stairs and their speed of movement? Some guidance on this is also presented in Table 19.1 and Equations 19.5–19.8. These considerations of the effects of smoke on escape behaviour become even more important when considering fire incidents in large buildings, involving large numbers of occupants, where survival has been critically influenced by exit choice and the speed and ability to move through smoke.[9] It is possible to model these effects by combining evacuation simulations with fire simulations, using fire dynamics models such as those described in Chapters 18 and 20 with evacuation models such as GridFlow,[10] CRISP[11] or EXODUS[12]).

19.6 Conclusions

Fractional effective dose modelling provides a powerful tool for calculating effects on escape capability, time to incapacitation and time to a potentially lethal exposure for humans exposed to fires. When combined with data from full-scale experimental fires or full-scale fires calculated using computational fire dynamics models, it can be used to assess fire hazards to occupants for fire safety engineering design, product evaluation or forensic fire investigations. As with almost all parameters used in fire engineering calculations, there are some uncertainties over the accuracy with which each individual FED equation is predictive of incapacitation end points in humans, and unlike some other fire parameters it is not possible to carry out the experiments required to obtain

precise data due to ethical limitations. Also, as described in Chapter 3, it is known that there are significant ranges of sensitivity to toxicant exposures in the human population. For some fire incidents, sufficient resources have been available to carry out detailed studies of the actual fire conditions to which people were exposed and the effects on their behaviour, incapacitation and survival. These studies have provided some validation of the methods used. Also, as described in the worked example, overall analysis of fire hazards often shows that fire conditions tend to deteriorate rapidly, so that possible variations in FED algorithms then have relatively small effects on calculated times to incapacitation. An important method for taking account of potential uncertainties and variations in different parameters in an overall analysis is application of risk assessment methods involving approaches such as Monte Carlo simulations.

The FED method has therefore proved to be effective in both the forensic and design contexts. It is considered that as the ability of fire dynamics computational methods to predict fire conditions and of evacuation simulation methods to predict escape behaviour improve, and as they are more frequently applied with FED calculations to assess fire hazards, the overall performance of these approaches will be further established.

19.7 References

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20

Modelling fire growth and toxic gas formation

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Abstract: The enormous complexity of the coupled phenomena of fire growth and toxic gas generation presents a huge challenge to predictive methodologies. Their prediction is hampered by the fact that the combustible materials involved in real fires are typically poorly defined, not having benefited from the detailed studies undertaken in the wider combustion community on idealised fuels. Moreover, the often significant effects of finite-rate chemistry greatly complicate representations of gas-phase combustion. Despite these difficulties, significant progress is now being made towards establishing more robust modelling frameworks. In particular a number of advanced CFD-based approaches are being developed which have the potential to include key phenomena influencing fire yields of toxic gas such as carbon monoxide. Further progress is constrained on the need for some degree of empirical calibration in simpler models, and by computational demands and a lack of knowledge of relevant input parameters amongst the more advanced approaches. None has been yet extensively tested in fire applications, and the bulk of modelling activity remains confined to the research domain.

Key words: fire modelling, fire growth, flame spread, pyrolysis, toxic gas, CFD.

20.1 Introduction

Fires produce heat and combustion products that are generally translated into high temperatures and concentrations of different compounds, many of them toxic. These temperatures and concentrations are a function of the different chemical reactions occurring in the combustion process and of the prevailing environmental conditions. Significant ventilation will not only result in more complete combustion, but will also tend to dilute the products, resulting in lower concentrations of toxic gas and reduced temperatures. The way in which the air is entrained will also affect the nature of the combustion reactions and the toxic gas evolution within the flowfield. Reactions will occur when fuel initially meets the oxidiser but also when the hot primary products of combustion interact with air entrained. Fire growth and toxic gas production therefore cannot be separated and need to be treated in a coupled manner. This

chapter focuses on the modelling methods which address these interlinked phenomena.

Except in some simple idealised scenarios, typified by laboratory tests, toxic gas yields are generally found in the context of 'natural' (or 'real') fires, where the fire develops to encompass new combustible materials according to their availability, and where the nature of the burning materials, and hence flammable combustibles, is typically very heterogeneous. Owing to the complexity of these processes, which span a huge range of time- and length-scales, many simplifications are required which will limit the generality, reliability and applicability of the models. These simplifications can involve the description of the fuel supply rate as well as the gas-phase combustion processes. Nevertheless, advanced modelling methods are now being developed with the intention of addressing some of these issues, in particular those based on computational fluid dynamics (CFD) with coupled solid-phase pyrolysis models.[1,2] Unlike their predecessors, which were concerned mainly with *transport* of heat and chemical species, advanced models tackle these coupled phenomena in a more comprehensive manner, which may ultimately provide a reasonable basis for establishing and extending representations of fire growth and the associated toxic gas production and distributions in fires.

Modelling fire 'growth' is a major undertaking in its own right including complex processes in the solid and gas phases. Thus there is a tendency to represent it in a highly simplified manner within CFD models, thereby normally restricting the validity to specific exposure conditions or idealised fire scenarios. A widely used baseline approach is to drive the fire simulation models by the prescriptions of fuel release rates. The latter are defined by simple models or linked to empirical values and the *prediction* of liberation of fuel volatiles from the fire source is bypassed. This strategy removes the need to solve the complex thermal processes occurring in the solid phase; nevertheless, it does not eliminate the need to predict 'flame spread'. Likewise, a common way to address the latter problem, dispensing with the need for detailed modelling of the solid/gas phase coupling, is by exploiting empirically derived spread rates. Such prescriptions, together with specifications of burning rates and global heats of combustion, are the basis of commonly used fire growth representations, such as the well-known t^2 fires,[3] as used in simpler fire models. A spectrum of more sophisticated approaches is also available, based on some form of 'flame spread model', where the boundary conditions for volatile generation appear coupled to the fire environment.[1,4] To adequately define the volatile release from solid surfaces, or an equivalent combustible gas inflow, both burning rate and area must be defined. The former can be established on the basis of pyrolysis models of different levels of complexity, where fuel supply is coupled to the heat feedback from the gas-phase combustion reaction, whilst the latter is obtained by means of a model of pyrolysis front progress that once more links heat transfer from the combustion reaction to the available flammable materials. It is

important to note that though the description of fuel generation and flame spread is necessary to establish the proper boundary condition for the CFD model, the importance of the fuel characteristics, beyond global heats of combustion, on the production of heat and toxic gas is still a matter of debate. The main use of these methods is currently in research applications.

Treatment of the subsequent gas-phase energy release process, as the fuel vapour is consumed, may also be addressed at many different levels. In the simplest models, heat and gases are represented by conserved scalars, or a crude 'heat source' model may be adopted to define the region within which it is assumed that energy release is occurring. Lacking a combustion model, sequential chemical reactions are therefore neglected. For these methodologies to be valid, it is necessary to assume that temperatures will drop downstream of the primary combustion region, reactions then being frozen. Whilst this might not be unrealistic in well-ventilated environments or at the earlier stages of the fire growth process, as the fire spreads, with increase in heat release rates and decrease in air availability, these assumptions break down and sequential chemical reactions can have an important effect on toxic gas concentrations and temperature distributions. Thus combustion models are required, and, even in their simplest form, i.e. with reaction rates linked purely to mixing, the distributed burning which is characteristic of gas-phase fire phenomena then arises as a true prediction of the model.

Apart from CFD, other simpler alternatives to representing fire growth also exist, ranging from specification of standard or parametric temperature–time curves (Eurocode 1 Annex A), i.e. effectively characterising the effects of the heat release in particular environments, through to more physically based models including semi-empirical flame spread models,[5] fire dynamics models[6] and zone models.[2] The latter may include simple representations of flame spread, but within a highly simplified fire representation. Given that transport and chemistry in the gas phase is not properly resolved, none of the above provides a detailed spatial description of the thermodynamic conditions which underpin toxic gas production. Moreover, it is only in models of a comprehensive nature, i.e. where the interrelated phenomena are linked together at a fundamental level, rather than coupled empirical representations, that any degree of generality in predictive capabilities might reasonably be expected.

Sufficiently detailed representations of fire growth provide the platform on which toxic gas predictions can be built. As described elsewhere in this book (Chapter 14) a range of different toxic gases are generated in fire, including asphyxiant and irritant gases, in quantities which are very much dependent on the combustion conditions. Models for toxic gas prediction are almost invariably concerned with the major species which give rise to fatalities in fires, in particular the asphyxiant carbon monoxide (CO), and the discussion that follows assumes that this is the prime species of interest. As also described in Chapter 14, under certain circumstances it is possible to derive engineering correlations relating

toxic gas yield to the broad characteristics of the underlying combustion conditions, in particular the equivalence ratio and temperature. Whilst of relevance and use in general assessment of hazards in certain well-defined scenarios, such engineering correlations have limits of applicability, and to be of general use, advanced models must produce robust predictions for a wide range of conditions. This requirement, and the overall complexity of toxic gas formation with involvement of finite-rate chemistry, place huge demands on predictive methodologies. Indeed, any such capabilities are not yet fully established and much of what is described here relates to ongoing study with research codes.

Historically, many attempts have been made to represent toxic gas yields in fire using empirical relationships (see Chapter 14). By their nature, these approaches tend to lack generality and are often not a great deal of use in a predictive sense. On the other hand, more fundamentally based approaches, using advanced modelling techniques, are also constrained in many respects, being limited both by an insufficient knowledge of the fundamental phenomena and computational restrictions. Nevertheless, there has been some success in application of modelling methods for simple fuels, particularly for relatively well-ventilated scenarios, and research continues on extending these methods into more challenging applications, in particular, to the under-ventilated conditions which are of great practical relevance. This chapter provides an overview of the state-of-the-art in this area and outlines a number of areas where further work is needed.

At the outset it is also sensible to consider the drivers for development of such methods, in terms of potential end users and areas of application. These may ultimately include:

- forensic investigations, where it is necessary to reconstruct the history of a particular fire in order to answer questions that may be raised in litigation;
- supplementing and extending the results obtained in standard testing, recognising the large costs involved in full-scale fire tests;
- design, where toxic gas predictions can, in principle, be factored into measures of toxic hazard, e.g. via fractional effective dose (FED) representations of tenability effects which in turn can be exploited in risk models; here, considering the complexity of the real phenomena, the emphasis must be on relative hazard levels, and consideration of 'reasonable worst cases', rather than absolute predictions of gas yields.

In each of these cases, caution is needed, owing to the challenging nature of the problems being addressed. Where possible, use should be made of supporting information, including reference to model validation in appropriate or similar scenarios, and use of alternative methods. In the longer term, a further aspiration would be to use simulation tools to investigate the roles of the different contributory phenomena, thereby supporting an enhanced scientific understanding of the underlying processes.

20.2 Fundamentals of computational fluid dynamics (CFD) fire modelling

The technique of CFD is now employed across a broad range of engineering disciplines for prediction of physical phenomena involving fluid flow. In many of these applications, e.g. aerodynamics, the relevant flows are basically isothermal, so there is no interest or need to look at the effects of buoyancy or heat release. However, because the basic governing equations are fundamental in nature, the method can in principle be applied to solution of any problem involving energy and mass transfer. Thus, it is finding increasing application in the realm of fire safety engineering and for simulation of the behaviour of fires in buildings in particular.[7,8] Many general reviews of turbulent combustion modelling have been produced, including those of Poinsot and Veynante,[9] Fox,[10] Peters,[11] Bilger[12] and Bilger *et al.*,[13] whilst fire applications are also considered in the review articles of Cox[14] and Novozhilov.[1]

Building fire applications are normally concerned with predictions of smoke movement due to its impact on life safety. Applications of CFD to problems where the transport of smoke is the dominant issue, i.e. where resolution of the details of the fire source itself and smoke concentration distributions are of secondary importance, are now commonplace and very acceptable predictions can be achieved over a wide range of scales and geometrical scenarios.[15] Smoke is normally represented as an inert marker in such models, with the details of the formation and destruction being neglected. Furthermore, despite their relative importance in deaths caused by fire, other minor products of combustion (e.g. carbon monoxide, CO, and hydrogen cyanide, HCN) are generally omitted altogether, or dealt with by overlaying the simple engineering approximations that are used in zone modelling, i.e. global equivalence ratio (GER) relationships.[16] For design applications, this framework may not be entirely unreasonable, since the intention is a strict separation of people leaving a building and toxic combustion products, implemented, for example, via minimum requirements for the height of the hot layer above an escaping individual.

This situation reflects the relative confidence in application of CFD techniques to fluid flow prediction, but also the extreme complexity and difficulty in representing the processes related to combustion of real fuels. Besides some basic deficiencies in the scientific knowledge regarding the details of the complex physical and chemical phenomena occurring in real fires, and the effects of such toxic products on humans, there are significant difficulties in the computational representation of minor products of combustion. Furthermore, even when the methods of solution are accessible, many significant constraints limit practical applications, including training of code users, insufficient or inappropriate model verification and validation, a lack of knowledge amongst approving bodies, and limits on computing resource.

Nevertheless, over the past three decades, substantial progress has been made in the development of powerful models for incorporation of detailed chemical calculations into combustion simulations.[7,8] Indeed, models based on 'flamelet' representations of combustion, developed in conjunction with bench-scale combustion experiments,[17,18] have been exploited in building fire simulations.[19,20] There are two key limitations to these methods – their fundamental restriction to applications involving simple fuels, where chemical kinetics are sufficiently well known, and their inability to properly treat finite-rate chemistry phenomena such as those involved in toxic gas production, e.g. in the formation and consumption of carbon monoxide; thus, whilst proving to be reasonably robust, even some way outside the regime of well-ventilated fires,[21,22] they are not expected to work well in highly vitiated fire environments, which include many of great practical relevance, for reasons that are further explained later.

The starting point for CFD models is an 'exact' system of coupled partial differential equations, known as the Navier–Stokes equations, that together describe the relevant phenomena in terms of mass, momentum, chemical species and energy. Though fundamental in nature, the exact solution of these equations requires the complete resolution of all length- and time-scales encompassed by the problem. In the turbulent combustion environments which are characteristic of fire, the solution of practical problems will remain well beyond the capabilities of even high performance computing (HPC) resources for the foreseeable future.[7,8]

It is therefore necessary to simplify the problem by various approximate procedures. Historically, there have been two major strategies used in fire simulation, i.e. Reynolds-averaged Navier–Stokes (RANS) and large eddy simulation (LES), both sourced from the wider combustion community but with certain fire-specific considerations. The former uses the concept of 'time averaging' to decompose the instantaneous variable, ϕ, into a time mean component, $\bar{\phi}$, and a fluctuating component, ϕ':

$$\phi = \bar{\phi} + \phi'$$

where

$$\bar{\phi} = \frac{1}{\Delta t}\int_{t}^{t+\Delta t} \phi \, \mathrm{d}t$$

In flows of variable density, such as fire, correlations between fluctuations in the quantity, ϕ', and the density, ρ', can be avoided by using mass-weighted averages[23] as follows:

$$\tilde{\phi} = \frac{\overline{\rho\phi}}{\bar{\rho}}$$

The decomposition is now expressed in terms of the mass-weighted mean, $\tilde{\phi}$, and fluctuation, ϕ'':

$$\phi = \tilde{\phi} + \phi''$$

$$\overline{\rho\phi''} = 0$$

Using this approach, the governing equations can be written in time-averaged form as follows.

Continuity:

$$\frac{\partial \bar{\rho}}{\partial t} + \frac{\partial}{\partial x_j}\left(\bar{\rho}\tilde{u}_j\right) = 0$$

Momentum:

$$\frac{\partial}{\partial t}\left(\bar{\rho}\tilde{u}_i\right) + \frac{\partial}{\partial x_j}\left(\bar{\rho}\tilde{u}_j\tilde{u}_i\right) = -\frac{\partial \bar{p}}{\partial x_i} + \frac{\partial(\bar{\tau}_{ij} - \overline{\rho u_i'' u_j''})}{\partial x_j} + \bar{g}_i$$

Energy:

$$\frac{\partial}{\partial t}\left(\bar{\rho}\tilde{h}\right) + \frac{\partial}{\partial x_j}\left(\bar{\rho}\tilde{u}_j\tilde{h}\right) = \frac{\partial \bar{p}}{\partial t} + \frac{\partial}{\partial x_j}\left(\frac{k}{c_p}\frac{\partial \tilde{h}}{\partial x_j} - \overline{\rho u_j'' h''} - \overline{\dot{q}_j^R}\right)$$

Species:

$$\frac{\partial}{\partial t}\left(\bar{\rho}\tilde{Y}_\alpha\right) + \frac{\partial}{\partial x_j}\left(\bar{\rho}\,\tilde{u}_j\tilde{Y}_\alpha\right) = \frac{\partial}{\partial x_j}\left(\overline{D\bar{\rho}\,\frac{\partial \tilde{Y}_\alpha}{\partial x_j}} - \overline{\rho\, u_j'' Y_\alpha''}\right) + \widetilde{\dot{\omega}_\alpha}$$

These equations are similar to the original Navier–Stokes equations but they now involve cross-product terms in the fluctuating components which are too expensive to compute directly (as could be achieved via direct numerical simulation (DNS)) and which must be approximated or 'modelled'. In particular, the velocity fluctuations give rise to the 'Reynolds stresses', i.e. resulting normal and shear stresses which affect the fluid dynamics. An approach known as Reynolds stress modelling, or second-order closure, may be adopted, but it is computationally demanding, requiring solution of further transport equations for each stress term. In practice, simpler techniques have been widely exploited to provide satisfactory engineering solutions, invoking the so-called 'Boussinesq eddy viscosity concept'. Here, an analogy is made with viscous stresses in laminar flow, with assumed linear stress–strain dependencies, relating the Reynolds stresses to the mean strain rate in the fluid via a modelled 'local eddy viscosity' or 'turbulent kinematic viscosity'. An equivalent turbulent diffusivity parameter can be used in the chemical species balance equations to relate cross-product terms to gradient diffusion (the 'gradient diffusion hypothesis').

Many approaches are available for modelling the turbulent viscosity itself, ranging from simple algebraic models based on dimensional reasoning, e.g. the Prandtl mixing length model, to one- and two-equation models, which require the solution of additional balance equations for parameters which characterise the turbulent nature of the fluid. The simpler models generally require tuning for

specific types of flow, and in practice the two-equation high Reynolds number $k-\epsilon$ model is widely used, with a requirement for solution of additional transport equations for the turbulence kinetic energy, k, and its dissipation rate, ϵ. For fires, it is important to use the buoyancy modified form of these equations.[24] Also, special attention may be required for certain regions of the flow, e.g. a low Reynolds number model may also be adopted for near-wall regions and corrections may be required for axisymmetric plumes to compensate the known tendency for underprediction of the radial spread rate. The computational costs of the basic approach are relatively modest, since there are only two extra equations on top of the original equation set.

In summary, each of the above Favre-averaged conservation equations and the balance equations for k and ϵ are now solved numerically, if the source terms can be closed, in the general form:

$$\frac{\partial}{\partial t}\left(\bar{\rho}\tilde{\phi}\right)+\frac{\partial}{\partial x_j}\left(\bar{\rho}\,\tilde{u}_j\tilde{\phi}\right)=\frac{\partial}{\partial x_j}\left(\Gamma_\phi\,\frac{\partial\tilde{\phi}}{\partial x_j}\right)+\tilde{S}_\phi$$

where ϕ is a generic (Favre-averaged) property of the fluid, S_ϕ is a source term and Γ_ϕ is an exchange coefficient appropriate to ϕ. (The use of ϕ as an instantaneous variable is consistent with common usage in CFD modelling, but is separate from its use in other chapters of this book where it represents the equivalence ratio.)

LES provides an alternative treatment to RANS in which the larger eddies, i.e. those which can be resolved at the scale of the computational grid, are solved directly, and turbulent effects at smaller scales are approximated using a subgrid scale (SGS) model. This is achieved by filtering (indicated by $^-$ over a character) instantaneous balance equations such that only the larger scales, in physical or spectral space, are explicitly resolved.[25] By this means a more faithful representation of the large-scale turbulence behaviour is achieved, but finer meshes may be required in order to provide adequate resolution, hence the technique is generally more computationally demanding.

A means of representing the turbulent viscosity of the fluid is required for the SGS model. An early approach by Smagorinsky[26] has since been widely adopted:

$$\mu_{\mathrm{LES}}=\bar{\rho}(C_{\mathrm{s}}\,\Delta)^2\left[2\bar{S}_{ij}\,\bar{S}_{ij}-\tfrac{2}{3}(\nabla\bar{u}^2)\right]^{1/2}$$

where the strain rate, S_{ij}, is:

$$S_{ij}=\frac{1}{2}\left(\frac{\partial u_i}{\partial x_j}+\frac{\partial u_j}{\partial x_i}\right),\quad i,j=1,2,3$$

The Smagorinsky constant, C_{s}, is empirically derived and a number of different values have been proposed for various types of flow.[26,27] Germano pioneered dynamic viscosity models[28] but these may not be justifiable in typical

fire applications, where it has been argued that even a constant viscosity may give acceptable results, owing to the fact that the flowfield is so dominated by the large-scale resolvable eddies.[29,30]

Whichever procedure is adopted to achieve turbulence closure, the full rigour of the initial balance equations is lost, being replaced by modelled properties. Moreover, the effects of turbulent fluctuations are not confined to the stresses controlling the fluid flow but can have a dramatic impact on chemical kinetics and radiation heat transfer, i.e. the furthest right-hand terms in the gas and energy equations presented above. The reasons are the same, because the cross-correlations of the fluctuating properties are unknown. The impact of these issues, and methods to overcome them, are the main focus of the rest of this chapter, spanning the global influence on combustion chemistry in Section 20.3 and the effects on toxic minor species, or pollutant chemistry in Section 20.4.

20.3 Combustion and pyrolysis models

A combustion model is a critical element of a CFD fire simulation, since it can be used to represent the spatial and temporal distribution of the rate of heat release arising from consumption of the parent fuel. Gas-phase combustion models differ in the means by which they accommodate the effects of turbulent fluctuations, and the following sub-sections describe the essence of the turbulence closure problem, together with some of the methods used to overcome it. Thereafter, the challenge of describing solid-phase pyrolysis, for prediction of flame spread, is briefly reviewed and the issues associated with effectively coupling the gas and solid-phase contributions are discussed.

20.3.1 Chemical source term closure

As mentioned above, the key aspect of the turbulent combustion modelling problem is the need to 'close' the source terms in the governing equations which relate to species and enthalpy, i.e. to the generation of products of combustion and prediction of the overall heat release rate. The closures are needed to an accuracy acceptable in describing the processes peculiar to fire. The effects of buoyancy on turbulent transport and fluid flow have already been referred to but it is now necessary to specifically consider the effects of fluctuations on chemical kinetics, ($\bar{\dot{\omega}}$), and radiant heat transfer ($\overline{\dot{q}_j^{\mathrm{R}}}$). Since both phenomena are generally highly non-linear in temperature, fluctuations can cause greatly enhanced levels of mean reaction rate and mean radiant heat flux, as explained below.

Assuming the simplest possible chemical kinetics, i.e. if the reaction mechanism can be reduced to a single global one-step reaction, the rate equation is:

$$F + rO \xrightarrow{k} (1 + r)P$$

Here, a unit mass of fuel, F, reacts with its stoichiometric mass requirement, r, of oxidiser, O, to provide $(1 + r)$ mass units of product, P. A simple Arrhenius expression describing the instantaneous rate constant for the reaction can be written:

$$k = B\mathrm{e}^{(-T_\mathrm{a}/T)}$$

where B is the pre-exponential factor for the reaction and T_a its activation temperature.

On replacing T by its mean and fluctuating components, and time-averaging, this becomes:

$$\bar{k} = B \exp\left(-\frac{T_\mathrm{a}}{\bar{T}}\right)\left[1 + \overline{T'^2}\left(\frac{T_\mathrm{a}^2}{2\bar{T}^4} - \frac{T_\mathrm{a}}{\bar{T}^3}\right) + \ldots\right]$$

The simple substitution of mean temperature into the Arrhenius rate expression would clearly be misleading. Evidently, the mean reaction rate can be substantially higher than one based upon consideration of laminar chemistry only and the turbulent rate may exceed the laminar value by over two orders of magnitude for some quite reasonable assumptions of activation temperature (20 000 K) and reactant and product temperatures (idealised as 500 K and 2000 K, respectively).[31] Radiative fluxes to solid surfaces, typically the main driver of flame spread, are affected by a similar phenomenon[32] where the magnitude of the second term in the expansion can exceed the first when the fluctuating components reach 40% of the mean values. Such fluctuation intensities are quite likely in fire plumes (e.g. Cox and Chitty[33]), so mean property representations are clearly inadequate.

It is therefore essential to properly account for the effects of turbulent fluctuations on chemical kinetics, both in terms of predictions of heat release rate and combustion products. A number of modelling techniques have been proposed to achieve this, with many aspects being common to both RANS[31] and LES treatments.[34] Some of the main approaches are described in more detail in the following subsections on combustion models, and in Section 20.4 from the perspective of predicting combustion products and toxic gas yields, with an emphasis on those models previously used, or showing most promise and relevance, for fire applications.

20.3.2 Eddy break-up combustion model

In the turbulent diffusion flame systems characteristic of fire, most chemical reactions can be considered fast compared with the relatively slow process of the physical mixing of fuel with oxidiser, hence are referred to as 'fast chemistry'. Thus, under some circumstances, it is possible to exploit a knowledge of the mixing rate alone in order to determine the overall rate of heat release. The first mixing rate model was based on the idea that the reaction progress in premixed

flames is determined by the intermingling, at micro-scale level, of fragments of unburnt reactants with hot products.[35] The rate of reaction was equated to the rate of dissipation of turbulent kinetic energy at the smallest scale in the flow, where viscous forces become dominant (the Kolmogorov length-scale):

$$\bar{S}_{\mathrm{f}} = -C_{\mu}\,\bar{\rho}\frac{\epsilon}{k}\left(\overline{Y_{\mathrm{f}}'^{2}}\right)^{1/2}$$

where $\overline{Y_{\mathrm{f}}'^{2}}$ is the variance in fluctuations of the fuel mass fraction obtained from a further balance equation in the generic form given above and C_{μ} is a constant. This model was later modified by Magnussen and Hjertager[36] for diffusion flames by assuming that $(\overline{Y_{\mathrm{f}}'^{2}})^{1/2}$ is proportional to the mean mass fraction and that the rate of reaction is further controlled by the deficient reactant:

$$\bar{S}_{\mathrm{f}} = -C_{\mu}\,\bar{\rho}\frac{\epsilon}{k}\min\left\{\bar{Y}_{\mathrm{f}},\ \frac{\bar{Y}_{\mathrm{o}}}{r},\ B\,\frac{\bar{Y}_{\mathrm{p}}}{(1+r)}\right\}$$

Thus, in the presence of products, rate control will switch from oxidiser in the vicinity of the fire source, to fuel at more remote locations. This expression is useful in allowing an approximate determination of the local rate of fuel consumption and combustion product generation without needing to take any account of detailed chemical kinetics or fluctuating scalar parameters.

Though relatively simple in concept, this model has also proved to be robust across a range of different combustion regimes, spanning both premixed and non-premixed combustion systems. Eddy break-up has also been adopted as an SGS model in LES.[37]

20.3.3 Presumed and transported probability density function (PDF)/filtered density function (FDF) methods

PDF and FDF methods in RANS and LES approaches, respectively, are underpinned by a representation of the turbulent combusting mixture as a statistical ensemble of microscopic laminar flame elements.[38] At the simplest end of the spectrum, the flamelets are taken to be steady, as per the classic 'steady laminar flamelet models' (SLFM). Thus, the local instantaneous composition and temperature within the turbulent flame flowfield are linked directly to that which might pertain in a steady laminar diffusion flame – with this information being supplied either from detailed chemical calculations or direct from experiment,[31] and parameterised, if necessary, by strain rate and other variables. These treatments have been particularly popular and successful for application to a number of non-premixed systems, such as fires, though there are a number of limitations and challenges, as discussed below. The more advanced approaches relax the steady assumption, but at the cost of greatly increased computational expense.

The species conservation equation can be conveniently recast in terms a conserved scalar, ξ, the mixture fraction,

$$\xi = \frac{\beta - \beta_o}{\beta_f - \beta_o}$$

as

$$\frac{\partial}{\partial t}\left(\bar{\rho}\tilde{\xi}\right) + \frac{\partial}{\partial x_j}\left(\bar{\rho}\,\tilde{u}_j\,\tilde{\xi}\right) - \frac{\partial}{\partial x_j}\left(\Gamma_\xi \frac{\partial \tilde{\xi}}{\partial x_j}\right) = 0$$

where $\beta \equiv Y_f - (Y_o/r)$ and the subscripts f and o refer to fuel and oxidiser respectively. ξ takes the value of unity in the fuel stream and zero in the oxidiser.

Since this equation contains no source term it bypasses the problem of turbulent closure. Instead it is assumed that all influences of turbulence on the kinetics are embedded within the behaviour of ξ. Solution for the mean mixture fraction, $\tilde{\xi}$, is achieved in much the same way as for $\tilde{\phi}$, since the mixture fraction is subject to the same transport processes of convection and diffusion. The outstanding problem is then to relate the instantaneous species mass fractions, Y_α, to the instantaneous behaviour of ξ and to provide a model of the latter.

One simple approach, the basis of the flamesheet combustion model, is to use a 'fast chemistry' assumption, taking equilibrium values of species yields to define state relationships, or in the limit of an assumed one-step irreversible reaction, no co-existence of reactants and oxidants.[1,39] However, the conditions in turbulent diffusion flames may be far from equilibrium, particularly in fuel-rich regions, and a methodology for partially relaxing this assumption, defining much more appropriate state relationships, is provided by the 'laminar flamelet concept'.[31] This is founded on the premise that the relationship between Y_α and ξ is locally the same in the turbulent flame as it is in a laminar flame, as suggested by Bilger[40] and broadly confirmed by experiments.[41] For simple hydrocarbons the laminar flame can be modelled theoretically, for example via simulations of opposed diffusion flame problems performed using detailed chemical kinetic codes.[42,43] For the more complex types of fuel of more practical concern in fire situations, the appropriate information might more realistically be derived from experimental measurements on representative laminar flames.[41,44–46]

In some circumstances it may also be important to account for the influence of other parameters, such as strain rate (or the scalar dissipation rate), heat loss and vitiation level, on the laminar flame profiles.[31] For example, the former phenomenon can be important in near extinction conditions in highly turbulent flames[47] but will usually be smaller in open turbulent jet flames;[17] it may often be a minor influence in the relatively benign mixing environments typical of compartment fires, and is normally neglected.[31,48] Heat loss is more complex since it is often dominated by soot, which has a comparatively slow formation chemistry. Attempts have been made to overcome this problem by establishing libraries of 'non-adiabatic' flamelets, relating heat loss to predicted soot

yields.[49] Though these have been relatively successful, fundamental limitations are still present due to the required assumptions on the location of the soot in the composition space. Both correlated and uncorrelated closures have been explored, but the reality will normally lie somewhere in between.[50] Finally, vitiation level has been adopted as a further dimension in flamelet libraries but thus far only implemented as an *a priori* assumption.[19,51]

Once state relationships are established, the mean species mass fractions can then be determined from a knowledge of the statistical character of the fluctuating property field, i.e.:

$$\tilde{Y}_\alpha = \int_0^1 Y_\alpha(\xi)\,\tilde{P}(\xi)\,\mathrm{d}\xi$$

where $\tilde{P}(\xi)$ is the PDF describing mixture fraction fluctuations. In engineering application it has been common to assume, a priori, a functional form for $\tilde{P}(\xi)$, which greatly simplifies the modelling problem. An alternative strategy, in which an additional transport equation for the joint PDF is solved using Monte Carlo methods, was pioneered for reactive flows by Pope and co-workers (e.g. Pope[52]). This removes the key model approximations from the representation of the combustion process and requires a modelled closure only for molecular transport. However, this is achieved only at the cost of significantly greater computational costs, with the order of 1000 particles per computational cell being required.[31]

The above methods are commonly referred to as 'presumed PDF' and 'PDF transport' methods, respectively, For the former, the PDF function is described by its first two moments, $\tilde{\xi}$ and ξ''^2. These can be obtained from solution of two further equations in the same form as the generalised governing equation presented above. Adopting an assumed form for $\tilde{P}(\xi)$, specifically the beta function (Euler integral of the first kind), has been found to be both economical and reasonably representative of the mixing involved. Whilst results for higher momentum flame systems have been shown to be relatively insensitive to the precise shape of the PDF, there is still some uncertainty as to whether this is so for buoyant fires and the applicability of a method which requires the reaction zone to be smaller than the Kolmogorov length-scale has also been questioned.[1,12,13,53]

A similar concept to the flamelet model is adopted in FDF approaches for LES SGS models[54] with the same advantage that the non-linear source terms involving chemical reactions and radiative emissions appear in closed form. Similar methods are again available, analogous to presumed or transported PDF methods in RANS.[34,55,56] However, as a consequence of the transitionally turbulent nature of the flow at the base of large fire plumes, serious under-predictions of reaction rates may result, due to violation of assumed statistical independence between the mixture fraction and dissipation in simple presumed FDF methods.[57] Special treatments are required to overcome this.[34] The major

advantage of transported FDF methods[54] is that they can readily be extended to include finite-rate chemistry.[34] However, the computational costs of these approaches are significant, approximating to an order of magnitude overhead on top of the basic LES computation, for the presumed FDF,[54] and many times more for transported FDF which, as a result, is currently restricted to relatively simple flows.[34]

20.3.4 Progress variable methods

One of the key limitations of the steady flamelet model is its inability to handle phenomena such as extinction and re-ignition. Though it may be possible to define a critical point in terms of the scalar dissipation rate above which extinction is inevitable, it must always be assumed that steady burning conditions prevail below this value, though in reality extinction and unstable burning are possible here too. For example, it is not possible in the SLFM to represent unignited reactants and the predicted state will always change suddenly from products to complete extinction, with no possibility for representation of any 'partially extinguished' intermediate states. One simple method for overcoming this problem is definition of an additional tracking scalar which, unlike mixture fraction, is non-conserved.[58] This is best characterised as a 'reaction progress variable', which follows the current extent of reaction, as in the flamelet/progress variable method (FPV). The progress variable parameter can be modelled by a single additional transport equation, thus making accessible intermediate mixture states. Contrary to the conventional methods adopted for flamelet generation, based on opposed diffusion flame simulations, a more general approach is adopted whereby quasi-steady diffusion-reaction equations are solved with complex chemical kinetics and multicomponent mass diffusion.

Pierce and Moin,[58] investigating pollutant formation in gas turbine combustors, showed that the basic FPV method is very well able to capture a lifted flame, unlike conventional flamelet models. However, carbon monoxide was still not adequately predicted due to some identified limitations in the PDF model. Ihme *et al.*[59] examined more elaborate models for the PDF of the reaction progress parameter with significant improvement using a presumed beta distribution instead of the original Dirac delta functions. Pitsch[60] and Ihme and Pitsch[61] later adopted another PDF model, known as a 'statistically most likely distribution' (SMLD), to establish the extended FPV model. The utility of the model was demonstrated in application to Sandia flame E, which exhibits enhanced interaction between turbulence and chemistry, with increasing levels of local extinction and reignition.[62] Toxic gas emissions were well represented, though some overprediction of carbon monoxide was found on the fuel side of the flame resulting from the fact that the steady flamelets adopted are not able to account for unsteady effects and hence overpredict fuel consumption in this region. In another variant of this approach, Yang *et al.*[63] adopted a progress

variable model in conjunction with a large eddy laminar flamelet model in order to describe the partially premixed conditions occurring in backdraft. These types of techniques are yet to be applied in fire studies but look very promising in view of the fairly modest computational overheads.

20.3.5 Unsteady flamelets

As mentioned above, a key problem of any methodology based on 'steady' flamelets is the fact that the fast chemistry assumption of simpler models is only partially relaxed. Thus, where the chemical kinetics depart significantly from this, the representation of the combustion rate itself may be compromised and to some degree inaccurate. In the last decade, a number of advanced modelling concepts which overcome this limitation have been developed in the combustion community, based on unsteady flamelet techniques.[64] In the Lagrangian flamelet model (LFM)[65] the streamwise evolution of local flame structure is treated in a Lagrangian-like sense to describe its transient behaviour, including slow processes; the main limitation is the restriction to idealised scenarios, i.e. parabolic flows where the flamelet time is related to the cumulative particle motion along specified paths. Barths *et al.*[66] proposed a more general model by introducing an Eulerian equation for flamelet probability, using fictitious marker particles to track their motion and solving a convective-diffusive Eulerian equation, known as the Eulerian particle flamelet model (EPFM). The method has been further developed[64,67] but despite promising results remains very much in the research domain.

20.3.6 One-dimensional turbulence (ODT)/linear eddy modelling (LEM)

DesJardin *et al.*[34] discuss the one-dimensional turbulence (ODT) methodology initially developed by Kerstein.[68] This is an SGS approach based on a postulated stochastic process which can incorporate both detailed chemistry as well as molecular transport phenomena. Initial studies of ODT and its predecessor, linear eddy modelling (LEM), have demonstrated that it can reproduce single-point statistical moments of flow variables for simple flows.[34,69] Application to buoyancy-driven flows is now being explored with the aim of predicting fire spread along vertical surfaces.[70]

20.3.7 Conditional moment closure (CMC)

Bilger[71] and Klimenko[72] independently proposed a 'conditional moment' closure model which offers a solution for the prediction of finite-rate kinetics by using conditionally-averaged quantities to close the chemical production terms. Typically, the species mass fraction, Y_α, is averaged conditionally on fixed

values of mixture fraction, ξ. By reducing the range of compositions contributing to the mean reaction rate determination, this is effective in reducing the impact of the non-linear variations which result from turbulent fluctuations. The moments of a particular chemical species, α, conditional on values of mixture fraction, ξ, for example,

$$Q_\alpha(\xi) = \frac{\langle \rho c_\alpha \,|\, \varphi = \xi \rangle}{\langle \rho \,|\, \varphi = \xi \rangle}$$

are determined from balance equations which also incorporate the simplifying assumptions of conditioned chemistry $\langle \dot{\omega}_\alpha \,|\, \xi \rangle$. Thus, comparatively complex chemical kinetics can then be included if simple closures are adopted for these source terms, capitalising on the substantially attenuated influence of scalar fluctuations. It has been demonstrated that this approach accurately predicts the finite-rate kinetics of turbulent hydrogen jet flames[73] and more recently in simple hood fire problems.[74] However, the improvement comes at a substantial cost, since a further dimension has been added to the problem, thereby requiring solution of sufficient additional transport equations to adequately characterise the conserved scalar space.[1] Thus, whilst very promising, it is likely that computational demands will continue to limit application to simple flame geometries and also to fuels for which reliable reduced kinetic schemes, involving a small number of reactive scalars, are available.

20.3.8 Pyrolysis models and flame spread

A variety of different models have been implemented for representation of pyrolysis, flame spread and fire growth in CFD codes.[1,4,30] They range from empirically linked models, using characterisations of burning behaviour obtained directly from bench-scale tests such as the cone calorimeter, sometimes corrected for difference in thermal exposures,[75] to more fundamentally based approaches. A distinction can be drawn between those methods which attempt to characterise the process by invoking detailed representations of the in-depth solid pyrolysis processes (e.g. Lautenberger and Fernandez-Pello[76]), and those which neglect or approximate these. The latter will tend to be more empirically dependent, whilst for the former, the computational overhead is typically quite high as there is a requirement that the solid-phase is resolved sufficiently well to capture the transient heating phenomena.[77] The more advanced models in this class incorporate a series of solid-phase chemical reactions coupled with complex heat and mass transport processes, the subject of ongoing research.[76] Whilst relatively complex in nature, the established mathematical formulations still do not fully describe all processes involved and thus are difficult to generalise. Furthermore, they include many fuel-dependent constants that have only been determined for a limited number of materials, the determination of these constants being in itself complex and in many cases requiring the use of

sophisticated optimisation techniques.[78] Thus, a lot of further work is required on these types of models before they can be used in any truly predictive sense, or applied to test conditions that depart significantly from those for which model parameters were originally fitted.

Toxic gas liberation

As well as generation in the gas phase, there are many practical scenarios where a significant component of overall yields of toxic gas is derived from generation from the solid phase. For example, at sufficiently high temperatures, carbon monoxide may be liberated directly off a surface via oxidation of chars, provided that oxygen is available, or intermediate chemical species may be produced which go on to form toxic gas in secondary reactions. The latter are strongly dependent on both the substrate composition and the exposure conditions, with polymers degraded in one or more routes including depolymerisation, random chain scission, chain-stripping and cross-linking with char formation.[79] Cellulose degradation is also highly complex, with carbon monoxide formed via secondary reactions in levoglucosan as well as directly from solid char. Modelling of all these processes is highly challenging, not least because of a lack of knowledge of the combustion chemistry for various real fuels, and further work is required.[80] This issue is discussed further in the next section.

20.4 Prediction of products of combustion and toxic gas

Whilst the chemistry of the primary heat-releasing reactions can normally be considered to be fast, the formation and burnout of carbon monoxide, soot and some other minor species are generally much slower and more comparable with turbulent mixing rates. In particular, the carbon monoxide oxidation process is relatively slow compared with the hydrogen–oxygen reaction system, and finite-rate chemistry appears to be important throughout the flame.[31] Therefore, the concentrations actually attained in real fire conditions depart significantly from those which might be expected on the basis of thermodynamic equilibrium alone (for which evaluation of concentrations is relatively straightforward, for pure fuels). For instance, in prediction of methane flames, the equilibrium level of carbon monoxide peaks at over 20% mass fraction near the stoichiometric contour, whilst empirically observed values in laminar flames do not exceed 4%.[31] Since it is these slow chemical reactions which are so important for the establishment of realistic assessments of the toxic hazard of fire gases and, through flame emissivities, radiant heat emissions, they cannot be neglected and any robust modelling approach must account for the balance between the kinetics and turbulent transport. In order to determine overall production rates

and distributions, the most critical element of any generalised predictive model is the estimation of the production rate itself, taking into account the effects of turbulent fluctuations. Species production rates depend in turn on the overall combustion process; thus, further discussion is set out in the following subsections, loosely related to the equivalent subsections used in Section 20.3, focusing mainly on carbon monoxide production.

20.4.1 Local equivalence ratio (LER)

Wang *et al*.[81] have demonstrated a model which references correlations derived from the GER concept in each cell of the CFD domain to establish a 'local equivalence ratio' model. Temperature effects are accommodated by selecting between two regimes, $< 800\,\mathrm{K}$ and $> 900\,\mathrm{K}$ but the carbon monoxide yield is instantaneous, i.e. it is purely a function of the local conditions.

20.4.2 Two-step eddy break-up (EBU)

Eddy break-up has been a popular approach in RANS fire models, but in basic form it has no intrinsic capability for representing toxic gas. Nevertheless, some attempts have been made to develop two-step eddy break-up models with explicit reference to carbon monoxide as a reaction intermediate,[21,22,82,83] or even multi-step approaches based on equilibrium chemistry.[84] However, any such methods contain embedded compromises with respect to intermediate species, being constrained to ignore turbulence–chemistry interactions, and thus remain rather crude approximations.

20.4.3 Multi-step chemistry

Another option is to generalise the simple one-step chemistry under the alternative assumption that chemical processes are rate controlling, i.e. adopting quasi-laminar chemistry. Reaction rates are then written in terms of mean temperature and species concentrations:

$$\overline{\dot{\omega}}_{\mathrm{CO}} = \dot{\omega}_{\mathrm{CO}}(\bar{T}, \bar{c}_i)$$

Simplified chemistries for alkane hydrocarbons have been available for many years[85–87] and mechanisms for reducing more complex chemistry have received a lot of attention in recent years.[88] In all of these, the chemical reaction rates are obtained from Arrhenius rate expressions, requiring an assumption of quasi-laminar chemistry; this is a significant assumption, though it may be justified in certain contexts, such as upper layer transport. Apart from these fundamental limitations, there are significant practical difficulties with expansion of the scalar field to be computed owing to the numerical stiffness of the coupled chemical source terms.[58] The computational effort is related mainly to the

number of species which must be modelled, rather than the number of reactions, and simplifying state relationships should be adopted wherever they can be justified.[48]

Bilger *et al.*[89] showed that flame structure predictions, including carbon monoxide, were substantially the same for a reduced four-step mechanism and a 'full' 58-step mechanism in a counter-flow methane air diffusion flame, whilst Welch and Marshall[90] found differences of the order 10–20% between the Held *et al.*[91] and Seiser *et al.*[92] mechanisms for heptane.

The approach adopted in version 5.1 of NIST's Fire Dynamics Simulator (FDS) code[30] is a variant of these methods using two steps and a well-ventilated limit yield. In the generation step, fuel is assumed to liberate carbon monoxide, with an instantaneous (infinitely fast) conversion, with stoichiometric ratios obtained from the coefficients sets for simple alkanes due to Westbrook and Dryer:[85]

$$C_xH_yO_z + \nu'_{O_2}O_2 \longrightarrow \nu_{H_2O}H_2O + (\nu'_{CO} + \nu_{CO})CO + \nu_S S$$

where S indicates soot.

Thereafter, the oxidation step regulates a partial conversion of carbon monoxide to carbon dioxide conditional on sufficient oxygen being available:

$$\nu'_{CO}\left[CO + \frac{1}{2}O_2 \rightarrow CO_2\right]$$

Two stoichiometric coefficients for carbon monoxide are introduced: ν'_{CO} is the carbon monoxide produced in the first step that can potentially be converted to carbon dioxide in the second step and ν_{CO} is the well-ventilated value.

In order to keep track of these yields the conventional single parameter mixture fraction is decomposed in to three mixture fraction parameters:

$$Z_1 = \frac{Y_F}{Y_F^I}$$

$$Z_2 = \frac{M_F}{M_{CO}[x - (1 - X_H)\nu_S]}\frac{Y_{CO}}{Y_F^I}$$

$$Z_3 = \frac{M_F}{M_{CO_2}[x - (1 - X_H)\nu_S]}\frac{Y_{CO_2}}{Y_F^I}$$

where Y_F^I is the fuel mass fraction at fuel source, x is the number of moles of carbon in the fuel and X_H is the hydrogen atom fraction in the soot. Each of Z_1, Z_2 and Z_3 are a conserved scalar and used for tracking mass fraction of fuel, carbon monoxide and carbon dioxide, respectively. Critical examination of the predictions across a wide range of fuels and combustion scenarios shows a lot of variation in the performance of the model and further work is under way to improve the predictions.[93]

20.4.4 Laminar flamelets

As mentioned above, flamelet models represent a degree of relaxation in the fast chemistry assumption, relating product concentrations of toxic gas to mixture fraction, via simple state relationships, for example for carbon monoxide:

$$Y_{CO} = Y_{CO}(\xi)$$

The product yield is then obtained by quadrature in the mixture fraction space:

$$\tilde{Y}_{CO} = \bar{\rho} \int_0^1 \frac{Y_{CO}(\xi)\tilde{P}(\xi)}{\rho(\xi)} \mathrm{d}\xi$$

The SLFM may also be generalised to accommodate variation of other key parameters, such as vitiation level,[51] and by accounting for this factor concentration profiles in a confined low Froude number flame in a vitiated environment have been plausibly reproduced.[21] However, as indicated in Section 20.3, there remain some significant limitations derived from the assumed instantaneous nature of the flamelets and it is anticipated that under more extreme conditions there will be significant departures from the laminar flame representations. For example, Hyde and Moss[22] performed homogeneous reactor computations based on a range of initial conditions (vitiation level and reactant temperature) and showed that the time to attain steady state exceeded 10 min under heavily vitiated conditions (1% O_2, 1300 K). Techniques to overcome this were outlined in Sections 20.3.4–20.3.7 above and discussion of some further aspects of relevance to toxic gas follows.

20.4.5 PDF transport models

PDF transport methods introduce large numbers of computational particles and obtain the evolution of the PDF by Monte Carlo simulation.[52] Reduced chemical schemes are adopted for the breakdown of simple hydrocarbons, permitting estimation of all relevant species yields. However, effective solution requires of the order of 10^3 statistical particles per computational cell, so that supercomputing resources are required for three-dimensional elliptical flows involving quite modest numbers of scalar variables, typically numbering ≤ 5. Furthermore, whilst predictions do replicate significant departures from the fast chemistry behaviour, even greater differences are shown in some experimental data indicating limitations in the model[47,48] and further work will be required before these methods are a practical solution tool. The equivalent approach in LES modelling is the transported FDF model, though recent studies have also shown little advantage in using this despite the potentially more accurate representation.[34]

20.4.6 Rate flamelets

For conditions when it can be assumed that the toxic gas chemistry is insignificant in the overall heat release it may be possible to decouple trace chemistry using additional post-processed balance equations, for example:

$$\frac{\partial}{\partial t}\left(\bar{\rho}\,\tilde{Y}_{\mathrm{CO}}\right)+\frac{\partial}{\partial x_j}\left(\bar{\rho}\,\tilde{u}_j\,\tilde{Y}_{\mathrm{CO}}\right)=\frac{\partial}{\partial x_j}\left(\overline{D\rho\,\frac{\partial Y_{\mathrm{CO}}}{\partial x_j}}-\overline{\rho\,u_j''\,Y_{\mathrm{CO}}''}\right)+\tilde{\dot{\omega}}_{\mathrm{CO}}$$

The mean source term, $\tilde{\dot{\omega}}_{\mathrm{CO}}$, can be directly linked to mixture fraction and closed through the PDF in a similar manner to the species concentration closure:

$$\tilde{\dot{\omega}}_{\mathrm{CO}}=\bar{\rho}\int_0^1\frac{\omega_{\mathrm{CO}}(\xi)\,\tilde{P}(\xi)}{\rho(\xi)}\mathrm{d}\xi$$

This approach has been widely and successfully adopted in regard to prediction of thermally generated nitric oxide, and similar models have been employed for smoke, see below. However, this type of closure is computationally cumbersome and is concerned mainly with accommodation of the effects of large scalar fluctuations, particularly the influence of temperature in rate processes having very high activation energies. For circumstances where these are not critical, mean properties can be used instead, as per Section 20.4.3.

20.4.7 Smoke effects

Soot modelling is a major topic in its own right and cannot be dealt with in detail here. Modelling approaches range from highly simplified prescribed yields which adopt a conserved scalar, thereby neglecting the details of the formation and oxidation process, to rate flamelet and PDF transport models similar to those described in the preceding two subsections.[1,4] Depending on the nature of the fire, the predictions may be critical in accurately representing the effects of radiative heat loss and its impact on the flame spread process. Thus, in addition to direct contributions to fire hazard in terms of respirable combustion products and visibility effects, there are knock-on effects on other toxic gas. In particular, soot particles are thought to have an important interaction with carbon monoxide chemistry and there are often strong correlations between soot and carbon monoxide generation rates. The mechanism is uncertain but may be associated with the fact that under fuel-rich conditions both compete for hydroxyl radicals.[79]

20.5 Applications

Table 20.1 presents an overview of some of the key features of modelling methods used for toxic gas prediction for fire in CFD environments. The yield model of FDS 4.0 (#6), the local equivalence ratio model (#1) and models based on steady flamelets (#2,3,4) all make reference to instantaneous carbon

Table 20.1 Examples of toxic gas prediction models as used in fire applications

#	Model name/ description	Chemistry	CFD code	Computational cost	Test cases	Advantages	Disadvantages
1.	LER model Wang *et al.*, University of Greenwich[81]	None (EDM)	SMARTFIRE CFX 4.2 (RANS)	Low	Range of reduced-scale and full-scale fire experiments (including corridors)	Simple extension of GER concept Includes a crude temperature dependency	Parametric approach Requires extensive calibration
2.	Constrained equilibrium flamelets Wen and Huang, Kingston University[94]	Detailed	CFX-FLOW3D	Moderate	Jet fire test, 135 m^3	Detailed CO chemistry is included	Cannot handle real fuels (e.g. wood) CO chemistry is instantaneous Not thoroughly validated
3a.	Two-step eddy breakup Hyde and Moss, Cranfield University[21,22]	Simple	SOFIE (RANS)	Low	Steckler compartment	Simple	CO chemistry is crude Not thoroughly validated
3b.	Flamelet-based CO model Hyde and Moss, Cranfield University [22]	Detailed	SOFIE (RANS)	Moderate Flamelet library is precomputed	Steckler compartment	Detailed CO chemistry is included	Cannot handle real fuels (e.g. wood) CO chemistry is instantaneous Not thoroughly validated
4.	Flamelet-based HCN/CO model Tuovinen, SP Swedish National Testing and Research Institute[51]	Detailed GRI 1.2	SOFIE (RANS)	Moderate Flamelet library is precomputed	ISO room corner test	Accounts detail chemistry	Not general fuels CO chemistry is instantaneous Vitiation level has to be prescribed Complex and time-consuming pre-processing

5.	CO/HC mass model Hu *et al.* University of Maryland[95]	Fast	FDS 4.05 (LES)	Low Solves 1 extra transport equation for fuel	Reduced-scale enclosure experiments at Univ. of Maryland	Simple and general model Extinction effects	Provides CO + HC predictions Poor extinction treatment – either fully burning or fully extinguished
6.	CO yield McGrattan, NIST Hu *et al*. USTC, Rinne *et al*. VTT[30,96,97]	None	FDS 4.0	Low	Tunnel fires	Simple	Very crude predictions
7.	CO production (two-step reaction with extinction) Floyd and McGrattan, NIST[93]	Fast	FDS 5.0 (LES)	Low Solves 3 extra transport equations	Beyler Hood Reduced-scale enclosure experiments	Does not require detail chemistry information Extinction effects	Not thoroughly validated Conserved progress variable definition
8.	CMC modelling of CO formation, Cleary and Kent, University of Sydney[74]	Detail GRI 3.0, CER	In-house code (RANS)	High	Toner's hood fire cases	Accurate combustion modelling Promising CO predictions	Computationally expensive Requires detailed chemistry Not thoroughly validated
9.	CO production (dedicated CO transport equation), Paul and Welch, The University of Edinburgh[98]	Simple	SOFIE (RANS)	Low Solves at least 1 extra transport equation	VTT 10×10 m^2 compartment[97]	Simple and general model Facilitates linkage to flame spread[80]	Less appropriate for turbulent conditions Not thoroughly validated

monoxide yields. Nevertheless, with SLFM, reasonable agreements have been obtained versus measurements in specific scenarios,[21,81] encompassing both freely burning (over-ventilated) fires and in hood fires, including under-ventilated conditions. However, Hyde and Moss[22] have also demonstrated that there are a range of real fire conditions where transient behaviour is expected to be important and the method is expected to break down under such conditions. Treatments to accommodate the effects of vitiation and heat loss in flamelet models (#3b,4) are valuable but the former has never been implemented in anything other than a priori mode.

Aside from the very demanding CMC approach (#8), further work is required on all of the models which have attempted to explicitly address finite-rate chemistry effects (#3a,9) and extinction (#5,7). In each case, modelling frameworks have been established, but where more extensive validation has been attempted only moderate success has been found and predictive capabilities have been shown to be very variable. This is associated with the fact that many of the input parameters are poorly defined and the modelling representations remain highly approximate. Nevertheless, both families of models, including #7 and #9, are benefiting from active ongoing research efforts and new capabilities are expected to be added, including further development of pyrolysis linking.[80]

20.6 Conclusions

The state-of-the-art regarding techniques used for simulation of toxic gaseous species in building fires is presented. Where distribution of toxic species occurs primarily via *transport* of combustion products, including carbon monoxide and smoke, CFD-based models may be harnessed to effectively predict hazard level evolution in space and time, and potentially harnessed for FED-based representations of human response. The main challenge lies in the more general case where toxic gas *production* is a major factor, typically occurring via gas-phase reactions in rich hot layers, or by direct release from solid-phase pyrolysis. Here, concentrations may vary significantly from chemical equilibrium levels and residence time effects become important via the underlying finite-rate chemistry.[16,31] However, powerful computational tools for prediction of these products, which might be critical in evaluating the threat to life safety, are now under development.[1,8]

Amongst the strategies described, most have not been extensively tested in application to building fire problems, and in fact a number are simply not computationally tractable for such applications. Powerful approaches to accommodating detailed chemistry, such as laminar flamelet models methods, are not well suited to handling the complexity of real fuels, or the finite-rate chemistry which pertains to toxic species production in typical fire environments. On the other hand, more detailed methods which have proliferated in recent years in the wider combustion community, such as CMC, are very

computationally demanding and remain primarily in the research domain. Nevertheless, some new treatments based on direct solutions of the kinetics, assuming quasi-laminar conditions in carbon monoxide transport, and those exploiting progress variable methods, show promise in providing tractable solutions to these types of problems. A great deal more effort is required to effectively link such models to solid-phase pyrolysis and flame spread.

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20.8 Nomenclature

B pre-exponential factor in Arrhenius chemical rate expression [varies]
c_i concentration of species, i [kg/m^3]
C_p specific heat of the mixture at constant pressure [J/kg/K]
C_μ empirical constant in eddy break-up reaction rate expression [–]
C_s Smagorinsky constant [–]
D molecular diffusion coefficient [$\mathrm{m^2\,s^{-1}}$]
F fuel [–]
g acceleration due to gravity [$\mathrm{m\,s^{-2}}$]
h static enthalpy [$\mathrm{J\,kg^{-1}}$]
k turbulent kinetic energy [$\mathrm{m^2\,s^{-2}}$]
reaction rate constant [varies]
M molecular weight [–]
O oxidiser [–]
P probability density function [–]
$\dot{q}^\mathrm{R}$ radiative energy flux [$\mathrm{W\,m^{-2}}$]
Q conditional average mass fraction [–]
r stoichiometric ratio [–]
S source term [varies]
reaction rate [$\mathrm{kg\,m^{-3}\,s^{-1}}$]
S_{ij} filtered strain rate [–]
t time [s]
T temperature [K]
T_a activation temperature [K]
u_i velocity component in direction i [$\mathrm{m\ s^{-1}}$]
v stoichiometric coefficient [–]
x distance [m]
number of moles of carbon in fuel [mol]

Y mass fraction [–]
Z mixture fraction [–]

β Schwab–Zeldovich variable representing excess fuel mass fraction [–]
ϵ turbulent energy dissipation rate [$m^2\,s^{-3}$]
ϕ general variable representing species or enthalpy scalars, etc. (in other chapters ϕ is used to represent the fuel-air equivalence ratio)
φ conditionally fixed value of micture fraction of ξ [–]
Γ diffusivity [$kg\,m^{-1}\,s^{-1}$]
ρ density [$kg\,m^{-3}$]
τ shear stress [$N\,m^{-2}$]
$\dot{\omega}$ reaction rate/energy release source term [$kg\,m^{-3}\,s^{-1}$]
ξ mixture fraction [–]
Δ filter width [m]

20.8.1 Subscripts

i,j,k three Cartesian coordinate directions
f fuel
LES large eddy simulation
o oxidiser
p product
α general species
ϕ general variable representing species or enthalpy scalars, etc.

20.9 References

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