FULL PUBLIC REPORT

2,2-dichloro-1,1,1-trifluoroethane (HCFC-123)

PRIORITY EXISTING CHEMICAL NUMBER 4

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Preface

This assessment is made under the National Industrial Chemicals Notification and Assessment Scheme (NICNAS). This Scheme was established by the *Industrial Chemicals (Notification and Assessment) Act 1989* (Cwlth) (the Act), which came into operation on 17 July 1990.

The principal aim of NICNAS is to help protect people and the environment from the harmful effects of industrial chemicals by finding out the risks to occupational health and safety, public health and the environment.

NICNAS has two major parts: one focussing on the risks associated with new chemicals before importation or manufacture; and another focussing on existing industrial chemicals already in use in Australia. As there are many thousands of existing industrial chemicals in Australia, NICNAS has a mechanism of prioritising assessments by declaring certain existing chemicals to be Priority Existing Chemicals (PECs). This report provides the full public report of a PEC assessment. A summary report is also publicly available and has been published in the Commonwealth *Chemical Gazette*.

NICNAS is administered by Worksafe Australia. Assessments under NICNAS are done in conjunction with the Commonwealth Environment Protection Agency and Department of Human Services and Health.

This assessment report has been prepared by the Director Chemicals Notification and Assessment in accordance with the Act. This report has not been subject to tripartite consultation or endorsement by the National Occupational Health and Safety Commission (the National Commission).

Copies of the full public report can be obtained by contacting the Chemical Assessment Division.

On publication of the Summary Report in the *Chemical Gazette* of 5 March 1996, the chemical will no longer be a PEC in accord with Section 62 of the Act.

For the purposes of subsection 78(1) of the Act, copies of full public reports may be inspected by the public at the Library, NOHSC, Plaza level, Alan Woods Building, 25 Constitution Avenue, Canberra, ACT 2600, between 9 a.m. and 5 p.m. each weekday except on public holidays.

A pamphlet giving further details of the PEC program and approved forms are available from Worksafe Australia. Please contact the Chemical Assessment Division at:

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1. Introduction

1.1 Declaration

The chemical, 2,2-dichloro-1,1,1-trifluoroethane (CAS No. 306-83-2), known as hydrochlorofluorocarbon 123 or HCFC-123, was declared by the Minister for Industrial Relations as a Priority Existing Chemical (PEC) under the *Industrial Chemicals (Notification and Assessment) Act 1989* (Cwlth) (the Act) by notice in the *Chemical Gazette* of 1 June 1993.

The declaration by the Minister was made on the basis that there were reasonable grounds for believing that the manufacture, handling, storage, use or disposal of the chemical could give rise to a risk of adverse health or environmental effects.

For HCFC-123 these grounds were:

- as a result of the phase out of chlorofluorocarbons (particularly CFC-11 and CFC-12), there is a potential for a significant increase in the use of HCFC-123 in Australia;
- there is a potential for a significant increase in occupational exposure to HCFC-123 and release to the environment;
- a study undertaken by Du Pont Chemicals (USA) in the Program for Alternative Fluorocarbon Toxicity Testing (PAFT) revealed an increase in benign tumours (multiple site) in rats following chronic inhalation exposure to HCFC-123; and
- HCFC-123 can break down in the lower atmosphere leading to the formation of persistent acidic substances, such as trifluoroacetic acid.

In accordance with section 55 of the Act, those introducing HCFC-123 into Australia applied for assessment of the chemical as a PEC. As HCFC-123 is not manufactured in Australia, applications were limited to importers.

1.2 Objectives

The objectives of this assessment are to:

- assess the potential health and environmental hazards of HCFC-123;
- characterise the occupational, public health and environmental risks arising from exposure to HCFC-123;
- determine whether these risks are adequately controlled with respect to current handling, use and disposal practices for HCFC-123 in Australia; and
- make appropriate recommendations to reduce potential risks to human health and the environment with respect to handling, use and disposal of HCFC-123.

1.3 Data collection

In order to meet the above objectives, the information required for assessment was identified in the declaration notice and obtained in accordance with section 58 of the Act. In addition to data submitted by the applicants, information was also received from:

- Alternative Fluorocarbon Environmental Acceptability Study (AFEAS);
- American Air Conditioning and Refrigeration Institute (ARI);
- American Society of Heating, Refrigeration and Air Conditioning Engineers (ASHRAE);
- Australian Conservation Foundation (ACF);
- Carrier Air Conditioning Pty Ltd;

- Commonwealth Department of Administrative Services (DAS);
- Commonwealth Fire Board;
- Deutche Forschungsgemeinschaft (DFG);
- Du Pont (Australia) Ltd;
- European Centre for Ecotoxicology and Toxicology of Chemicals (ECETOC);
- International Agency for Research on Cancer (IARC);
- International Programme on Chemical Safety (IPCS);
- International Register for Potentially Toxic Chemicals (IRPTC);
- Japan Chemical Industry Ecology-Toxicology and Information Center (JETOC);
- Pacific Chemical Industries Pty Ltd;
- Programme for Alternative Fluorocarbons Toxicity Testing (PAFT);
- Standards Association of Australia;
- the Trane company;
- Tyco International;
- United Nations Environment Programme (UNEP);
- UK Health and Safety Executive;
- US Environmental Protection Agency (US EPA); and
- York International.

Further information was obtained from a comprehensive literature survey. In addition, a number of site-visits were undertaken to a variety of chiller installations for the purpose of data collection, which included a Worksafe Australia-conducted air monitoring survey.

2. Background

2.1 The Montreal Protocol

Global concern over the depletion of the stratospheric ozone layer by chlorofluorocarbons (CFCs) and halons resulted in the Vienna Convention for the Protection of the Ozone Layer (adopted in March 1985) and its Montreal Protocol on Substances that Deplete the Ozone Layer (1987).

Under the Montreal Protocol the production and importation of halons and CFCs are to be totally phased out by 1994 and 1996 respectively. The Montreal Protocol does not prohibit the use of CFCs beyond the phase out date, but the use of halons is to be phased out altogether by 1996.

The 1992 Copenhagen Amendment to the Montreal Protocol regulates manufacture and import of hydrochlorofluorocarbons (HCFCs) with a total phase out by 2030.

Around 150 countries, have signed the Montreal Protocol, including Australia, which formally ratified the Copenhagen Amendment on 10 July 1994.

There is global concern regarding CFCs and the greenhouse effect. CFCs cause approximately five per cent of global warming to date if their direct (11 per cent radiative forcing) and indirect (six per cent ozone depletion) effects are taken into account.[1]

2.2 The Australian situation

In 1989 the Australian Environment Council (now the Australian and New Zealand Environment and Conservation Council—ANZECC) endorsed and published the *Strategy for Ozone Protection*. This document was developed by Commonwealth, State and Territory governments in association with industry, environmental and consumer groups.

The ANZECC *Revised Strategy for Ozone Protection in Australia*,[2] which includes new information on technologies and chemical replacements for ozone depleting substances, was published in April 1994. This strategy is compatible with the Montreal Protocol phase out time line for CFCs and halons.

In Australia the phase out of halons, CFCs and HCFCs will be brought about under the *Ozone Protection Act (1989)* (Cwlth), which is implemented by the Environment Protection Agency (EPA).

With regard to halons, the phase out in production and importation was achieved in 1992. The use of halons is to be banned by 1996 and halon-filled fire extinguishing equipment will not be permitted unless an Essential Use Permit is granted by the EPA. Similarly, the manufacture and importation of all CFCs is also to be phased out by 1996, although currently no restriction has been implemented with respect to use.

Early in 1995 the EPA released the summary paper *The Phase out of Hydrochlorofluorocarbons in Australia*[3] in response to Recommendation 93/12 of the ANZECC *Revised Strategy for Ozone Protection in Australia*. This paper proposes amendments to the *Ozone Protection Act (1989)* to substantially phase out the supply of HCFCs in Australia by the end of 2015. A very limited supply may still be permitted until 2030 (or any earlier date set by the Montreal Protocol agreement) primarily to service HCFC-123 centrifugal chillers.

In line with the Copenhagen Agreement, a number of initiatives have been implemented in order to assist in the disposal and recycling of CFCs and halons in Australia such as the establishment of the Halon Bank by the Department of Administrative Services Centre for

Environmental Management (DASCEM) and the Ozone Depleting Substances (ODP) Reclaim Fund, established by the fluorocarbon industry.

2.3 HCFCs as interim alternatives to CFCs and halons

The phase out of CFCs and halons has created an urgent need for acceptable substitute chemicals. Currently the most suitable replacements for many of the applications of these substances are halogenated chlorofluorocarbons (HCFCs).

Although the ozone-depleting and global warming potential of HCFCs are considerably lower than those of their fully halogenated analogues (CFCs and halons), they are only being considered as interim (transitional) replacements until more acceptable alternatives are developed, for example, substances with zero ozone depleting and global warming potential.

In Australia, HCFC-123 is currently being used as an interim replacement for CFC refrigerants (mainly CFC-11) and as a component of certain fire extinguishants which are being introduced as interim replacements for Halons 1211 and 1301.

Under the US EPA Significant New Alternatives Program,[4] HCFC-123 is regarded as an acceptable interim replacement for:

- CFC-11, CFC-12, CFC-500, and CFC-502 in industrial process refrigeration; and
- CFC-113 in precision cleaning.

HCFC-123 can act as a replacement in blends containing HCFC-123 as acceptable interim replacements for:

- Sterilant blends containing CFC-12; and
- Halons 1211 and 1301 in fire suppression.

Other uses for which HCFC-123 has been proposed overseas are as an expansion (blowing agent) in polyurethane foam manufacture and in solvent applications.

2.4 Scientific testing and assessment of CFC and halon alternatives

Some of the world's major CFC producing companies have co-operated to set up AFEAS and PAFT. The aim of these programs is to generate information on the potential effects of CFC and halon alternatives on the environment and human health in order to promote safe, viable alternatives.

The first of several PAFT programs,* which includes extensive toxicological testing of HCFC-123, has recently been completed and the studies made available for this assessment.

Under NICNAS, HCFC-123 is the first CFC/halon alternative to be assessed as a PEC, although a number of such alternatives have been notified and assessed (or in progress) as New Chemicals. These include the refrigerants HFC-32, HFC-143a, FC-218 and the extinguishants HFC-227ea, PFC 410 and FIC-1311.

Reviews of HCFC-123 by international organisations have been carried out by the European Centre for Ecotoxicology and Toxicology of Chemicals[5] and the International Programme on Chemical Safety.[6]

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* PAFT 1, launched in 1987.

3. Applicants

Association of Fluorocarbon Consumers and Manufacturers
Suite 1 Unit 6
The Bay
29 Bentham Street
Yarralumla ACT 2600

Elf Atochem (Australia) Pty. Ltd.
Level 6
65 Berry Street
North Sydney NSW 2060

Lovelock Luke Pty. Ltd.
497 Blackburn Road
Mount Waverly VIC 3149

North American Fire Guardian Technology (Australia) Pty. Ltd.
26 Britannia Street
Pennant Hills
Sydney NSW 2120

4. Chemical identity

4.1 Chemical name

HCFC-123 is listed on the Australian Inventory of Chemical Substances (AICS) as ethane, 2,2-dichloro-1,1,1-trifluoro-.

4.2 Registry numbers

CAS number	306–83–2
EINECS number	206–190–3
RTECS number	KI 1108000

4.3 Other names

- 1,1-Dichloro-2,2,2-trifluoroethane.
- 2,2-Dichloro-1,1,1-trifluoroethane.
- Dichlorotrifluoroethane.
- Dichloro(trifluoromethyl)methane.
- FC-123.
- Fluorocarbon 123.
- Freon-123.
- Fron-123.
- Halon-232.
- HCFC-123.
- Hydrochlorofluorocarbon 123.
- Propellant 123.
- R-123.
- Refrigerant 123.
- Trifluorodichloroethane.

4.4 Trade names

4.4.1 Pure substance

- Asahiklin AK-123.
- Demeon 123.
- Environ 123.
- FE-232.
- Forane 123.
- Genetron 123.
- Halotron.
- HFA-123.
- Solkaflam 123.
- Solkane 123.
- SUVA *Centri-EP*.
- SUVA *Centri-LP*.

4.4.2 Blends containing HCFC-123

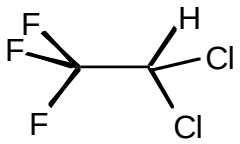
No refrigerant blends containing HCFC-123 are currently in use in Australia. However, the following blends are extinguishing agents:

- Halotron-I.
- HCFC-Blend A.
- HCFC-Blend C.
- HCFC-Blend D.
- NAF P-III.
- NAF S-III.

4.5 Molecular formula

$CHCl_2CF_3$

4.6 Structural formula



4.7 Molecular weight

152.91

4.8 Conversion factors

- 1 ppm = 6.25 mg/m^3 (@ 20°C).
- 1 mg/m^3 = 0.160 ppm (@ 20°C).

4.9 Chemical composition

4.9.1 Specification of HCFC-123

Commercial sample (Du Pont)		Details
HCFC-123		99.6–99.8%
Water		10 ppm (max)
HCl		0.1%
Isomer content:		1% (max)
1,2-dichloro-1,1,2-trifluoroethane	(HCFC-123a)	0.33%
1,1-dichloro-1,2,2-trifluoroethane	(HCFC-123b)	0.04%
Residue		0.01 (vol%)
Total unsaturates		20 ppm

4.9.2 Impurities

Table 1: Common impurities reported in several samples of HCFC-123

Impurity	Sample 1	Sample 2	Sample 3	Sample 4	Sample 5
CFC-11	40 ppm	<30 ppm	—	—	<30 ppm
CFC-12	<5 ppm	15 ppm	—	—	—
CFC-113	1400 ppm*	350 ppm*	179 ppm	270 ppm*	39 ppm
CFC-114	8 ppm	222 ppm	12 ppm	38 ppm	<2 ppm
CFC-114b1	25 ppm	505 ppm	—	—	57 ppm
CFC-216	80 ppm	183 ppm	46 ppm	—	92 ppm
CFC-1112a	<4 ppm	<4 ppm	—	16 ppm	<2 ppm
CFC-1113	—	—	—	10 ppm	<2 ppm
CFC-1317mx	<4 ppm	<4 ppm	—	15 ppm	<2 ppm
HCFC-121	—	—	—	36 ppm	—
HCFC-123a	4.1%	12.6%	4.1%	5.2%	4.7%
HCFC-123b	—	—	—	—	369 ppm
HCFC-124	—	—	—	22 ppm	—
HCFC-124a	—	—	—	19 ppm	—
HCFC-133a	<5 ppm	28 ppm	—	22 ppm	<2 ppm

* Includes HCFC-123b (same GC retention time).

Sample 1 Montague FC-123[7]
Sample 2 Chiba FC-123[7]
Sample 3 Phillips[8]
Sample 4 Du Pont[9]
Sample 5 Du Pont[10,11,12]

4.10 Chemical composition of HCFC-123 blends

4.10.1 Specification of HCFC Blend A (NAF S-III)

HCFC-123	**4.75%**
Chlorodifluoromethane (HCFC-22)	82%
1-chloro-1,2,2,2-tetrachloroethane (HCFC-124)	9.5%
Isopropenyl-1-methylcyclohexene	3.75%

4.10.2 Specification of HCFC Blend C (NAF P-III)

HCFC-123	**55%**
1-chloro-1,2,2,2-tetrachloroethane (HCFC-124)	31%
1,1,1,2-tetrafluoroethane (HFC-134a)	10%
Isopropenyl-1-methylcyclohexene	4%

4.10.3 Specification of HCFC Blend D (Halotron-I)

HCFC-123	**93%**
Proprietary additive (unknown)	~7%

5. Physical and chemical properties

5.1 Physical state

HCFC-123 is a clear, colourless liquid with a slight ethereal odour.

5.2 Physical and chemical properties

The physicochemical data listed in Table 2 relates to commercial grade HCFC-123.

Table 2: Physical and chemical properties of HCFC-123

Property	Value	Conditions
Boiling point	27.6°C	760 mm Hg
Freezing point	-107°C	—
Critical temperature	185°C	—
Critical density	0.53 g/cm^3	—
Liquid density	1.464 g/cm^3	25°C
Viscosity	0.45 centipoise	25°C
Specific gravity	1.462	25°C
Vapour density	6.38 g/L (saturated vapour)	—
Vapour pressure	670 mm Hg 0.76 bar 4.9 bar	25°C 20°C 80°C
Evaporation rate	< 1 (CCl_4 = 1)	—
Henry's Law constant	0.096 atm/m^3/mol	25°C
Water solubility	2.1 g/L 3.9 g/L	25°C 75°C
Partition coefficient	log $P_{o/w}$ 2.9*	—
	log $K_{o/w}$ 2.3†	—
pH	Neutral	—
Dissociation constant	Not applicable	—
Flash point	Not applicable	—
Autoignition temperature	Not applicable	—
Flammability	Non-flammable	—

* Estimated from QSAR.

† Estimated by HSDB.

5.3 Reactivity and stability

5.3.1 Hydrolysis

HCFC-123 is hydrolytically stable.

5.3.2 Incompatibility

Incompatible with alkali or alkaline earth metals, for example, powdered Al, Zn and Be.

5.3.3 Polymerisation

HCFC-123 does not polymerise under normal temperature and pressure.

5.3.4 Thermal decomposition

At high temperatures (open flame, glowing metal surface etc.) HCFC-123 may decompose to form free halogen, HF, HCl, dichloroethylene and carbonyl halides, for example, phosgene. Less than one per cent thermal decomposition of HCFC-123 occurred at 300°C (24 hours duration). The main decomposition products were CFC-113 and CFC-114.[13]

5.4 Environmental properties

The properties listed in Table 3 relate to the physicochemical behaviour of HCFC-123, HCFC-123 blends and related substances in the atmosphere.[14]

Table 3: Atmospheric properties of HCFC-123 and related substances

	HCFC-123	CFC-11	NAF S-III	NAF P-III	Halon 1211	Halon 1301
ODP	0.02	1.0	0.05	0.02	5	12–13
GWP	0.02	1.0	0.04	0.08	np	1.4
EAL	1.4	50	1.4–13.3	1.4–14	20	65

ODP Ozone depleting potential.
GWP Global warming potential.
EAL Estimated atmospheric lifetime (years).
np No information provided.

6. Methods of detection and analysis

6.1 Identification

HCFC-123 can be characterised by:

- Infra-red (IR) spectroscopy;
- Nuclear magnetic resonance (NMR) spectroscopy;
- Mass spectroscopy; and
- Raman spectroscopy.

6.2 Atmospheric monitoring

6.2.1 Fixed monitoring and detection systems

A number of fixed monitoring systems are available for HCFC-123 vapour detection in the workplace. The different types of detection employed in these systems include IR absorption, IR photo-acoustic, halide ion and metallic oxide resistance sensors. The detection limit for most automated monitors is reported at 1–2 ppm HCFC-123 (upper limit 200 ppm), although optimum accuracy is achieved above 5 ppm. In practice however, cross-sensitivity to other airborne hydrocarbons (including other refrigerants) at chiller installations, interferes with the specificity of HCFC-123 monitoring, particularly at low levels (< 10 ppm). The most specific refrigerant detection is achieved using IR technology, although IR monitors will respond to other gases which absorb at similar wavelengths. IR monitors adjusted for HCFC-123 do not readily respond to CFC-11, CFC-12, CFC-500 and HCFC-22.

Most fixed monitoring systems are linked to alarm and ventilation systems, and in some cases to chiller shutdown, which are triggered at preset HCFC-123 levels. Some of the more sophisticated systems can be linked to a number of detectors and can provide readings for each detector independently. In addition to instantaneous monitoring, some systems incorporate an 'integrator' facility which provides a cumulative exposure reading, that is, a continuous calculation of the TWA exposure level. Both instantaneous and TWA monitoring can be linked to alarms.

Although not strictly a method of refrigerant monitoring, an indication of refrigerant leakage can be obtained from monitoring the quantity of uncondensed gas bubbles in the chiller liquid line. Commercial sensors are available that trigger an alarm when a low level of refrigerant liquid is detected over a predetermined time schedule, thus maintaining continual surveillance of the system charge.

The Australian Standard for Refrigerating Systems (AS 1677)[15] and the US ASHRAE Safety Code for Mechanical Refrigeration[16] specify requirements for fixed refrigerant monitoring/detection systems.

6.2.2 Portable monitors

Sampling

Routine atmospheric monitoring can be undertaken by personal or static sampling. Methods have been reported using activated charcoal tube (100/50 mg) or Tedlar® gas bag (one litre) sampling strategies. Strategies used for HCFC-123 use sampling pumps set at 20–50 cm^3 per minute for charcoal tube sampling and 750–1500 cm^3 per minute for Tedlar® gas bag sampling. Charcoal tube samples were desorbed with carbon disulphide or isopropyl alcohol

with desorption efficiencies close to 100 per cent over the concentration range of 5–100 ppm HCFC-123 for isopropyl alcohol.

Organic vapour badges (which do not require pumps) are available for passive sampling of HCFC-123 with a sampling rate of around 30 cm^3 per minute and a 99 per cent desorption (using methylene chloride) efficiency.

Analysis

A method devised by Du Pont utilising GC/FID[17] has been adapted from the US National Institute of Occupational Safety and Health (NIOSH) analytical method No. 1020* which is recognised by the American Conference of Governmental Industrial Hygienists (ACGIH) and the US Occupational Safety and Health Administration (OSHA). The detection limit for this method of analysis is reported to be less than 0.94 ppm. This method has also been used for the routine purity analysis of HCFC-123 (liquid) and has been used to quantify over 20 specified chlorinated alkane impurities at a detection limit of 1–2 ppm.

Direct (peak) monitoring of HCFC-123 in air has been carried out by portable gas chromatograph analysis[18] and IR (non-dispersing) vapour analysers (models used include the Miran 1B and LAN-1). Continuous monitoring is possible using these methods. The detection limit for either method of analysis is around 1–2 ppm HCFC-123 and is suitable for measuring up to several hundred parts per million.

Indicator tubes (Gastec®) have also been used to monitor workroom air levels of HCFC-123 in the ranges 0-1600 ppm.[19] Analysis of pyrolysis products of HCFC-123 (HCl and HF) has been carried out using Draeger® calorimetric detector tubes.[20]

6.3 Biological monitoring

Although no methods were made available for assessment with regard to the biological monitoring of HCFC-123, a search of the literature revealed methodologies, using IR spectrometry, for measuring halocarbons in expired air[21] and fluorocarbons, using GC/head space analysis in body fluids.[22] These methods have not been validated for use as routine biological monitoring methods.

* Devised for 1,1,2-trichloro-1,2,2-trifluoroethane (CFC-113).

7. Use, manufacture and importation

7.1 Use

In Australia, the main use of HCFC-123 is as a refrigerant in low pressure centrifugal chillers for air conditioning systems and is a technically suitable replacement for CFC-11. Smaller amounts of HCFC-123 refrigerant are being used to replace CFC-12 in retrofitted high pressure chillers.

Smaller amounts of HCFC-123 are used in the fire protection industry in fire extinguishant blends, which are being introduced to replace halon extinguishants. Two such blends currently imported into Australia are NAF S-III (HCFC Blend A) and NAF P-III (HCFC Blend C) which have been introduced to replace Halons 1301 and 1211 respectively. NAF S-III is being used as a "total flooding agent" in fixed systems and NAF P-III as a "streaming agent" in portable extinguishers. Both blends are particularly suitable for fires involving computer or electrical equipment.

Government authorities in other countries, notably the US, have sanctioned the use of HCFC-123 for other uses, such as an expansion (blowing) agent in polyurethane foam manufacture, in solvent applications and in sterilant blends.

7.2 Manufacture

HCFC-123 and extinguishant blends containing HCFC-123 are not manufactured in Australia, nor are there any plans to do so in the near future.

7.3 Importation

HCFC-123 is imported into Australia either as a pure chemical or in fire extinguishant blends. Approximately 80 tonnes of HCFC-123 (as refrigerant and extinguishant) were imported between 1992 and 1995.

7.3.1 HCFC-123 refrigerant

Pure HCFC-123 is imported in heavy duty steel drums, ranging in size from 45–300 kg.

It is estimated that approximately 20 tonnes of HCFC-123 was supplied to the air conditioning market from mid-1992 to mid-1993.

It has been estimated that there may be a 10-fold increase in chillers operating on HCFC-123 by 2010.[23] This equates to an increase of around 50 chillers per year. Assuming the average capacity of a centrifugal chiller to be 500 kg of refrigerant, approximately 25 tonnes per year of HCFC-123 could be required in the foreseeable future for stocking of new and retrofit machines. Additional incremental quantities of HCFC-123 would also be required to replace refrigerant loss to the environment (maximum of one per cent per year) which according to the above estimate, currently stands at approximately one tonne per year, and would increase by approximately a quarter of a tonne per year to a maximum of five tonnes in 2010. Thus the maximum usage of HCFC-123 refrigerant in the future is estimated at around 30 tonnes per year.

Other estimates of HCFC-123 refrigerant use are higher. One estimate by a major supplier of HCFC-123 is that total sales (all sources) may reach 80 tonnes per year by the end of 1995.[24] A national survey carried out by the Victorian EPA provides projections of HCFC use in

Australia.[25] The survey lists 1992 and 1993 usage of HCFC-123 refrigerant as 17 tonnes each year, with a projected future usage of up to 200 tonnes per year. The Association of Fluorocarbon Consumers and Manufacturers (AFCAM) recently revised this estimate downwards to 85 tonnes.

7.3.2 HCFC-123 in extiguishant blends

NAF S-III and NAF P-III, which contain approximately five per cent and 55 per cent HCFC-123 respectively, are imported into Australia in 1030 kg cylinders.

Imports of NAF S-III and NAF P-III, together with the HCFC-123 equivalent amounts are shown in Table 4.

Table 4: Australian import volumes for extiguishant blends containing HCFC-123[26]

Year	Extinguishant blend	Extinguishant (kg)	HCFC-123 (kg)
1992	NAF S-III	8,250	400
1993	NAF S-III	10,500	500
1994	NAF S-III	9,250	450
1994	NAF P-III	1,000	550

Projections of HCFC use in Australia provided by the Victorian EPA survey[25] lists 1993 usage of HCFC-123 in extinguishant blends as less than 500 kg. Such an estimate is in agreement with sales figures for NAF S-III for 1993.

In the EPA report, future usage of HCFC-123 in extinguishant blends is estimated at 5000 kg per year. This estimate does not include streaming agents. In view of the significantly higher content of HCFC-123 in NAF P-III, future consumption figures for extinguishant use may be an underestimate. However, uncertainties remain concerning likely extent of HCFC usage in fire protection as a preference exists for clean agents that will not be phased out.

8. Exposure assessment

There is the potential for environmental, occupational and public exposure to HCFC-123 resulting from its use as a refrigerant in centrifugal chillers in the air conditioning industry and as an ingredient in extinguishants in the fire protection industry.

8.1 Sources of human and environmental exposure

HCFC-123 does not occur naturally in the environment nor is it manufactured in Australia. Release into the environment may occur during:

- transport, storage, recycling and disposal of refrigerant or extinguishant;
- operation (normal operation and malfunction) of centrifugal chillers;
- maintenance of centrifugal chillers, for example, leaks and spills; and
- fire extinguishant discharge.

8.1.1 Transport and storage

HCFC-123 refrigerant is imported into Australia in factory sealed drums, the largest being 250 kg. Both NAF S-III and NAF P-III extinguishants are imported into Australia in 1030 kg cylinders, containing approximately 50 kg and 600 kg of HCFC-123 respectively. Exposure during transport, handling and storage may result from leakage of inadequately resealed drums or damaged containers or during filling operations where the contents of large containers are transferred to smaller containers. New chillers are usually supplied complete with refrigerant holding charge. Therefore, a potential exists for exposure during transport and installation of new equipment.

8.1.2 Operation of centrifugal chillers

Emissions of HCFC-123 from centrifugal chillers can occur during normal operation. Chillers represent an enclosed system in which the refrigerant and water circuits are isolated. Chillers using HCFC-123 operate under reduced pressure, which means that under normal conditions air will leak into the chiller system rather than refrigerant leaking out. Air must be purged from the system in order for the chiller to function efficiently. Purged air contains a certain amount of refrigerant which will be released to atmosphere. By using a high efficiency purge with good maintenance techniques it is reported that this loss can be minimised to about five per cent of purged air,[27] which is equivalent to about one per cent* of the refrigerant charge per year.[28] Refrigerant charges vary from around 350 kg–1500 kg, depending on the size of the chiller. In addition, refrigerant can be lost from chiller malfunction or operational malpractice. For example, corroded or damaged water tube heat exchangers in the chiller condenser may lead to leakage of refrigerant into the water circuit, which may be emitted to the atmosphere from the water cooling tower.

Documented reports of chiller malfunction or operational malpractice leading to HCFC-123 loss include:

- an incidental release of HCFC-123 from purge vent line/piping resulting from a chiller retrofit† with incompatible materials;[29] *

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* A recent report of a long term study on a retrofitted chiller (charge: 612 kg HCFC-123) indicates that refrigerant losses of <1% can be achieved.[37]

† Chillers not specifically built to run on HCFC-123 usually require conversion in order to do so. This process is termed "retrofitting". There are two types of retrofit: 1. conversion of a high pressure chiller to a low pressure chiller; and 2. conversion of a low pressure centrifugal chiller designed to run on another refrigerant (for example, CFC-11).

- emissions of HCFC-123 (>950 ppm in breathing zone) resulting from evacuation of a purge vent line following the pumping of purge exhaust into the rupture disc vent;[19] and
- accidental release of around 1200 kg of HCFC-123 refrigerant due to an incorrect chiller start-up procedure.[30]

Such events are rare and it has been estimated that a serious malfunction such as a catastrophic leakage might occur on a national basis less than once per year per 2,000 installed chillers.[28]

8.1.3 Maintenance of centrifugal chillers

Once installed, centrifugal chillers require ongoing maintenance and repair. This is carried out by experienced technicians both on a routine basis and in response to systems failure or malfunction. Certain maintenance procedures can result in escape of refrigerant. The most significant sources of HCFC-123 loss during chiller maintenance are hereafter characterised in more detail.

Refrigerant transfer procedures

Refrigerant transfer involves the removal (often referred to as refrigerant recovery) and subsequent replacement of refrigerant from the chiller system, and is performed in conjunction with the initial start up of newly installed equipment and with repair jobs and retrofits. For this purpose, the refrigerant charge is transferred to recovery/storage vessels.

In summary, the process involves pulling a deep vacuum on the recovery vessel. When the vacuum inside the vessel exceeds that of the chiller evaporator, liquid HCFC-123 flows from the chiller to the recovery vessel. Once the liquid HCFC-123 has been removed from the chiller the residual refrigerant vapour may then be removed by reversing the hose connections to pull a deep vacuum on the chiller vessel.

Recharging the chiller involves a reversal of the above procedure, that is, pressurising the recovery vessel whilst evacuating the chiller.

The main source of HCFC-123 exposure during transfer operations occurs during connection and disconnection of transfer lines/hoses from the recovery unit and chiller. Additionally, HCFC-123 vapour may be vented from the vacuum pump outlet. Refrigerant release may also occur when residual amounts of HCFC-123 in portable gas cylinders are transferred to other storage vessels.

Leak testing

Under normal operating circumstances, leaks in the system (excluding the purge unit) are not a potential source of refrigerant exposure, due to the negative pressure of the system. However, the process of testing for leaks, which is carried out following repair work or as a result of specific diagnoses (for example, excessive purging), may result in HCFC-123 release from the chiller system.

Leaks may be detected with the refrigerant charge in the chiller unit by: (a) raising the chiller pressure to induce refrigerant emission;† or (b) purging the empty chiller with nitrogen (or a mixture of nitrogen with an "inert" refrigerant such as R-22) under atmospheric pressure. Both these procedures are potential sources of HCFC-123 vapour emissions should a leak(s) be present in the system. Furthermore, process (b) may result in additional levels of refrigerant release should the nitrogen charge (which will contain residual HCFC-123 vapour) be released to the atmosphere.

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* HCFC-123 is more corrosive than other chlorofluorocarbon refrigerants to certain types of plastic/rubber materials used in existing chiller equipment and hence certain components, such as motor windings, hoses, seals and valves, may require replacement with more resistant materials.

† This method is commonly employed where an automatic pressure raising system, which raises chiller pressure during the off cycle, has been installed.

Lubricant and filter changes

Chiller oil becomes contaminated with refrigerant (up to five per cent residual refrigerant, depending on oil temperature) during normal operation and hence the drainage of oil and removal of the oil filter are potential sources of HCFC-123 exposure.

The purge filter and refrigerant core drier (ceramic filter) also become contaminated with refrigerant vapour during normal operation and require periodical changing as a minor service procedure. Some purge units are also fitted with carbon filters which can be reprocessed (currently not undertaken in Australia) to recover refrigerant. As with oil filter replacement, the removal of these filters are also a source of HCFC-123 exposure.

Compressor stripdown

During major service and repair operations, the chiller compressor may be opened up, referred to as stripdown. Although such operations usually require the prior removal (transfer) of refrigerant charge, they represent the largest potential source of HCFC-123 release from maintenance activities as residual refrigerant vapour. The amount of HCFC-123 vapour released during stripdown procedures is, to a large extent, dependent on the efficiency of the refrigerant transfer procedure.

8.1.4 Fire extinguishant discharge

Discharge of HCFC-123 from fire extinguisher systems occurs during normal operation and represents a significant potential source of exposure. HCFC-123 is currently used in Australia as an ingredient in 'total flooding' and 'streaming' agents used in fixed* and portable† extinguishers respectively. Both systems are enclosed and the extinguishant is isolated (until discharge) and as such leaks are unlikely.

Discharge of extinguishant may also occur during installation and testing however such potential exposures may be reduced should future State and Territory legislation prohibit the discharge of HCFC-containing extinguishants during testing operations, as is currently the situation with halon extinguishant systems.

8.1.5 Disposal/recycling

According to the *Ozone Protection Act (1989)*, ozone depleting refrigerants must not be released to the atmosphere.

Contaminated HCFC-123 from refrigerant use can be recycled to remove moisture and contaminants, such as dirt, metallic particles and sludge. This process involves recovery of refrigerant from the chiller, mechanical filtration and purification through evaporation. The product is pumped into suitable storage tanks for re-use. Recycling is therefore a potential source of HCFC-123 exposure.

Reprocessing as distinct from recycling involves the breakdown of refrigerant and its reconstitution into a new product conforming to the specification of the original material. Reprocessing is not a source of exposure in Australia as appropriate facilities for reprocessing are not available. As such, this process would currently have to be undertaken internationally.

Disposal is another potential source of HCFC-123 exposure. Any contaminated refrigerant (or extinguishant) that is not suitable for recycling or reprocessing should be disposed of according to State and Territory regulations. Acceptable options for disposal include high temperature incineration or plasma arc destruction. Such facilities are not currently available in Australia and, as such, local disposal is unlikely. It is intended that under Commonwealth legislation the

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* **Total flooding system.** A system consisting of a supply of extinguishant arranged to discharge into and fill (to a predetermined concentration) an enclosed space surrounding a fire hazard. Total flooding systems require the use of an extinguishant that exists in vapour form at room temperature.

† **Streaming agents.** Act on a fire hazard in its liquid form by direct application.

manufacturer or importer of HCFC-123 will be required to accept recovered HCFC-123 and be responsible for its storage, recycling or destruction. A number of initiatives have been implemented in order to assist in the recycling of CFCs and halons in Australia such as the establishment of the Halon Bank by DASCEM and the ODP Reclaim Fund established by the Fluorocarbon industry.

8.2 Occupational exposure to HCFC-123

8.2.1 Major sources of exposure to refrigerant

The major source of occupational exposure to HCFC-123 refrigerant is from chiller maintenance and repair. Chiller maintenance technicians are the main population at risk. Other sources of exposure include accidental spillage from refrigerant drums and leaks caused by chiller malfunction. Procedures likely to give rise to the most significant worker exposures are:

- refrigerant transfer;
- leak testing; and
- chiller stripdown.

Exposures to maintenance personnel during refrigerant transfer occur during connection and disconnection of transfer lines/hoses from the recovery unit and chiller, where both vapour escape and spillage of liquid refrigerant may occur. Additionally, HCFC-123 vapour may be vented into workroom air during vacuum pump operation. Exposure may also occur to workers involved in transfer of residual (up to 0.5 kg per 200 kg cylinder) refrigerant from portable gas cylinders to other storage vessels. This process is typically carried out at locations other than the chiller installation and represents an additional workplace where exposure may occur.

Exposures to maintenance personnel during leak testing may occur during pressurisation of the condenser should a leak be present and from release of the inert gas (nitrogen) holding charge, if vented into workroom air, which may contain a significant amount of residual HCFC-123 vapour.

Many chiller repairs require some degree of chiller opening/dismantling, often referred to as stripdown (stages 1 to 3), depending on the type of work being undertaken. Such work may lead to significant leakages of HCFC-123 vapour into the workplace depending on the degree of stripdown and the amount of residual refrigerant in the chiller.

8.2.2 Extent of exposure to maintenance technicians

The extent of exposure of maintenance technicians to HCFC-123 is dependent on the number of hours spent at chiller installations (running on HCFC-123 refrigerant) and the type of maintenance/repair work carried out.

It has been estimated that in Australia there are currently around 100 chillers operating on HCFC-123 in New South Wales[27] and that up to 4000 chillers in service nationwide are suitable for conversion to this refrigerant.[23] It has also been estimated that there will be more than 1000 chillers (both new and retrofitted machines) operating on HCFC-123 by 2010. Approximately 100 maintenance technicians are required per thousand machines.[31]

Maintenance technicians spend 20–1200 hours per year on chiller maintenance (minor and major) of which 16–320 hours might be expected for refrigerant transfer procedures.[28,32] In addition, 40–250 hours per year may be spent attending to system breakdowns/repairs. Thus a maintenance technician would spend one to 30 hours per week on maintenance and repair operations.

A maintenance technician may also spend 10–40 hours per week at chiller installations undergoing machine logging tasks.[32] Such tasks, often referred to as routine servicing or scheduled maintenance procedures, do not usually involve activities that may result in release of

refrigerant. Therefore, exposure of service technicians to HCFC-123 during logging operations would not normally occur except as a result of existing contamination of installation room air.

The maximum daily shift for a maintenance technician is 10 hours. In most cases, a technician would be unlikely to exceed six hours in the chiller room.[28]

8.2.3 Air monitoring studies (refrigerant)

Monitoring for HCFC-123 refrigerant has been carried out at a number of centrifugal chiller installations to characterise exposures during the various maintenance operations and repair processes carried out by maintenance technicians.

Meridian monitoring study

A US-based study by Meridian Research Incorporated (on behalf of the US EPA) was carried out at five chiller installations to measure exposure of workers to HCFC-123 engaged in routine maintenance checks and refrigerant transfer.[33]

The chiller installations were chosen according to specific criteria to achieve a representative range of possible exposure conditions. The primary criteria included size of equipment; leaks during normal operation; compliance with safety codes; age of equipment; refrigerant recovery procedures; and type of ventilation.

Personal air samples were collected for each technician using charcoal tube personal sampling pumps. In addition, static monitoring was undertaken (two to three hours) at a number of potential leak sources (oil reservoir, liquid service valve and empty refrigerant drum) using the same charcoal tube method. The methods used for sampling and analysis were based on NIOSH Method 1020. Concurrent monitoring (undertaken by Du Pont) using a portable GC was also carried out at three of the installations.

In this study concentrations of HCFC-123 measured by either static (nine samples), portable GC or personal sampling (14 samples) were all below the detection limit of 1 ppm, even during refrigerant transfer procedures.

Trane monitoring studies

A US-based study carried out by the Trane Company measured concentrations of HCFC-123 in chiller equipment rooms at 12 different sites selected to achieve a representative range of possible exposure conditions.[18]

Monitoring was carried out using both portable GC (140 samples) and charcoal tube static samplers (26 samples) followed by laboratory GC. Static sampling locations within the equipment rooms were selected according to the potential for refrigerant leakage.

HCFC-123 was detected at four sites, the results of which are presented in Table 5.

Table 5: Summary of positive HCFC-123 results from Trane monitoring study

		Static sampling (TWA)			
	Location of sampling	Sample 1 (ppm)*	Sample 2 (ppm)†	Sample time	Peak levels (ppm)‡
Site 1	Above empty HCFC-123 storage drum	0.64	0.49	4 hr	25 (29)
Site 2	Near detected leak from pump-out vapour connection on condenser	<0.40	<0.40	4 hr	18 (9)
Site 3	Near detected leak from eductor tap on condenser	<0.39	<0.39	4 hr	18–35 (11)
Site 4	Near detected leaks from purge vent line and half-empty HCFC-123 drum	5.9	13.6	20 min	22–122 (11)

* Taken 18 inches above floor (same vertical plane as sample 2).

† Taken five feet above floor.

‡ Detectable level(s) from multiple spot sampling. Total number of samples taken at each site is in parenthesis.

< Less than limit of quantitation shown.

In this study static samples were all below 1 ppm (TWA), except at a one site where levels of around 14 ppm (TWA) were reported (in the breathing zone) near to a leaking purge vent line and refrigerant drum. The sampling period reported at this installation was only 20 minutes. The highest peak reading (approximately 12 ppm) was also measured at this installation.

A follow up study by the Trane Company[29] was carried out at three different chiller sites to monitor exposure of technicians to HCFC-123 during tasks involving refrigerant transfer (two tasks); oil and oil filter change (four tasks); and a number of major service procedures (13 tasks).

Personal air samples (21 samples) were collected (four to eight hours in duration) during these procedures. The methods used for sampling and analysis were based on NIOSH Method 1020. All personal samples were below 2 ppm (TWA) and only three were greater than 1 ppm (TWA).

In addition, a Lan portable IR vapour analyser was used to measure instantaneous (peak) concentrations during these service procedures. Most peak readings (18/20) were taken for less than five minutes, with a maximum sampling time of 10 minutes. The majority of peak measurements (15/20) in this study were below 10 ppm HCFC-123. The highest peak levels encountered were during refrigerant transfer (15 ppm, 10 seconds), oil change procedures (23 ppm, five minutes), purge filter change (18 ppm, 50 seconds) and air run (18 ppm, five minutes).

Carrier monitoring study

A US-based study by the Carrier corporation[19] on a single 200 ton (610 kg refrigerant capacity) retrofitted centrifugal chiller monitored ambient levels of HCFC-123 during refrigerant transfer oil and oil filter change; refrigerant filter change and removal of a valve inspection plate. In this study, a 98 per cent recovery was reported following refrigerant transfer.

Instantaneous monitoring was carried out using both Lan and Miran IR vapour analysers, Gastec® gas sensor tubes and an Inficon® halogen leak detector. Sampling locations within the equipment room were selected according to potential refrigerant leakage. In addition, service technicians were fitted with charcoal tube personal monitors.

Breathing zone peak monitoring levels for all the above procedures were higher than 80 ppm HCFC-123. (Sampling time was two to five minutes and exact levels were not reported.)

Individual results for personal monitors were not reported, however time weighted average (TWA) exposures over a 12-hour period were reported to range 2–5 ppm HCFC-123.

To assess worker exposure dynamics resulting from a refrigerant spill, one litre of HCFC-123, estimated as being the maximum quantity of residual refrigerant that might be lost through disconnecting charge lines during refrigerant transfer, was deliberately released into the chiller room. Breathing zone (peak) levels rose slowly (about 50 ppm per minute) to a maximum level of 500 ppm, which then decreased at a rate of around 25 ppm per minute.

Worksafe Australia monitoring study

A survey by Worksafe Australia was conducted in 1993 to evaluate worker exposure during repair operations carried out on a single retrofitted* centrifugal chiller (580 kg capacity). Work activities included refrigerant evacuation, removal of refrigerant filter (Cuno) shut-off valve and leak testing.

Personal (three technicians) and static air monitoring was carried out using charcoal tube sampling pumps and peak levels were obtained using a portable Miran IR vapour analyser.

Both static (six hours duration) and personal (four to six hour duration) samples were found to be below one ppm (TWA).

Peak exposures (one to three minutes), ranging from 30 ppm HCFC-123 to several hundred, were measured on several occasions during the repair procedures, which included leaks during hose disconnection; emissions from vacuum pump outlet; refrigerant filter change and removal of shut-off valve. The highest levels were measured following completion of a preliminary leak test (soapsud method), when the nitrogen charge was evacuated to atmosphere in the plant room. A peak vapour concentration of several hundred ppm HCFC-123 was measured (during a three minute period) in the breathing zone around the area of nitrogen release.

8.2.4 Major sources of exposure to extinguishant

Although engineers may be potentially exposed to HCFC-123 from HCFC-blend extinguishants during installation and testing of extinguisher systems, exposure from this source is unlikely to be significant under normal working conditions, particularly as restrictions are expected with respect to discharges during testing.

By far the greatest potential source of exposure to HCFC-blend extinguishants will be from extinguisher discharge. Although total flooding systems constitute the highest potential for exposure to HCFC-123 from extinguishant discharge, they are designed to discharge into unoccupied areas. Therefore, exposure to workers from this source will be low. However, high levels of HCFC-123 from total flooding agents may be present several hours after discharge (particularly in poorly ventilated areas) and may constitute a significant source of exposure to emergency personnel attending fire situations, for example, police and paramedics.

On the other hand, because of their manual operation, portable fire extinguishers constitute the most likely source of occupational exposure to HCFC-blend extinguishants. Two occupational groups are potentially exposed: professional firefighters; and other workers attending to fire hazards. Actual worker exposure to HCFC-123 will depend on the size of extinguisher, the concentration of HCFC-123 in the HCFC-blend, the size of the hazard area in which the extinguishant is discharged and the deployment of personal protective equipment (PPE).

8.2.5 Extent of exposure for firefighters and installation engineers

Information on the extent (numbers of workers and duration) of exposure to HCFC-123 from firefighting or installation and testing of extinguisher systems was unavailable for assessment.

Information required includes estimates of the number of systems/units (fixed and portable) in commission, the frequency of testing and numbers of fire events. In light of current and projected import volumes, the extent of occupational exposure to HCFC-123 blend extinguishants is expected to be low.

8.2.6 Air monitoring studies (extinguishant)

Two US-based studies have been carried out by Meridian Research Inc. to assess firefighter exposure to HCFC-123 following discharge of the streaming agent Halotron-1 (HCFC Blend D) during both outdoor and indoor firefighting scenarios. Halotron-1 contains around 93 per cent HCFC-123 in an unspecified inert material.[34]

Outdoor discharge study

In a study carried out on behalf of the US EPA, a number of outdoor firefighting exercises were monitored using Halotron-1 to extinguish JP-5 jet fuel. Each fire hazard was attended by a single firefighter wearing complete protective equipment, including self-contained breathing apparatus (SCBA), using either a hand-held (20 pound) or semi-portable (150 pound) extinguisher.[35]

Personal breathing zone air samples were obtained for each of 16 fire events using personal sampling pumps attached to Tedlar® sampling bags. Samples were analysed by GC-FID. In addition, monitoring of acidic (HCl and HF) pyrolysis products of HCFC-123 was carried out using Draeger® vapour detection tubes. The results of this study are presented in Table 6.

Results were fairly consistent for 'running fuel fire' and 'pit fire' hazards with personal exposure levels in the range 7–24 ppm HCFC-123. However, results for 'pan fire' and 'dual engine fire' were highly variable, with an exposure range of 23–100 ppm and 94–870 ppm HCFC-123 for each hazard respectively. Also detected in this study were acidic pyrolysis products of HCFC-123 (by Draeger® tube). Hydrogen fluoride levels were detected at 3 ppm (the exposure standard according to the National Commission's *Exposure Standards for Atmospheric Contaminants in the Occupational Environment* [36]) and hydrogen chloride was detected at 1.5 ppm.

Table 6: Results of HCFC-123 air monitoring from outdoor discharge of Halotron extinguishant during fire suppression exercises

Fire hazard	Fire event number	Discharge duration (seconds)	HCFC-123 (ppm)	Pyrolysis products	
				HCl (ppm)	HF (ppm)
Pan fire	1	4	100	—	—
	2	4	31	ND	—
	3	4	ND	—	ND
	4	5	23	—	—
Dual engine fire	5	3	100	—	—
	6	2	720	—	3
	7	2	94	ND	—
	8	2	870	1.5	—
Running fuel fire	9	12	24	ND	—
	10	17	24	—	ND
	11	11	7	—	—
	12	7	15	—	—
Pit fire	13	33	12	ND	—
	14	37	17	—	3
	15	11	ND	ND	—
	16	14	8.5	ND	—

ND Not detected (below quantitation limit).

HCl Hydrochloric acid.

HF Hydrofluoric acid.

A 20 pound Halotron extinguisher was used for fire event nos. 1–12.

A 150 pound Halotron extinguisher was used for fire event nos. 13–16.

Indoor discharge study

In the indoor study, both personal and static monitoring of HCFC-123 levels from Halotron-1 discharges were monitored in an aircraft hanger. Each discharge was carried out by a single firefighter (wearing complete protective equipment including SCBA) using either a hand-held or semi-portable (150 pound) extinguisher.[20]

Personal air samples were collected using personal sampling pumps attached to Tedlar® sampling bags and area samples using charcoal tubes. In addition instant (peak) monitoring was carried out with a MIRAN IR vapour analyser. Tedlar® bag and charcoal tube samples were analysed by GC-FID.

Results from personal monitoring of hand-held (20 pound Halotron) and semi-portable (150 pound Halotron) extinguishers indicate maximum exposures during discharge (one minute duration) of 20 ppm and 300 ppm HCFC-123 respectively. Personal exposure levels were not as high as predicted from air dilution models.[20]

In general, peak levels of HCFC-123 were higher the nearer the area monitored to the discharge point for both types of extinguisher, ranging 100–630 ppm (after five minutes) for hand-held, and 650–1000 ppm (after 30 minutes) for semi-portable extinguishers. Similar trends were seen from static monitoring where TWA levels for 30 minutes after discharge ranged 30–140 ppm for hand-held, and 380–560 ppm HCFC-123 for semi-portable extinguishers.

The results from static (TWA) and peak sampling are presented in Table 7.

8.3 Environmental exposure

The main use of HCFC-123, currently at a level of approximately 30 tonnes annually, is in low pressure chillers, where it can replace CFC-11. Smaller amounts are used to replace CFC-12 in retrofitted high pressure chillers and in extinguishant blends for fire protection.

The major environmental sources of HCFC-123 from low pressure chillers is loss during normal running (via purging) and maintenance (via leakage and spills) of industrial chiller installations. Annual refrigerant loss during normal operation of low pressure chillers has been estimated as less than one per cent of the charge. [28,37]

Catastrophic leaks may occur from chiller system malfunction, but such incidents are expected to occur very rarely (perhaps once every few years) in Australia.

HCFC-123 has been detected in the background air at Cape Grim, Tasmania, in 1993 by GC-MS techniques, at concentrations less than 0.01 parts per trillion (ppt) (less than 0.00000001 ppm). This means that by 1993, less than 100 tonnes of HCFC-123 was in the global atmosphere.[38]

A survey of American and Canadian contractors[39] indicates that emissions of refrigerant are accounted for as follows:

Equipment leaks	41.5 %
Mishandling during service	17.9%
Contamination (motor burn)	14.1%
Contamination (oil, water and acid)	12.2%
Improper purging	12.2%
Other	2.1%

The Australian Refrigeration and Air Conditioning Code of Good Practice[40] contains a range of measures for minimising environmental exposure to refrigerants. The most important measures with respect to reducing environmental exposure are outlined below.

Under the Air Conditioning Code, retrofitting a system to use HCFC-123 (or any alternative refrigerant) can only be carried out after consultation with equipment/component manufacturers. Labelling, colour coding and nameplates must be changed following retrofit to permanently indicate the refrigerant contained and type of lubricant. All ozone depleting substances must be recovered and either recycled, reprocessed or held for disposal.

Because of the negative operating pressure, leaks do not normally result in emissions of HCFC-123, as air tends to leak in rather than refrigerant leak out. Low pressure chillers must therefore be purged periodically of any air in the system. The Air Conditioning Code requires that all new and existing equipment be fitted with a high efficiency purge unit that recovers refrigerant. Purge losses must not exceed 0.8 kg per kilogram of air.

Leak testing of connecting pipe work is required under the Air Conditioning Code before charging of refrigerant systems. For systems to be repaired, the Air Conditioning Code requires that both refrigerant liquid and vapour be recovered, with pressure reduced to 3 kPa in the case

of low pressure chillers. Where pressurisation is used to prevent ingress of air during shutdown of low pressure chillers, the Code requires that a high pressure limit switch be installed.

To minimise leaks during operation, regular inspection and/or installation of suitable sensing and alarm systems are recommended under the Code. Chiller technicians must not add refrigerant to systems known to be leaking, or return such equipment to service unless restored to a leak-free condition.

Table 7: Results of HCFC-123 air monitoring from indoor discharge of Halotron extinguishants.

Sampling time (min)	20 pound unit					150 pound unit				
	Discharge point	Area 1*	Area 2†	Area 3‡	Area 4§	Discharge point	Area 1*	Area 2†	Area 3‡	Area 4§
Peak levels										
5	400–500	360	200–300	100–500	630	—	—	—	—	—
15	210–350	46	140	—	—	—	—	—	—	—
20	39	34	40	28	37	—	—	—	—	—
30	—	—	—	—	—	1000	700	700	700	650
40	20	13	18	13	12	—	—	—	—	—
45	7	7	7	6	—	—	—	—	—	—
60	—	—	—	—	—	145	—	—	180	180
90	4	3	4.5	4	4	—	—	—	—	—
120	3	2	2.5	2	2	10	11	9	9.5	7
170	—	—	—	—	—	4	5	3	4	2
TWA levels										
0–30	—	51–126	86–141	29–98	83–103	—	386	557	378	549
30–60	—	13–14	13	7–12	4–13	—	183	308	176	309
60–90	—	6–13	4–6	3–5	3–5	—	64	84	77	96
90–120	—	2	2.5	2	2.5	—	24	30	22	29
120–150	—	<1	1	1	<1	—	11	7.5	11	7.5
150–180	—	—	—	—	—	—	5	9	5	3

* 30 feet (approx) from discharge point.

† 50 feet (approx) from discharge point.

‡ 80 feet (approx) from discharge point.

§ 160 feet (approx) from discharge point.

Use of HCFC-123 in fixed flooding and portable extinguishers entails inevitable atmospheric release, but will only occur in fire situations. No data were available on quantities likely to be released to the environment, but the current contribution to total HCFC-123 emissions is considered to be small as imports are currently at a low level and fires occur infrequently.

Release of HCFC-123 during installation, inspection and testing of gaseous fire extinguishants should not occur when these activities are undertaken in accordance with the Fire Protection Industry Association of Australia's (FPIAA) Code of Practice.[41]

Minor losses may result from transport, storage, recycling and disposal operations.

Despite the relatively small import volumes at present, there is scope for considerable increase in use of HCFC-123 in low pressure chillers and extinguishant blends, although their growth potential may not be fully realised given their scheduled phase out.

8.4 Public exposure

Under normal conditions, the public is unlikely to be exposed to HCFC-123 refrigerant. There is potential for minor leakage or spillage of HCFC-123 during routine chiller maintenance. However, given that air conditioning equipment is usually housed in plant rooms or other inaccessible locations, it is not anticipated that public exposure will arise from such activities. There is a small possibility that a major failure of a large air conditioning system could lead to a significant exposure of the building occupants. Exposure from environmental sources is also unlikely as HCFC-123 will not be intentionally released into the atmosphere, or otherwise disposed of in Australia.

There is also a potential for circulating water in the air conditioning system to become contaminated with HCFC-123 from leaking tubes or waterbox in the chiller. Leakage will flow in the direction of the vacuum, that is, from water pipe to refrigerant. However, depending on conditions such as water temperature and air conditioning system integrity—such as condition of modulating valves—a potential does exist for low level exposure to residual refrigerant for building occupants in the water system.

Under normal discharge conditions, no public exposure to HCFC-123 will occur from fixed fire extinguisher systems, particularly as fixed systems are designed for discharge into non occupied areas. Inadvertent exposure of building occupants to total flooding agents from fixed systems of up to 5000 ppm HCFC-123 and up to 100,000 ppm total fluorocarbons could be attained in an enclosed, unventilated environment. A potential also exists for hazardous exposures to HCFC-123 for occupants revisiting the hazard area, as significant levels may reside several hours after extinguishant discharge.[20]

Intermittent exposure of the public may occur following discharge of portable fire extinguishers containing HCFC-123. In addition, persons may be exposed to thermal decomposition products of HCFC-123, including phosgene, HCl, HF and to products arising from reactions between HCFC-123 and burning material. However, indoor extinguishant discharges are expected to be rare events, thereby restricting the number of persons who would be exposed in this manner. Furthermore, the duration of exposure to high concentrations of HCFC-123 arising from discharge of a portable extinguisher is not expected to be prolonged, given the relatively small volume of extinguishant involved.

9. Toxicokinetics and metabolism

9.1 Human studies

No data were available on the absorption, distribution, metabolic transformation or elimination of HCFC-123 *in vivo*.

An *in vitro* study[42] with human liver microsomes indicated that HCFC-123 is metabolised by cytochrome P450 enzymes, primarily by CYP 2E1. The major biotransformation product was trifluoroacetic acid (TFA). Chlorodifluoroacetic acid and inorganic fluoride were also identified in addition to a further (minor) uncharacterised metabolite. In this study[42] significant variation existed in the rate of formation of TFA in liver samples from seven subjects, which was directly related to the amount of CYP 2E1 protein present, but was neither age nor sex related. The rate of TFA formation by human liver microsomes was between 1.5 and 16 times faster than in rat microsomes.[42,43]

9.2 Animal studies

9.2.1 Absorption

Partition coefficients for HCFC-123 have been determined in various tissues.[43,44,102] Results indicate lipophilic characteristics and, as such, absorption and distribution are expected to occur readily.

The uptake of ^{14}C-HCFC-123 from whole body inhalation exposure has been studied in both rats and guinea pigs.[43] The rate of uptake of HCFC-123 (1000–5000 ppm) in rats (three to five animals) was estimated by measuring the disappearance of radioactivity in a closed chamber study. In this study, uptake was reported to be saturated above 2000 ppm in males. In the study by Vinegar et al[44] uptake was biphasic with a rapid initial absorption during the first 30 minutes followed by a slower rate of uptake. The author states that pharmacokinetic modelling of metabolic constants indicates a single saturable pathway.

In a supplementary study, two rats and two guinea pigs were exposed to two injections (into a closed recirculating exposure chamber) of 2000 ppm ^{14}C- HCFC-123 at three-hour intervals. Uptake of 50–60 per cent of the applied radioactivity was estimated in rats and greater than 90 per cent in guinea pigs.[43]

9.2.2 Distribution

The distribution of ^{14}C-HCFC-123 has been investigated in rats and guinea pigs following two injections (into a closed recirculating exposure chamber) of 2000 ppm ^{14}C- HCFC-123 at three-hour intervals.[43] After 48 hours, around two per cent of HCFC-123 was recovered in organs of rats and up to six per cent in guinea pigs. In rats, the liver contained most of the radiolabelled HCFC-123, followed by testes, kidneys, lungs and brain, pancreas and spleen. A similar distribution profile was seen in guinea pigs.

9.2.3 Metabolism

Biotransformation

It has been estimated from uptake and elimination studies (in rats and guinea pigs) that around 25 per cent of the absorbed dose of HCFC-123 undergoes biotransformation.[43,45] No significant differences were seen in the extent of HCFC-123 oxidation between microsomes from male and female rats.[42]

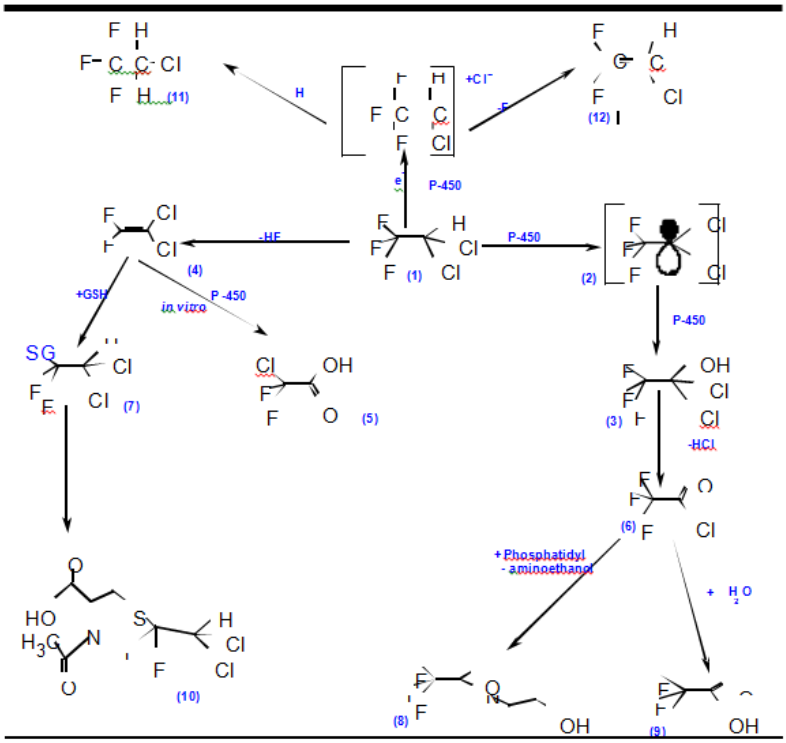
Several *in vivo* and *in vitro* studies have clearly established that the major urinary metabolite in rats is TFA.[43,46,47] *In vitro* studies in rat (and human) microsomes have shown that in the absence of NADPH or with the use of heat inactivated microsomes, TFA was not detected, indicating the involvement of cytochrome P-450.[42,43] Moreover, evidence obtained from studies with diallyl sulphide, a selective mechanism-based inhibitor of CYP 2E1, indicates a major role for this isoform in the HCFC-123 biotransformation by the liver.[42,43] Other minor metabolites of HCFC-123 (detected in rat and guinea pig urine) were N-trifluoroacetyl-2-aminoethanol and N-acetyl-S-(2,2-dichloro-1,1-difluoroethyl)-L-cysteine. Chlorodifluoroacetic acid was detected *in vitro* (in rat and human liver microsomal fractions) but not *in vivo* in rats or guinea pigs.

HCFC-123 has also been reported to undergo a cytochrome P-450 catalysed reductive metabolism in rats to form 2-chloro-1,1,1-trifluoroethane (HCFC-133a) and 2-chloro-1,1-difluoroethene (CDE).[46,47] Trace amounts of both metabolites were found in liver, with HCFC-133a detected also in expired air and kidney.[46] Both these reductive metabolites have also been identified *in vitro* but only under anaerobic conditions (<5% oxygen).[42,48]

Metabolic studies[42,43,45,46] indicate that the major biotransformation pathways for HCFC-123 is as shown in Figure 1.

Studies on the rate of HCFC-123 uptake, protein binding and TFA excretion in rats indicate that biotransformation of HCFC-123 is the rate limiting pathway with respect to the observed saturation of these processes and that saturation occurs at exposures above 1000 ppm.[45, 49] More recently, a study on blood levels of TFA in rats, indicated that HCFC-123 inhibits its own metabolism at high exposure levels, as a 50 per cent decrease of peak TFA levels (in blood) was seen 1000–10,000 ppm HCFC-123,[44] a finding confirmed by Dodd et al.[47] Metabolic rate constants developed for HCFC-123 in a PBPK model were K_m = 1.0 mg/L and

Figure 1: Major metabolic pathways for HCFC-123 as determined from in vivo and in vitro studies (adapted from Dekant 1993)[43]



1. HCFC-123.
2. 1,1-dichloro-2,2,2-trifluoroethyl radical.
3. 1,1-dichloro-2,2,2-trifluoroethanol.
4. 1,1-dichloro-2,2-difluoroethene.
5. Chlorodifluoroacetic acid.
6. 1,1,1-trifluoroacetyl chloride.
7. Glutathione conjugate of 1,1-dichloro-2,2-difluoroethene.
8. N-trifluoroacetyl-2-aminoethanol.
9. Trifluoroacetic acid.
10. N-acetyl-S-(2,2-dichloro-1,1-difluoroethyl)-L-cysteine.
11. 2-Chloro-1,1,1-triflourethane (HCFC-133a).
12. 2-chloro-1,1-difluoroethene.

Protein binding

Binding of HCFC-123 metabolites to tissue proteins (including blood proteins) has been demonstrated in rats and guinea pigs. [43,45] Studies with HCFC-123 and structural analogues indicate that trifluoroacetylchloride is the metabolite associated with this binding. [6,45]

The highest levels of protein binding have been detected in liver[43] where N-trifluoroacetylated lysine adducts have been identified in microsomal and cytosolic proteins.[45] The extent of binding to liver proteins in rats and guinea pigs exposed for six hours to 2000 ppm HCFC-123 was 0.4–0.7 nmol HCFC-123 per mg protein.[43] Immunochemical detection of trifluoroacetylated liver proteins in rats exposed for six hours to 100, 1000 and 10,000 ppm HCFC-123 indicate that little binding occurred at 100 ppm and that the rate of adduct formation is saturated above 1000 ppm.[45] Phenobarbitone pretreatment has been shown to increase the extent of hepatic protein binding in rats and mice.[45]

Low levels of covalent binding of HCFC-123 metabolites were also detected in other organs of rats and guinea pigs,[43] including kidney, lung and brain following exposure to 2000 ppm HCFC-123 (the only level tested). In this study, covalent binding in testes and pancreas were reported as not being above background levels.[43]

9.2.4 Elimination and excretion

The main route of HCFC-123 elimination, based on inhalation data for other CFCs and halothane, is likely to be via exhalation as unchanged HCFC-123.[6] In rats, steady-state expired breath concentrations of HCFC-123 were proportional to exposure concentrations at 100, 1000 and 10,000 ppm HCFC-123 and decreased rapidly on cessation of exposure, to around 10 per cent of steady-state level in 15 minutes on cessation of exposure, indicating that exhalation is a major route of HCFC-123 elimination.[44]

Similar studies by Dodd et al[47] and Vinegar et al[44] demonstrated that blood levels of HCFC-123 rapidly decreased (by about 90 per cent in two hours) when exposure ceased. The studies also showed that blood TFA levels continued to increase post-exposure (between five and 20 hours) followed by slow elimination (estimated elimination half-life ($t_{\frac{1}{2}}$) of two to four hours[47]). Fat concentrations of HCFC-123 decreased by 98% between one and eight hours post exposure.[44] The data from this study clearly demonstrated that HCFC-123 from tissues other than blood contributed to blood TFA levels.

HCFC-123 is excreted in urine trifluoroacetic acid (TFA), N-acetyl-S-(2,2-dichloro-1,1-difluoroethyl)-L-cysteine, N-trifluoroacetyl-2-aminoethanol and inorganic fluoride.[43] Approximately 25 per cent of the estimated uptake was recovered in the urine during 48 hours post-exposure of rats and guinea pigs to 2000 ppm ^{14}C-HCFC-123.[43] Urinary excretion of TFA was increased or reduced by selective induction and inhibition of cytochrome P-450.

Vinegar et al[44] also demonstrated that the urinary TFA elimination rate in rats was linear up to 48 hours post-exposure and that saturation occurred above 1000 ppm. Similar findings have been reported from other studies where urinary TFA elimination was saturated between 1000–4,500 ppm[49] and fluoride elimination saturated between 300–1000 ppm HCFC-123.[50]

Data from pharmacokinetic, biotransformation and urinary excretion studies indicate that hepatic elimination of TFA is the rate limiting step with respect to HCFC-123 metabolism.[43,44,102] Rate constants for urinary TFA excretion in Sprague Dawley rats were K_m = 11.5 mg/L and V_{max} = 44.6 mg/kg/24 hr for males, and K_m = 3.7 mg/L and V_{max} = 35.5 mg/kg/24 hr for females.[43]

10. Effects on experimental animals and in vitro bioassays

Toxicological studies made available for assessment have been evaluated and are summarised in this section. Study protocols were assessed against OECD guidelines,[51] the use of which are recommended in the NICNAS *Handbook for Notifiers*[52] and the National Commission's *Approved Criteria for Classifying Hazardous Substances*.[100] Where studies were carried out in accordance with OECD guidelines, this has been noted as it provides some indication of the methodology. For all studies, results were considered valid provided the scientific quality and reporting of the data was considered adequate. Conclusions as to the significance of the findings with respect to potential human health effects and classification can be found in section 12.

10.1 Acute toxicity studies

10.1.1 Oral toxicity

HCFC-123 was administered as a single dose (in corn oil by gavage) to male rats (ChR:CD), one animal per group, at doses ranging 2,250–11,000 mg/kg body weight.[53] The approximate lethal dose (ALD*) was approximately 9000 mg/kg body weight, where death occurred within one hour. Rapid respiration and prostration were reported after oral administration of doses at and above 3,400 mg/kg body weight. No effects were reported at the lowest dose level. Only a summary of the study was provided for assessment.

10.1.2 Dermal toxicity

Limit tests for dermal toxicity have been carried out in rats and rabbits according to OECD Guideline 402. HCFC-123 (>99% pure) was applied at a single dose of 2000 mg/kg body weight for 24 hours to occluded, intact skin of five male and five female Crl:CD BR rats, and five male and five female New Zealand albino rabbits. Animals were observed for 14 days post application. No animals died during these studies. Slight to moderate erythema was seen in rabbits (six out of 10 animals) up to five days post treatment. No gross pathological abnormalities were observed in either species.

* The lowest dose administered that causes mortality in at least one animal.

Table 8: Summary of acute inhalation lethality studies

Test animal	Exposure	Duration	Mortality ratio	Study end point, lethality	Clinical observations and pathology	Comments	Ref.
Rat (Albino)							
2 males/group	12,500 ppm 25,000 ppm 50,000 ppm 100,000 ppm	30 min 15 min 15 min 2 min	0/2 0/2 0/2 2/2	LC_{50} (15 min) > 50,000 ppm	Incoordination, prostration, unconsciousness at all exposure levels. Congestion and oedema observed in lungs and kidneys of dead animals	Purity of HCFC-123 only 71%. Animals (2) died up to 3 days following exposure.	Clayton (1964)**Error! Bookmark not defined.**
Mouse							
10 animals/group	NR	30 min	NR	LC_{50} (30 min) = 74,000 ppm	No effects reported.	Experimental data not provided. Sex of animals not reported. Purity of test material not indicated. Sex and strain unspecified.	Raventos, Lemon (1965)[i]
Rat (Charles River-CD)							
6 males/group	16,480–18,900 ppm 30,000–40,500 ppm	4 hr 4 hr	0/6 2/6	LC_{50} (4hr) = 35,000 ppm	Immediate unresponsiveness, loss of balance, hyperaemia, irregular breathing, lacrimation and death at lethal exposure levels. Marked congestion in lungs, kidney, liver of dead animals.	Purity of test material (commercial grade) not indicated. Experimental data inadequate.	Clayton (1966)**Error! Bookmark not defined.**
Rat (Charles River-CD)							
6 males/group	20,700 ppm 32,000 ppm 33,700 ppm 42,100 ppm 52,500 ppm 55,000 ppm	4 hr 4 hr 4 hr 4 hr 4 hr 4 hr	0/6 3/6 3/6 4/6 6/6 6/6	LC_{50} (4hr) = 32,000 ppm	Loss of mobility, lethargy, prostration, unresponsiveness and dyspnoea (effects reversible in surviving animals). No gross pathology or histopathology carried out.	Purity of test material not indicated.	Hall and Moore (1975)**Error! Bookmark not defined.**

Table 8 (cont): Summary of acute inhalation lethality studies

Test animal	Exposure	Duration	Mortality ratio	Study end point, lethality	Clinical observations and pathology	Comments	Ref.
Rat (Charles River -COBS)							
10 males/group	0 g/m^3 49 g/m^3 145 g/m^3 234 g/m^3 236 g/m^3 261 g/m^3 660 g/m^3 767 g/m^3	6 hr 6 hr 6 hr 6 hr 6 hr 6 hr 24 min 20 min	0/10 0/10 0/10 2/10 1/10 4/10 10/10 10/10	LC_{50} (4hr) = 329g/m^3 (52,640 ppm)	Discolouration of lung, liver, thymus and small Intestine seen at the highest 3 dose levels. Histopathology not reported.	Purity of test material not indicated.	Coate (1976)**Error! Bookmark not defined.**
Chinese Hamster							
5 males/group	10,000 ppm 14,000 ppm 22,000 ppm 26,000 ppm 31,000 ppm	4 hr 4 hr 4 hr 4 hr 4 hr	0/5 0/5 0/5 0/5 5/5	LC_{50} (4hr) = 28,400 ppm	Muscular incoordination and prostration at all exposures. No gross or histopathological effects.	Protocol according to OECD 403. Purity of test material not indicated.	Darr (1981)[ii]

NR Not reported.

i. Raventos J. and Lemon P.G., 'The Impurities in Fluothane: Their Biological Properties', *Br J Anaesth*, **37**:716–737, 1965.

ii. Darr R.W., *An Acute Inhalation Toxicity Study of Fluorocarbon 123 in the Chinese Hamster*, Report No. MA-25-78-15, Allied Corporation, Corporate Medical Affairs, Morristown, 1981.

10.1.3 Inhalation toxicity

Lethality

A number of acute inhalation lethality studies for HCFC-123 have been carried out in rats, mice and hamsters, and are summarised in Table 8. The studies carried out in male rats indicate an LC_{50} (four hours) in the range 32,000–53,000 ppm.[56,57,58,59] Reversible CNS effects such as loss of mobility and balance, lethargy, prostration and dyspnoea were reported in the range 12,500 ppm to 42,000 ppm. A test carried out according to OECD guidelines (No. 403) in Chinese Hamsters (males) indicates an LC_{50} (4 hours) of 28,400 ppm.[55] In this study, CNS effects (such as muscular incoordination and prostration) were seen at all exposure levels.

Liver effects

In an acute inhalation study, male Hartley guinea pigs (10 per group) were exposed to 0, 1000, 10,000, 20,000 and 30,000 ppm HCFC-123 for four hours.[60] All animals were sacrificed 48 hours post exposure. Histopathological lesions (seen in all exposure groups) were limited to the liver (no effects on kidney or heart) and included centrilobular and multifocal vacuolar fatty change, degeneration and necrosis. ICDH, ALT and AST were significantly increased in animals exhibiting severe effects. There was significant variation in the susceptibility to hepatotoxicity both within and between treatment groups and a clear dose response relationship was not observed.

Behaviour

In an acute behavioural toxicity (inhalation) study[61], Charles River-CD male rats (six per group) were exposed to HCFC-123 at concentrations of 0, 1000, 2500, 5000 and 10,000 ppm for one hours. The most sensitive effects elicited were failures in unconditioned reflexes (lift, grip and vertical bar). The estimated EC_{50} (one hours), for these effects was approximately 4,000 ppm HCFC-123. No effects were observed at 2,500 ppm. All effects were reversible with animals fully recovering within 24 hours post exposure.

Cardiac sensitisation

In an acute cardiac sensitisation study, groups of male Beagle dogs, pre-treated with an intravenous injection of adrenalin (0.008 mg/kg), were exposed by inhalation (five minutes) to HCFC-123 at concentrations of 10,300 ppm, 20,900 ppm and 40,600 ppm.[62] A challenge dose of adrenalin produced severe arrhythmia, ventricular fibrillation and cardiac arrest at the two highest concentrations (seven out of nine animals) but no response was noted at the lowest exposure level. The EC_{50} (five minutes) for cardiac sensitisation in dogs was calculated to be 19,000 ppm (119 g/m^3). CNS depression was observed at all exposure levels.

10.2 Irritation studies

10.2.1 Skin irritation

HCFC-123 (pure) was evaluated for skin irritation potential in male and female New Zealand albino rabbits.[12] The study was carried out according to OECD Guideline 404. No erythema or oedema were observed up to 72 hours following occlusion (four hours) of intact skin with 0.5 ml (730 mg) of HCFC-123. The sensitivity of this study was confirmed by a positive control substance.

10.2.2 Eye irritation

The potential for HCFC-123 to induce eye irritation was investigated in albino rabbits, sex and strain unspecified.[63] HCFC-123, as 0.1 ml of undiluted or 0.2 ml of 50% HCFC-123 in propylene glycol, or 0.1 ml of pure propylene glycol, was placed in the conjunctival sac of the right eye of two animals. After 20 seconds the treated eye of one animal in each group was

washed with water for one min. Observations of the cornea, iris and conjunctiva were made after one and 4 hours, and at days 1, 2, 3, 7 and 14.

In the animals treated with undiluted HCFC-123, mild to moderate conjunctival irritation (washed and unwashed eye) and mild to slight corneal opacity (washed eye only) were observed up to three days after dosing. Similar effects were seen in animals treated with 50% HCFC-123 in propylene glycol, except that moderate to severe conjunctival irritation was seen in unwashed eyes and moderate corneal opacity was observed in the unwashed eye. Propylene glycol *per se* had no effect on the cornea or iris (washed or unwashed eye) but did elicit mild to slight conjunctival irritation (washed and unwashed eye). Although this study did not conform to OECD test guidelines it was considered adequate.

10.3 Skin sensitisation study

The sensitisation potential of HCFC-123 was tested in a group of 10 male albino guinea pigs.[64] In the induction stage of the test, 0.1 ml of a 1% solution of HCFC-123 in dimethyl phthalate was administered by intradermal injection once a week for three weeks. Two weeks after the final injection the animals were challenged with an application (0.05 ml) of 10% (approx 7 mg HCFC-123) and 50% (approx 35 mg HCFC-123) HCFC-123 in propylene glycol vehicle to intact shoulder skin. No signs of sensitisation were seen 48 hours after challenge and no signs of irritation were evident during the study.

10.4 Repeated dose (inhalation) studies

10.4.1 Sub-acute toxicity (14–28 days)

Several short-term repeated dose inhalation studies have been performed in rats, with an additional study in guinea pigs, summaries of which are presented in Table 9. In each case, HCFC-123 was administered for six hours per day, five days per week, for two to four weeks at concentrations ranging 1000–20,000 ppm.

The main target organs for HCFC-123 elicited effects in these studies were the CNS, liver and testes. CNS effects were seen at and above 5000 ppm and were reversible overnight. In rats, HCFC-123 caused increased liver to body weight ratio; depressed serum triglyceride, cholesterol and glucose levels;[68] elevated serum AST, ALT and ALP activities;[65,67] increased ß-oxidation activity;[68] hepatic centrilobular fatty change;[67,68] hepatocyte hypertrophy;[68] increases in the number of hepatic mitochondria and peroxisomes; and an increase in hepatocyte mitotic activity, that is, cell proliferation index (CPI).[68] Changes in hepatic morphology and serum biochemistry developed at 1000 ppm, and changes in most parameters were dose-related. Levels of ß- oxidation activity, increased peroxisome numbers and changes in hepatic morphology (weight and cellular changes) indicate that HCFC-123 is a mild peroxisome proliferating compound in rats. Species differences in toxicity were evidenced by the lack of peroxisome proliferation and decreased liver weight in guinea pigs. In addition guinea pigs developed hepatocyte necrosis as opposed to hypertrophy (in rats).[68]

In rats, increased testes weights were observed at 1000 ppm HCFC-123, together with elevated serum androgen concentrations, Leydig cell hyperplasia (one animal only), seminiferous tubule atrophy and degeneration, epididymal hypospermia and germinal cell necrosis at exposure levels greater than 18,000 ppm. Testicular effects were not seen in guinea pigs. Testicular peroxisome proliferation was not reported in any of the studies assessed.

A slight increase in pancreatic peroxisome proliferation was seen in guinea pigs, however no changes in pancreatic peroxisome proliferation were seen in rats or guinea pigs exposed to the WY-14643 (known peroxisome proliferator) which serves to question the significance of this finding. Similarly, the slight decrease in pancreatic peroxisome proliferation seen in rats in the same study was not considered biologically significant.[68] Slight increases in pancreatic mitotic

activity (CPI) were seen in both species, although no changes in pancreas morphology were seen. In the same study, insulin levels were statistically decreased in rats exposed to HCFC-123. This finding was considered to be a physiological response to decreased glucose levels rather than an indicator of diminished pancreatic function, although data for WY-14643 confound this conclusion.[68]

The study in rats and guinea pigs by Warheit[68] was devised as a follow-up mechanistic study to the two-year (chronic inhalation) study, carried out by Malley[50] (see 10.4.3). This study is discussed in more detail in section 12.3.7 on carcinogen hazard assessment.

Table 9: Summary of sub-acute inhalation toxicity studies

Test animal	Exposure protocol	Duration	Gross observations/ body & organ weights	Clinical and pathological effects	Comments	ref
Rat (ChR-CD)						
10 males/group	0, 9,100–9,700 ppm (measured concentration)	6 hr per day, 5 days per week, for **2 weeks**	Loss of motor coordination; unresponsive to noise. Kidney weight (rs+)*.	No effects on blood chemistry except AST (s+)* at end of study and 14 days post-exposure. Histopathology - unremarkable.	Purity of test material not indicated. Clinical and pathological tests carried out on 5 animals at end of study and 14 days post-exposure.	(1) Kelly (1975)[i] (2) Trochimowicz et al (1977) [ii]
Rat (Crl-CD BR)						
10 males and 10 females/group	0, 1,000 [a], 5,000[b], 10,000[c] 20,000[d] ppm (approximate concentrations)	6 hr per day, 5 days per week, for **4 weeks**	Anaesthetic effects (e.g. unresponsive to noise) in [b] [c] & [d] (dose related). Body weights (-) in all test groups (dose related in males) and (s-)* in [c] & [d]. Liver weight (rs+)* in all test grps (females - dose related). (rs+)* in [d] males. Testes weight (rs+)* in [a] [c] & [d].	Degeneration (uni & bi) of seminiferous tubules and epididymal hypospermia in 6/10 animals in [d] (cf 2/20 control animals). Liver Cyt-P450 (s-)* in all female test grps and in [b] [c] & [d] in males (dose related). Plasma AST (s+)* in [c] & [d] males, ALT (s+)* in [d] males. Urinary fluoride (+) in all grps. (s+)* in [d] both sexes & [c] females.	Protocol according to OECD 412. Animals recovered from anaesthetic effects overnight. Hepatic fatty change seen in test animals (12% of test animals) was not dose related and was not considered biologically significant. Testicular lesions seen in animals exposed to 20,000 ppm were reported as moderate to severe whereas in controls these lesions were reported as minimal to moderate. No biologically significant changes seen in cytochrome b5 activity	Kelly (1989)[iii]
Rat (CD BR)						
6 males/group	0, 977 [a], 4,510[b], 19,500[c] ppm (measured concentrations)	6 hr per day, 5 days per week, for **4 weeks**	Anaesthetic effects in [c]. Body weights (-) in all test groups. Liver weight (as+)* (rs+)** in [c]. Testes weight (rs+)* in all test groups.	Hepatocyte hypertrophy & centrilobular fatty change in all test grps. Peroxisome and mitochondria prolif. (s+)** in [b] & [c]. SER (s-)** in [b] & [c]. (all dose related). Plasma AST (s+)** in all test grps, ALT (s+)* in [a & c], ALP (s+)** in [c], trig (s-)** in all test grps, chol (s-)** in [b] & [c].	Protocol according to OECD 412. TFA measured in urine. Leydig cell hyperplasia, tubular atrophy and epididymal hypospermia seen in I/6 animals in [c]. No biologically significant changes seen in Liver Cyt-P450 and cytochrome b5 activity. Beta-oxidation activity (towards palmitoyl CoA) = 1.9, 2.0 & 3.3 times control levels in [a] [b] & [c] respectively	Lewis (1990)**Error! Bookmark not defined.**

Table 9 (cont): Summary of sub-acute inhalation toxicity studies

Test animal	Exposure protocol	Duration	Gross observations/ body & organ weight	Clinical and pathological effects	Comments	ref
Rat (Crl-CD BR)						
17 males/group	0 18,200 ppm (mean exposure level)	6 hrs per day, 5 days per week, for **4 weeks**	Body weights (s-)* Liver weight (rs+)* Testes weight (as+)(rs+)* ASO (as-)*	Hepatocellular hypertrophy (+) in all test animals. Atrophy (uni & bi) of seminiferous tubules in 3/5 animals. Germinal cell necrosis & syn/sl in 4/5 animals. Liver peroxisome prolif. & CPI (s+).* Trig/Chol/Gluc./Ins (s-).* CCK/Oestradiol/Test (+)	Peroxisome proliferation assay not carried out with testicular tissue. Liver peroxisome prolif. measured by ß-oxidation activity (towards palmitoyl CoA)–4.7 times control levels. LH also measured –no change from controls. Although reported as not statistically. significant, testosterone levels were 50% higher than controls	Warheit (1993)[iv]
Guinea pig (Hartley -BR VAF/PLUS)						
17 males/group	0 9,400 ppm (mean exposure level)	6 hr per day, 5 days per week, for **4 weeks**	Body weights (s-)* Liver weight (as-)(rs+)* Testes (as-)* ASO (as-)(rs-)*	Centrilobular fatty change (+) in all test animals. Hepatocyte necrosis (+) in 3/5 animals. No testicular lesions. Testes CPI (+). Liver peroxisome prolif. (-) CPI (+). Trig/Chol/Gluc./Ins (s-).* Serum CCK/Test (-).	Although reported as not stat. significant, testosterone levels were 50% lower than controls. Initial exposure level for HCFC-123 was 20,000 ppm. Level was reduced to 9,400 ppm due to severe weight loss. Three treated guinea pigs died during study.	Warheit (1993) [iv]

* $p \leq 0.05$	a	absolute weight	Chol	cholesterol	trig	triglycerides
** $p \leq 0.01$	[a], [b] etc	test group designations	Gluc	glucose	test	testosterone
+ increase	ALP	alkaline phosphatase	Ins	insulin	TFA	trifluoroacetic acid
- decrease	ALT (GPT)	alanine transaminase	CPI	cell proliferation	r	relative weight
	ASO	Accessory sex organs	LH	luteinising hormone	s	statistically significant
	AST (GOT)	aspartate transaminase index	prolif	proliferation	SER	smooth endoplasmic reticulum
	CCK	cholecystokinin	syn/sl	syncytia/sloughing	uni & bi	unilateral & bilateral

i. Kelly D.P., *Two-week Inhalation Toxicity Studies with Cover Sheet and Letter*, Report No. 149–76, Haskell Laboratory, Du Pont de Nemours, Newark, Delaware, 1975.

ii. Trochimowicz H.J., Moore B.L., Chiu T., 'Subacute Inhalation Toxicity Studies on eight Fluorocarbons, *Toxicol. Aool. Pharmacol. (Abstracts)*, 41:198–199, 1977.

iii. Kelly D.P., *Four-week Inhalation Toxicity Study with HCFC-123 in Rats*, Report No. HLR 229–89, Haskell Laboratory, Du Pont de Nemours, Newark, Delaware, 1989.

iv. Warheit D.B., *Mechanistic Studies with HCFC-123*, Report No. 828-92, Haskell Laboratory, Du Pont de Nemours and Co., Newark, 1993.

10.4.2 Sub-chronic (90 days) toxicity

A number of sub-chronic inhalation studies have been carried out in rats and dogs and are summarised in Table 10. In each case, HCFC-123 was administered for six hours per day, five days per week at concentrations ranging between 300 and 10,000 ppm.

The main effects seen in these studies were CNS depression and liver injury, with limited evidence of effects on kidney function.

Reversible CNS effects were recorded in both species at and above 1000 ppm. Neurobehavioural screening (including grip strength, landing foot splay, startle response, tail pinch and righting reflex) showed no treatment related effects in a neurotoxicity study[69] except a statistically significant reduction in arousal at 1000 and 5000 ppm HCFC-123. No treatment-related effects on the brain or nerve tissues were revealed by histological examination.

In 90-day studies in rats, HCFC-123 caused dose-related increases in liver weight at the lowest level tested (300 ppm) together with hepatocyte atrophy, focal necrosis (in males) and mixed cell inflammation at and above 500 ppm. Levels of ß-oxidation activity, increased peroxisome numbers (measured at 5000 ppm only) and changes in hepatic morphology (weight and cellular changes) indicate that HCFC-123 is a mild peroxisome proliferating compound in this species. Significant elevations in serum ALT, AST and ALP activities were seen at 1000 ppm in two rat studies. However, the absence of hepatic histopathological changes in these studies serve to question the biological significance of these enzyme increases. Significant decreases in serum triglyceride and glucose levels were also seen at 1000 ppm in all test groups in addition to decreases in serum cholesterol in females .[70,71,72] Dogs also displayed elevated ALP activities at and above 1000 ppm and elevated AST, ALT and liver discolouration, hypertrophy, and necrosis at 10,000 ppm.[71]

Relative kidney weights were increased in female rats at 1000 ppm, accompanied by elevated blood urea nitrogen (BUN) levels (in males and females). BUN levels were also significantly increased in dogs exposed to 10,000 ppm.[71] Although statistically increased, the biological significance of increased BUN levels was questioned by study authors as changes were reported to be within the range of normal variation.

Testicular weights were increased in rats at 300 ppm and above. Severe hypospermia and unilateral tubular atrophy was seen in a single rat exposed to 5000 ppm.[72]

Table 10: Summary of sub-chronic inhalation toxicity studies

Test animal	Exposure	Duration	Gross observations/body & organ weights	Clinical and pathological effects	Comments	Study ref.
Rat (ChR) albino						
35 males & 25 females per group	0 500 [a] 1,000 [b] 5000 [c] ppm	6 hr per day 5 days per week for **90 days**	Body weights (s-)** in [c] males & in [b] & [c] females. Liver weight (rs+)* in all female test grps & in [c] males. Adrenal weight (as-)* in [b] males. Kidney weight (as-)* (rs+)* in [c] female & (as-)* in all test grps (males).	Mild focal necrosis (+) in all males & (+) in [a] & [b] females; MCI (+) in all test groups. Hepatocyte atrophy / tel [+] in all males & in [c] females. Gluc (-) in [a] & [b] females.	Purity of test material not indicated. Serum insulin in male animals returned to normal range 30 days post exposure. Urinary fluoride (+) in [b] males & (+) in all test grps (females). 10 male & 5 female animals were allowed 30 days recovery period at end of study. In these groups no significant differences were seen in body / organ weights or in terminal histopathology (except MCI (seen in [c] females).	Brewer & Smith (1977)**Error! Bookmark not defined.**
Rat (ChR-CD)						
27 males & 27 females per group	0, 1,000 [a] 10,000 [b] ppm	6 hr per day 5 days per week for **90 days**	Anaesthetic effects (e.g. lack of motor coordination & unresponsiveness) in [b]. Body weights (-) in both test grps. Liver weight (as+)(rs+)* in both test grps. Testes weight (r+) in both test grps. Adrenal weight (r+) in both test grps (male). Kidney weight (r+) in both test grps (female).	Histopathology—unremarkable. AST (s+)* in both test grps (males); ALT (s+)* in males in [a]; ALP (+) in both test grps (males) & (+) in [b] females; LDH (+) in [b]. BUN (s+)* in both test grps (males) & in [a] females; Gluc (s-)* in both test grps (female) & in [b] males; Prot (s-)* in both test grps.	Animals recovered from anaesthetic effects 15–30 mins post-exposure. Histopathology carried out on 6 animals per test group. Only summary of results available for assessment. Lower organ to body weight in testes; adrenal and kidney may reflect lower body weights. Urinary fluoride (+) in both test grps.	Doleba-Crowe (1978)**Error! Bookmark not defined.**
Dog (Beagle)						
4 males per group	0 1000 [a] 10,000 [b] ppm	6 hr per day 5 days per week for **90 days**	Anaesthetic effects (e.g. lack of motor coordination & unresponsiveness) in [b].	Gross histopathology—discolouration of livers in [b]. Hepatic hypertrophy, necrosis and inflammatory cell infiltration In [b]. AST (+) in [b]; ALT (+) in [b]; ALP (s+)* in both test grps. BUN (+) in [a] & (s+)* in [b]; Gluc (+) in both test grps.	Animals recovered from anaesthetic effects 15–30 mins post exposure. Only summary of results available for assessment. No compound related pathological effects were seen at 1000 ppm.	Doleba-Crowe (1978)**Error! Bookmark not defined.**

Table 10 (cont): Summary of sub-chronic inhalation toxicity studies

Test animal	Exposure	Duration	Gross observations/body & organ weights	Clinical and pathological effects	Comments	Study ref.
Rat (Crl-CD BR)						
10 males and 10 females per group	0 300 [a] 1000 [b] and 5000 [c] ppm	6 hr per day 5 days per week for **90 days**	Anaesthetic effects (e.g. unresponsive to noise) in [c]. Body weights (-) in [b] & [c]. Liver weight (rs+)* in [b] & [c] males and females. Testes weight (r+) in all test grps.	Histopathology—unremarkable. Hepatic peroxisome prolif (s+)* in all test grps (female) & in [b] & [c] males. Trig/Gluc (s-)* in all test grps; Chol (s-)* in [b] & [c] females. BUN (s+)* in [b] & [c] both sexes & in [a] females. AST (s+)* in [b] & [c] males & (-) females in all test grps; ALT (s+)* in [b] & [c] males & (-) females in all test grps; ALP (s+)* in [b] & [c] males; LDH (s+)* in [c] males. Urinary fluoride (+) in all test grps & (s+)* in all male test grps & [c] female.	Animals recovered from anaesthetic effects overnight. Body weight gain (s+)* in all test grp (females) up to test day 48. Severe hypospermia & unilateral tubular atrophy seen in 1/10 animals at 5000 ppm. Liver peroxisome prolif measured by ß-oxidation activity (towards palmitoyl CoA) and electron microscopy in [c] test groups. ß-oxidation activity in males = 1.9, 3.4 & 3.7 and females = 2.6, 2.2 & 2.4 times control levels in [a] [b] & [c] respectively	Malley (1990)**Error! Bookmark not defined.**
Rat (Sprague-Dawley CD)						
10 males and 10 females per group (Neurotoxicity study)	0 300 [a] 1000 [b] 5000 [c] ppm	6 hr per day 5 days per week for **13 weeks**	Anaesthetic effects (half & fully closed eyes) in [b] & [c]. Behavioural changes (lower arousal) in [b] & [c] males. Bodyweights (s-)* in [b] & [c] females from week 2 onwards. Relative brain weight—unaffected	Histology of brain, medulla/pons, cerebellar cortex, spinal cord, ganglia, dorsal and ventral root fibres and peripheral nerves (sciatic, sural and tibial) was unremarkable. No other tissues were examined.	Behavioural changes did not increase in severity with time, and disappeared during recovery period (weeks 13 to 17). Body weights increased following withdrawal of treatment. There were no effects on food consumption.	Coombs (1994)**Error! Bookmark not defined.**

+	Increase.	a	Absolute weight.	LDH	Lactate dehydrogenase.
-	Decrease.	ALP	Alkaline phosphatase.	MCI	Mixed cell inflamation.
*	$p \leq 0.05$.	ALT	Alanine transaminase.	Prolif	Proliferation.
**	$p \leq 0.01$.	AST	Aspartate transaminase.	Prot	Total protein.
[a], [b] etc	Test group designations.	BUN	Blood urea nitrogen.	r	Relative weight.
		Chol	Cholesterol.	s	Statistically significant.
		Gluc	Glucose.	Tel	Telangiectasis.
		Ins	Insulin.	TFA	Trifluoroacetic acid.
				Trig	Triglycerides.

10.4.3 Chronic (two-year) toxicity

A combined chronic inhalation toxicity/oncogenicity study was carried out by Malley.[50] Crl:CD BR rats (80/sex/group) were exposed to 0, 300, 1000 and 5000 ppm (0, 2, 6, 31 g/m^3) HCFC-123 for six hours per day, five days per week for 24 months. The purity of the test material was reported to be 99.8%. The study was carried out according to OECD Guideline No. 453.

In this study, serum biochemistry was carried out at six, 12, 18 and 24 months and histopathology at 12 and 24 months. Historical oncogenicity data for Charles River (Sprague-Dawley) rats, obtained from the performing laboratory was used for comparative purposes.

The main target organs for treatment related effects in this study were the liver, testes and pancreas. The incidence of tumours in these organs is summarised in Table 11.

Hepatic effects

Perturbations in serum biochemistry (carried out on groups of 20 rats per sex at 6 month intervals) were inconclusive with respect to diagnosis of hepatocellular dysfunction. Although elevations were seen in serum ALP, ALT and AST activities, (highest at 5000 ppm HCFC-123) increases were considered to be within normal biological variation. Similarly, significant decreases in serum triglycerides, cholesterol and glucose levels (seen at 12 and 18 months) may be related to the hypolipidaemic potential of HCFC-123 rather than to overt liver dysfunction.

Groups of five rats per sex were assessed for hepatocellular proliferation (CPI) and peroxisome proliferation at 12 months. Treatment related differences in mitotic activity (CPI) were not observed at 5000 ppm and hence other test groups were not evaluated. A dose-related increase in hepatic peroxisome proliferation (as assessed by increased ß-oxidation enzyme activity) was seen in male rats with increases of 2.3, 3.1 and 4.0 fold at 300, 1000 and 5000 ppm HCFC-123 respectively. In females, significant increases were only seen at the two highest doses, where 1.7 and 3.1 fold increases were measured. The smaller increases in female rats may be due to the unusually high ß-oxidation activity in controls.

No compound-related gross or microscopic changes were observed at any exposure level in either males or females at 12 months.

At 24 months exposure to 5,000 ppm HCFC-123, liver weights were significantly increased and accompanied by discolouration and hepatic masses in both sexes. Histopathology revealed a number of treatment related effects including cystic degeneration and cellular alteration at 1000 and 5000 ppm, cholangiofibrosis (females), necrosis (males), centrilobular fatty change, biliary hyperplasia and ectasia at 5000 ppm.

At 24 months significant increases in the incidence of hepatocellular adenomas (both sexes) and cholangiofibromas (females) were seen at the highest exposure level, although a significant increase in hepatocellular adenomas was also seen in females at 300 ppm (see Table 11). No increase in hepatic tumours was seen at 12 months. Increases in certain malignant tumours were also seen at 24 months but were either metastatic in origin or similar to historical controls and therefore not considered compound related.

Testicular effects

Testicular weights were increased at 24 months at all exposure levels, but were not statistically greater than controls. Male rats exhibited dose-related increases in unilateral seminiferous tubular atrophy and focal interstitial (Leydig) cell hyperplasia, significant at 5000 ppm and 1000 ppm respectively. Epididymal hypospermia occurred at 5000 ppm HCFC-123.

Although increases were also seen in interstitial (Leydig) cell adenomas, especially bilateral adenomas at all exposure levels, a dose-response relationship was not observed (see Table 11), and statistical significance was only seen at 5000 ppm, although when the tumour types are

combined, significance is seen at all exposure levels. Malignant neurofibrosarcoma seen in a single rat at 1000 ppm was metastatic in origin and therefore not considered compound related.

Pancreatic effects

An increase in pancreatic nodules was seen at 24 months. Histopathology revealed a significant increase in acinar cell focal hyperplasia (in both sexes) at and above 1000 ppm. Pancreatic weights were not determined at necropsy.

An increased incidence of exocrine pancreatic acinar cell adenomas was seen at all exposure levels except in females at 1000 ppm, however the incidence in females was neither statistically significant or dose related (see Table 11). Sex differences in adenoma incidence were reflected by differences seen in acinar hyperplasia.

Increases in certain malignant tumours (exocrine and endocrine pancreas) were also seen at 24 months but were either metastatic in origin or similar to historical controls and therefore not considered compound related.

Other effects

Animals exposed to 1000 and 5000 ppm exhibited higher survival rates compared to controls. Animal body weights and body weight gain were significantly decreased at 5000 ppm at 12 months and at 1000 ppm in females at 24 months. Decreased kidney weights in both males and females and increased adrenal & lung weights in males were also observed at this exposure level.

Increases in tumours were also seen in other tissues at 24 months but were either not considered biologically significant, were metastatic in origin or exhibited a similar incidence to historical controls and therefore not considered dose related.

Significant biochemical changes (at 24 months) not reported under specific organ effects (above) include increased serum albumin in above 1000 ppm (both sexes) and decreased serum globulin levels above 300 ppm in females and 1000 ppm in males.

Rats exposed to 5000 ppm HCFC-123 showed evidence of CNS effects, that is, less responsive to auditory stimuli compared to controls. Females exposed to 5000 ppm manifested a significant increase in ovarian atrophy and ovarian cysts. Histological evaluation of the retina indicated a significant increase in diffuse retinal atrophy in both sexes at all exposure levels.

Males and females exposed to 5000 ppm exhibited a 50 per cent decrease in neutrophils at 24 months. Monocytes were decreased to a similar extent in females at 1000 and 5000 ppm.

Table 11: Summary of tumour incidence in target organs (from chronic inhalation study) **Error! Bookmark not defined.**

Tumour description				Number of animals with tumours/number examined							
				Control		300 ppm		1000 ppm		5000 ppm	
Organ	Tumour	Type	Origin (organ or cell type)	Male	Female	Male	Female	Male	Female	Male	Female
Liver	Histiocytic sarcoma	M	Unknown	1/67	0/65	1/66	0/67	5/66	0/67	1/66	0/69
	Hepatocellular adenoma	B	—	3/67	0/65	2/66	5/67*	2/66	2/67	8/66*[1]	7/69*[2]
	Hepatocellular carcinoma	N	—	1/67	0/65	1/66	1/67	0/66	0/67	1/66	1/69
	Lymphosarcoma	M	Unknown	0/67	0/65	1/66	0/67	0/66	0/67	3/66	0/69
	Leukaemia	M	—	0/67	2/65	2/66	1/67	3/66	2/67	1/66	1/69
	Adenocarcinoma	M	Pancreas/Prostate	0/67	0/65	0/66	0/67	1/66	1/67	1/66	0/69
	Cholangiofibroma	B	—	0/67	0/65	0/66	0/67	0/66	0/67	0/66	6/69*[2]
			Total Hepatic Tumours	**5/67**	**2/65**	**7/66**	**7/67**	**11/66**	**5/67**	**15/66**	**15/69**
Exocrine Pancreas	Adenocarcinoma	N	Acinar cell	1/67	0/65	0/66	0/66	0/64	0/67	2/66	0/69
	Adenoma	B	Acinar cell	1/67	0/65	4/66	2/66	12/64*	0/67	14/66*	2/69
	Neurofibrosarcoma	N	—	0/67	0/65	0/66	0/66	1/64	0/67	0/66	0/69
	Histiocytic sarcoma	M	Unknown	0/67	0/65	1/66	1/66	1/64	0/67	0/66	0/69
	Leukaemia	M	—	0/67	1/65	1/66	0/66	2/64	0/67	0/66	0/69
	Lymphosarcoma	M	Unknown	0/67	0/65	0/66	0/66	0/64	0/67	1/66	0/69
Endocrine Pancreas	Adenoma	B	Islet cell	6/67	3/65	5/66	4/66	7/63	3/67	1/66	0/69
			Total Pancreatic Tumours	**8/67**	**4/65**	**11/66**	**7/66**	**23/64**	**3/67**	**18/66**	**2/69**
Testes	Adenoma	B	Interstitial cell[3]—unilateral	3/67	N/A	6/66	N/A	4/66	N/A	8/66*	N/A
	Adenoma	B	Interstitial cell[3]—bilateral	1/67	N/A	6/66	N/A	5/66	N/A	6/66*	N/A
	Neurofibrosarcoma	M	Unknown	0/67	N/A	0/66	N/A	1/66	N/A	0/66	N/A
			Total Testicular Tumours	**4/67**	**N/A**	**12/66***	**N/A**	**10/66***	**N/A**	**14/66***	**N/A**

This table comprises tumour incidence data for organs where compound-related tumours were seen at terminal (24 months) sacrifice (includes rats that died in extremis after interim [12 month] sacrifice).

* $p \leq 0.05$

N/A not applicable

1 Includes 3 animals with multiple tumours.

2 Includes one animal with multiple tumours.

3 Known also as Leydig cell.

B Benign .

M Malignant (metastatic).

N Malignant (neoplastic).

10.5 Reproductive toxicity studies

10.5.1 Developmental toxicity studies

Developmental toxicity (inhalation) studies with HCFC-123 have been performed in rats and rabbits.

Two studies have been conducted according to OECD guideline No. 414 in Charles River albino rats. In one study, 25 dams were exposed to 0 or 10,000 ppm of HCFC-123.[73] In the other study, 20 dams were exposed to 0 or 5000 ppm.[74] In both studies dams were exposed to HCFC-123 by inhalation for six hours per day during days 6–15 of gestation. Reduced weight gain and CNS depression were observed at 5000 and 10,000 ppm respectively, however there was no evidence of adverse effects on foetal viability, growth or development.

Similarly, there was no evidence of developmental effects in New Zealand white rabbits (24/group) exposed by inhalation to 0, 500, 1500 or 5000 ppm of HCFC-123 for 6hr/day, during days 6–18 of gestation.[75] In the range-finding study, (1000, 5000, 10,000 and 20,000 ppm HCFC-123, six hours per day through gestation days 6–18) increased resorption rate and lower foetal weights were seen at the two highest concentrations, together with foetal tail defects at 20,000 ppm.[76] Maternal toxicity, seen as dose-dependent reduced weight gain and inappetence was seen in this study.

10.5.2 Two generation reproduction toxicity study

A two generation inhalation reproduction toxicity study was carried out in Crl: CD (SD) BR VAF/plus rats[77] in accordance with OECD 416. Animals were exposed to 0, 30, 100, 300 or 1000 ppm (0.19, 0.63, 1.88 and 6.26 mg/L) HCFC-123. The F_0 (parental generation) animals, 32 animals/sex/group, were exposed for six hours per day, seven days per week from six weeks of age for 38 weeks. All animals were exposed during pregnancy, except between day 20 to post-partum day four.

The F_1 generation (28 pups/sex/group) were derived from the F_0 generation. During the pre-weaning period direct exposure was confined to the lactating (F_0) parent. The F_1 generation were then exposed from four weeks of age through to weaning (approximately 28 weeks) of their litters (F_2 generation).

Among F_0 rats, depression in body weight gain was seen in males at 100 ppm and above between weeks 14 and 26 only. Body weight gain was significantly lower in females at 1000 ppm during the third week of pregnancy (11% lower), but not during lactation. Food intake was decreased in females during lactation at and above 300 ppm. Significant perturbations in circulating cholesterol and triglyceride levels were observed in F_0 rats. Triglycerides (when measured at 38 weeks of age) were depressed at 300 and 1000 ppm (both sexes) and among 100 ppm females. Relative liver weights were significantly increased in all treated F_0 animals. Dose related histological changes were also present at 300 ppm and above, and consisted of enlarged and vacuolated centrilobular and/or periportal hepatocytes in both sexes.

HCFC-123 did not influence pre-mating interval, copulation index or the pregnancy rate of F_0 rats. No consistent changes in serum cholecystokinin (CCK) were observed. A decrease in milk fat content was observed at all dose levels, although no dose response relationship was observed. Male hormonal assays (at 14 weeks) revealed significantly increased levels of luteinising hormone (LH) at and above 300 ppm. No treatment related histological abnormalities were seen in the reproductive organs of either sex. There were no significant treatment-related effects on the number of implantation sites, embryonic losses, sex ratio, litter size or the number of live-born pups. Mean pup weights (F_0 offspring) were significantly decreased (around 10%) from day 14 post-partum to weaning at exposures (dose-related) at and above 100 ppm. Sexual maturation was slightly delayed in males at 300 and 1000 ppm.

In the F_1 generation, body weight gains were significantly reduced at 300 and 1000 ppm for female and male adults and at 1000 ppm for females during pregnancy (11–20% lower) but not during lactation. Food intake was decreased during lactation in females at 100 (days 4–6), 300 and 1000 ppm. Relative hepatic weights were increased among F_1 weanlings and adults at 300 ppm and 100 ppm respectively. Histological changes, triglyceride and cholesterol perturbations (seen in adults only) were similar to F_0 generation. Significantly reduced relative pituitary and ovarian weights were seen in females at 300 and 1000 ppm respectively, although no treatment related histological abnormalities were present in the reproductive organs (both sexes—adult F_1 rats). Male hormonal assays revealed significantly decreased levels of progesterone at and above 100 ppm.

HCFC-123 did not influence pre-mating interval, copulation index, pregnancy rate or pup sex ratio of the F_1 generation or effect serum CCK concentration or milk fat content. The number of implantation sites was significantly reduced at 1000 ppm, with a consequent diminution in litter size and litter weights, although foetal survival was not compromised. Mean pup weights in F_1 offspring (F_2 generation) were significantly decreased (around 20%) from day seven post-partum to weaning at all exposure levels. During this period (from post-partum day four) direct exposure was confined to the lactating parent.

10.6 Genotoxicity studies

10.6.1 In vitro bioassays

Microbial mutation assays

The mutagenic potential of HCFC-123 has been investigated in *Salmonella typhimurium* (point mutation) and *Saccharomyces cerevisiae* (gene mutation).[78,79,80,81]

In the most recent study,[81] HCFC-123 tested (suspension and plate assays) as a vapour and liquid did not induce any significant increases in the observed numbers of revertant colonies in any strain (TA98, TA100, TA1535 TA1537, TA1538) of *Salmonella typhimurium*, either in the presence or absence of an auxiliary metabolising system (S9). The toxic effects observed at the highest exposure level (thinning of background level and/or reductions in colony numbers) confirm that HCFC-123 was tested to an effective maximum dose (750 mg/vessel or 150,000 ppm vapour). Positive controls confirmed that the bacterial strains were responding satisfactorily. The results of this study are in agreement with previous studies carried out by Barsky,[78] Brusick[79] and Longstaff et al.[80]

Only one study[81] conformed to OECD guidelines (OECD 471) and deficiencies were apparent in earlier studies. In addition, the study in *Saccharomyces cerevisiae* (strain D4) was considered inadequate for assessment due to the fact that no positive controls were included, the concentrations of HCFC-123 test doses were not stated and the number of replicates was not stated.[79]

Cytogenetic tests

Two cytogenetic tests have been performed using cultured human lymphocytes in which HCFC-123 was tested both in the liquid and gaseous phase.[82,83] Both studies were carried out according to OECD Guideline No. 473. The sensitivities of both studies were confirmed by similar clastogenic responses to the positive control substances. The results of these tests are summarised in Table 12.

HCFC-123 elicited a dose-related increase in chromosomal aberrations in human lymphocytes *in vitro* in both studies. Metabolic activation was required to induce a clastogenic response after three hours HCFC-123 exposure (vapour phase assay). However, after 24 hours a significant increase in aberrations was seen in both liquid and vapour assays without a metabolising system.

Table 12: Summary of in vitro cytogenetic studies

Test system	Exposure protocol	Dose	Mean mitotic index	Number of cells with aberrations (excluding gaps)
Human (male) lymphocytes (Dance[82])				
300 lymphocytes scored per dose	3 hr (without S9)	0% v/v	25.2	1
		0.005% v/v (73 μg/ml)	19.6	2
		1.1 % v/v (146 μg/ml)	21.7	3
		1.2 % v/v (292 μg/ml)	21.7	3
		CBC (2ug/ml)	14	91
HCFC-123 (liquid phase)	3 hr (with S9)	0% v/v	23.8	1
		1.1 % v/v (146 μg/ml)	21.8	2
		1.2 % v/v (292 μg/ml)	14.7	6
		1.4 % v/v (584 μg/ml)	6.6	5
		CP (6 ug/ml)	8.4	106
	24 hr (without S9)	0% v/v	30.7	2
		0.0025% v/v (36 μg/ml)	27.4	3
		1.5 % v/v (73 μg/ml)	21.5	10*
		0.02% v/v (292 μg/ml)	9.7	31†
		CBC (2μg/ml)	22.9	70
Human (male) lymphocytes (Edwards[83])				
300 lymphocytes scored per dose	3 hr (without S9)	0% v/v	24.9	1
		7.5% v/v (75,000 ppm)	23.9	3
		15% v/v (150,000 ppm)	17.9	0‡
		30% v/v (300,000 ppm)	10.3	5‡
		CBC (2μg/ml)	18.5	60
HCFC-123 (vapour phase)	3 hr (with S9)	0% v/v	22.2	4
		7.5% v/v (75,000 ppm)	24.1	3
		15% v/v (150,000 ppm)	21.0	4
		30% v/v (300,000 ppm)	9.5	23‡§
		CP (6 μg/ml)	15.2	107
	24 hr (without S9)	0% v/v	16.6	1
		2.5% v/v (25,000 ppm)	19.1	9†
		5% v/v (50,000 ppm)	13.2	18§
		10% v/v (100,000 ppm)	5.9	24§
		CBC (2μg/ml)	13.5	118

* 0.05>p>0.01
† 0.01>p>0.001
‡ Increase in number of polyploid cells.
§ p<0.001

CP Cyclophosphamide (positive control).
CBC Chlorambucil (positive control).
S9 Exogenous metabolic activation system.

Cell transformation test (Styles assay)

A negative response was reported for HCFC-123 when tested in baby hamster kidney fibroblasts (BHK21 cells) with and without metabolic activation in a Styles assay. No supporting data were provided except that transformation was determined by the observation of sustained cell growth (in semisolid agar) and that the criterion for a positive result was a transformation frequency in excess of five times the spontaneous rate. The sensitivity of the study was confirmed by appropriate positive control substances.[80]

10.6.2 In vivo bioassays

Cytogenetic test

HCFC-123 has also been tested *in vivo* for its ability to induce chromosomal aberrations in peripheral lymphocytes in rats.[84] In this study, rats (10 males per dose level) were exposed by inhalation to HCFC-123, in the dose range of 300 to 5000 ppm, for six hours per day, five days per week for 14 weeks. There was no evidence of HCFC-123 induced clastogenicity in the

peripheral lymphocytes at 5000 ppm. Several deficiencies in experimental design (such as no analysis of lymphocytes at lower exposure levels and a lack of cell toxicity at the upper dose tested) were noted in this study. An increase in the number of cells with aberrations was observed for the positive control cyclophosphamide (20 mg/kg given by intraperitoneal injection).

Micronucleus test (bone marrow)

Groups of NMRI mice (five animals per sex per group) were exposed, nose-only, to 2000 ppm, 6000 ppm and 18,000 ppm HCFC-123 for six hours.[85] The incidence of micronucleated polychromatic or normochromatic erythrocytes in each treatment group was within the normal range of the negative control. Similarly the ratio of polychromatic to normochromatic erythrocytes in both male and female animals did not differ from control values. The sensitivity of the test was confirmed by a statistically significant increase in the number of micronucleated polychromatic erythrocytes in the positive control group.

Unscheduled DNA synthesis

HCFC-123 was tested for DNA damaging effects in rat hepatocytes, in two independent experiments, following 6 hours inhalation exposure to 12,500 ppm and 20,000 ppm.[86] In both experiments, five male rats per group were used and 60 hepatocytes were scored per animal. Based on the evaluation of both the mean net nuclear grain count and percentage of cells in repair, HCFC-123 did not cause unscheduled DNA synthesis (UDS) in rat liver *in vivo*. The sensitivity of the test system was validated by an induction of UDS in the positive control group receiving N-nitrosodimethylamine and non-significant UDS in the negative control group. Results were consistent for both experiments.

10.7 Summary of toxicological data

Table 13 summarises results of all assessed studies, including critical effects together with NOAELs or LOAELs (where determined).

Table 13: Summary of toxicological data

Type of study	Route of administration	Animal/ test system	Result(s) (critical effect/toxicological endpoint)	Section
Acute toxicity				
Lethality	Oral	Rat (m)	ALD = 9000 mg/kg b.w.	10.1.1
	Dermal	Rat Rabbit	LD_{50} > 2000 mg/kg b.w.	10.1.2
	Inhalation	Rat (m) Mouse Hamster (m)	LC_{50} (4hr) = 32,000 - 53,000 ppm LC_{50} (30 min) = 74,000 ppm LC_{50} (4hr) = 28,400 ppm	10.1.3 10.1.3 10.1.3
Liver effects	Inhalation	Guinea pig	Hepatotoxic at lowest test dose (1000 ppm)	10.1.3
Behaviour	Inhalation	Rat (m)	EC_{50} (1hr) = 4000 ppm No effects at 2,500 ppm	10.1.3
Cardiac sensitisation	Inhalation	Dog (m)	EC_{50} (5 min) = 19,000 ppm No effects at 10,300 ppm	10.1.3
Irritation				
	Skin	Rabbit Guinea pig (m)	Non irritant Non irritant	10.2.1
	Eye	Rabbit	Slight irritant	10.2.2
Sensitisation				
	Skin	Guinea pig	Negative	10.3
Repeated dose toxicity				
Sub-acute	Inhalation	Rat	CNS depression (NOAEL = 1000 ppm) Hepatic effects (LOAEL = 1000 ppm) Testicular effects (NOAEL = 10,000 ppm)	10.4.1
		Guinea pig (m)	CNS depression Hepatic toxicity	10.4.1
Sub-chronic	Inhalation	Rat	CNS depression (LOAEL = 1000 ppm) Hepatic effects (LOAEL = 300 ppm; NOAEL[1]= 100 ppm)	10.4.2 10.5.2
Sub-chronic	Inhalation	Dog	CNS depression (NOAEL = 1000 ppm) Hepatic effects (NOAEL = 1000 ppm)	10.4.2
Neurotoxicity	Inhalation	Rat	No effects observed	10.4.2
Chronic	Inhalation	Rat	CNS depression (NOAEL = 1000 ppm) Benign tumours (LOAEL = 300 ppm) Non-neoplastic effects[2] (LOAEL = 300 ppm)	10.4.3
Reproductive effects				
Fertility	Inhalation	Rat	Effects only at maternally toxic doses	10.5
Development	Inhalation	Rat Rabbit	No adverse effects[3] Effects only at maternally toxic doses	10.5
Genotoxicity (in vitro)				
Mutation		S. typhimurium S. cerevisiae	Negative Inadequate study	10.6.1 10.6.1
Chromosomal aberration		Human lymphocytes	Positive	10.6.1
Cell transformation		BHK21 cells	Negative	10.6.1
Genotoxicity (in vivo)				
Chromosomal aberration		Rat lymphocytes	Negative	10.6.2
Micronucleus induction		Mice	Negative	10.6.2
UDS		Rat	Negative	10.6.2

1. Determined (at 28 weeks) in two-generation reproductive toxicity study.
2. Histopathological effects in liver, pancreas and testes.
3. Decreased pup weight (at 30 ppm) was not seen at birth and may be a lactational effect.

m Males only (male and female animals used unless stated).
ALD Approximate lethal dose.
LOAEL Lowest observed adverse effect level.
NOAEL No observed adverse effect level.
UDS Unscheduled DNA synthesis.

11. Human health effects

No human health effects data for HCFC-123 were available apart from a single report of effects following acute exposure.[30] However, health effects from exposure to structural analogues (including other HCFCs, CFCs and halons) are well documented.

As HCFCs show similar toxicological profiles to CFCs and halons in animals,[6,87] similarities might also be expected in humans. Thus, a consideration of effects produced by CFCs and halons in humans is considered relevant to the assessment of potential human health hazards from exposure to HCFC-123.

11.1 Acute effects

In humans, acute health effects from exposure to CFCs and halons include CNS effects, cardiopulmonary effects, hepatic effects and asphyxiation.

Effects such as dizziness, headaches and nausea were reported in around 40 workers exposed to HCFC-123 following the rupture of an industrial chiller.[30] Leakage of HCFC-22 refrigerant at a skating rink resulted in the one death and 34 cases of acute intoxication that included nausea, CNS depression, cough, etc.[88]

Bronchospasm, bradycardia and T-wave inversion have been reported in human studies with bronchodilator and commercial aerosols containing CFC-11 and CFC-12. Exposure of chiller maintenance technicians to 10,000 ppm (50 g/m^3) CFC-12 for two hours led to a reduction in ventilatory lung capacity and a significant decrease in heart rate.[87] Similar effects were seen in volunteers exposed to 27,000 ppm CFC-12 for up to one minute.[89] Volunteers exposed to 4500 ppm CFC-113 for up to two hours suffered significant impairment of manual dexterity and concentration .[99] NIOSH reported the deaths of 12 workers due to asphyxiation or cardiac arrhythmia resulting from excessive exposure* to CFC-113 used as a solvent.[87] Another occupational death was reported[87] from exposure to CFC-113 vapour at a concentration of around 1000 g/m^3 (130,000 ppm). Fatalities have been reported from the use and abuse of aerosol products containing CFC propellants.[89,90]

Effects reported from exposure to bromofluorocarbon (halon) fire extinguishants include; paraesthesia, tinnitus, anxiety, slurred speech, electroencephalographic changes and eye and respiratory irritation.[89]. Convulsive seizures and respiratory arrest have been documented in firefighters exposed to chlorobromomethane.[99] Human volunteers exposed to Halon 1301 showed electrocardiographic irregularities at exposures 70,000–150,000 ppm with paraesthesia and other CNS effects above 100,000 ppm.[99] Fatalities have been reported for Halon 1211, [91] including a death from exposure to an estimated concentration of around 120,000 ppm Halon 1211 resulting from discharge (around three kilograms) of extinguishant into a confined space (7000 litre chamber).

Halothane (HCFC-123b1) toxicity has been well documented in humans. Exposure levels of 10,000–40,000 ppm (one to four per cent) during anaesthesia have been associated with cardiac effects and toxic hepatitis (known as 'halothane hepatitis'), both of which have resulted in fatalities, although extremely rare with halothane hepatitis.[92,93] It is currently thought that halothane hepatitis may be an immune-mediated disease and the fact that halothane and HCFC-123 exhibit similar patterns of trifluoroacetylated liver proteins,[94] and serum antibodies[95] (in animal studies) has led to concern over HCFC-123 being capable of eliciting a similar hepatic response in humans.[95,96] It has also been suggested that a potential may exist

* Data not provided.

for cross-sensitisation between HCFC-123 and structurally analogous anaesthetic agents.[95] Hepatic toxicity has been well documented in humans from exposure to other halogenated alkanes, including methyl chloride, 1,1,1-trichloroethane, 1,1,2,2-tetrachloroethane and mono- and di-bromoethane.[99]

11.2 Dermal effects

Some fluorocarbon liquids remove oils from the dermis, causing irritation and development of dry, sensitive skin, particularly after repeated contact.[89]

Limited evidence of skin sensitisation exists for both CFC-11 and CFC-12 from use in deodorant sprays.[87]

11.3 Chronic effects

No electrocardiogram or pulmonary function effects were seen in human volunteers exposed to 250–1000 ppm CFC-11 or CFC-12 (venous blood levels of up to 4.7 mg/L) for eight hours per day for up to four weeks.[87]

Approximately 200 workers (male and female), reportedly exposed to HCFC-22, CFC-113 and HCFC-142b—in addition to other identified CFCs—were studied by Filicheva.[97] Neurological disorders, including neurovegetative system disturbances and polyneuritis of the upper extremities, were reported in approximately 70 per cent of workers. Reduced erythrocyte haemoglobin levels and sedimentation rate in addition to moderate leucocytosis were also reported. Exposure profiles were not reported in this study. In another study, 50 workers exposed to 45–4,700 ppm CFC-113 for around 2.5 years showed no signs or symptoms of adverse effects.[89]

Hospital personnel exposed to HCFC-22 during preparation of frozen tissue sections exhibited a higher (3.5-fold excess) incidence of coronary heart disease,[89] although an epidemiological study in workers exposed to HCFC-22 and other CFCs showed no excess mortality from cardiovascular or malignant disease .[99]

Evidence for 'toxic hepatitis' (see section 11.1) caused by low level repeated exposure to halothane is inadequate and hence would similarly not be expected from repeated exposure to HCFC-123.

Although epidemiological studies have reported associations between exposure to anaesthetic vapours (including halothane) and the occurrence of cancers, spontaneous abortions and congenital abnormalities in female hospital personnel, the evidence is considered inadequate.[89,98]

11.4 Toxic combustion products

Pyrolysis of CFCs and HCFCs (including HCFC-123) can lead to the formation of a number of toxic products including free halogens, HCl and HF and phosgene (carbonyl chloride). Cases of phosgene poisoning have been reported following thermal decomposition of CFC-11 propellant.[89] Signs and symptoms of Cl_2, F_2, HCl, HF and phosgene poisoning include eye and respiratory irritation, vomiting, dyspnoea and cyanosis. Acute exposure to 50 ppm phosgene; 50–250 ppm F_2, HCl or HF and 1000 ppm Cl_2 may be fatal.[99] Isopropenyl-1-methylcyclohexene is added to extinguishant blends containing HCFC-123 to reduce the quantity of certain pyrolysis products. With respect to HCFC-blend fire extinguishants, toxic products may also arise from the reaction of thermal decomposition products with the material on fire.

12. Human health hazard assessment and classification

This section integrates data on kinetics and metabolism, animal toxicity and human effects in order to characterise potential human health hazards from exposure to HCFC-123 and classify these hazards. The classification criteria used are the National Commission's *Approved Criteria for Classifying Hazardous Substances*[100] (the Approved Criteria), except for reproductive toxicity, where European Union criteria[101] are used.

Where adequate human data are not available, information from experimental studies (animal and in vitro bioassays) form the basis for assessment. In extrapolating results from experimental studies to humans, consideration has been given to relevant issues such as quality of data, weight of evidence, metabolic and mechanistic profiles and relevance of exposure levels.

12.1 Toxicokinetics and metabolism

In vivo studies indicate that HCFC-123 is metabolised similarly in rats and guinea pigs in terms of uptake (absorption via inhalation), tissue distribution and extent and rate of elimination of metabolites in urine.

Partition coefficients for HCFC-123 in various tissues indicate that absorption is expected to occur readily. HCFC-123 is taken up mainly by the liver, kidney and testes in rats and guinea pigs.

In vitro studies indicate that HCFC-123 is metabolised by the same cytochrome P-450 isoenzyme (CYP 2E1) in both animal and human microsomal preparations. In both systems the main metabolites are TFA and chlorodifluoroacetic acid.

Biotransformation studies indicate that the major HCFC-123 metabolite *in vivo* is TFA. Approximately 25% of the administered dose is recovered in rats and guinea pig urine. Data suggest that Cytochrome P-450 mediated biotransformation of HCFC-123 to TFA is suppressed above 1000 ppm in rats.

Evidence indicates that reactive oxidative metabolites (possibly trifluoroacetyl chloride) are associated with acute hepatotoxicity. Liver protein adducts (increased by phenobarbitone pretreatment) are formed with HCFC-123 in rats and guinea pigs. Although distribution to other tissues occurs, no evidence of covalent binding was seen in testes or pancreas (both target organs for toxicity from repeated dose studies with HCFC-123).

The available evidence indicates that HCFC-123 is metabolised similarly in rats and guinea pigs. Furthermore *in vitro* evidence indicates that metabolism is likely to be similar in humans. The increased rate (> 10 fold) of biotransformation of HCFC-123 to TFA seen in human liver cell preparations (compared to rat liver cell preparations) indicates that quantitative differences in oxidative metabolism and elimination may exist *in vivo* between humans and rodents with resultant changes in toxicity profiles.

12.1.1 Comparative metabolism with halothane

A number of similarities exist between HCFC-123 and halothane metabolism. Halothane toxicity and metabolism has been extensively investigated due to its use as an anaesthetic agent in humans. Metabolic comparisons between the two substances are therefore valid with respect to providing an insight into potential mechanisms of toxicity for HCFC-123 and relevance to humans. Of the information provided for assessment HCFC-123 and halothane elicited similar acute hepatotoxic profiles in guinea pigs and similar propensities for peroxisome proliferation

in rats. Only HCFC-123 has been shown to induce tumours in animal bioassays. Halothane did not induce tumors in inhalation studies in rats and mice.[98] Mice were exposed *in utero* and then three times weekly for 78 weeks at the maximum tolerated dose, or 24 times at several dose levels. The rats were exposed to a low level of halothane alone or in combination with nitrous oxide.

HCFC-123 and halothane exhibit similar biotransformation profiles, undergoing both oxidative and reductive metabolism. Both substances undergo oxidative metabolism to trifluoroacetyl chloride (the putative metabolite associated with protein binding) and TFA (the putative metabolite associated with peroxisome proliferation) in addition to reductive metabolism (minor pathway) to HCFC-133a and 2-chloro-1,1-difluoroethylene (CDE). There is evidence to suggest that with HCFC-123 this metabolic pathway only occurs under conditions of reduced oxygen. Consequently, under normal conditions of use this pathway is likely to be more relevant to halothane than to HCFC-123 metabolism.

At high levels HCFC-123 is metabolised[44,45] (in rats) to TFA to a greater extent (approximately 50%) than halothane, despite the fact that HCFC-123 is less lipophilic than halothane[102] and hence, is not expected to be so readily absorbed. These results were confirmed *in vitro*.[42] Both halothane and HCFC-123 are reported to suppress their own metabolism to TFA at around 1000 ppm.[44]

Protein binding profiles are very similar for HCFC-123 and halothane with a similar degree of trifluoroacetylated liver protein adducts at equivalent exposure levels.[45,60] In addition, liver samples from HCFC-123 and halothane exposed guinea pigs exhibited similar cross reactivity to anti-trifluoroacetylated antibodies.[60]

Despite the lower lipophilicity of HCFC-123 compared to halothane, available studies indicate that the amount of hepatic protein binding and TFA formation are similar for both compounds. In summary, the similarities between HCFC-123 and halothane in chemical structure, metabolism (including protein binding) and acute toxicity[60] in animal studies, indicate a potential for similarities in toxicity profiles in humans.

12.2 Toxicity of HCFC-123 impurities

Toxic impurities are found in commercial grade HCFC-123.

1,2-dichloro-1,1,2-trifluoroethane (HCFC-123a) has been identified as the major impurity in HCFC-123 and is usually present in concentrations of less than 5% v/v (up to 13% v/v has been reported—see section 4). Studies in rats indicate similar toxicity profiles for HCFC-123a and HCFC-123 with respect to liver damage and hepatic peroxisome proliferation.[68] Although in this study HCFC-123a, but not HCFC-123, elicited minor pancreatic effects (acinar cell inflammation and degeneration), this was not considered significant, particularly as similar pancreatic effects were associated with TFA, the major metabolite of HCFC-123. Therefore, it is unlikely that HCFC-123a *per se* is primarily responsible for any of the critical effects seen from repeated exposure to HCFC-123, but probably contributes (additive effect) to the overall toxicity profile of HCFC-123.

In addition to HCFC-123a, other halogenated hydrocarbon impurities found in HCFC-123 (listed in Table 1) amount to a total of around 0.5% v/v. Saturated hydrocarbons comprise most of these impurities, with 1,1,2-trichlorotrifluoroethane (CFC-113) being the most ubiquitous, present at levels up to 0.2%. The maximum concentration of unsaturated hydrocarbon impurities in HCFC-123 is estimated to be around 0.02%. At such low concentrations it is considered unlikely that either saturated or unsaturated hydrocarbon impurities contribute to the toxicity profile of HCFC-123.

12.3 Health effects evaluation

12.3.1 Acute effects

No data exist on the oral and dermal toxicity of HCFC-123 in humans. Studies in animals show that HCFC-123 has low acute oral toxicity (ALD of approximately 9000 mg/kg in rats) and low dermal toxicity (LD_{50} > 2000 mg/kg in rats and rabbits). In rats and hamsters, the acute inhalation LC_{50} (four hour) for HCFC-123 is low, 28,000–53,000 ppm (175–330 mg/L).

In a single acute inhalation study carried out in guinea pigs, hepatotoxicity was seen at the lowest test level of 1000 ppm (6.25 mg/L) HCFC-123. Similar lesions were described in the same study with the HCFC-123 analogue, halothane. Such lesions were reported as reversible (by one week post-exposure) in other studies on halothane exposed guinea pigs.[103] Halothane is associated with both fatal (rare) and non-fatal hepatitis in humans. Similarities in metabolism, immunotoxicology and hepatic lesions between halothane and HCFC-123 in rats and guinea pigs support the possibility that acute exposure to high levels of HCFC-123 may elicit a similar toxicological profile to halothane in humans.

Acute reversible CNS effects have been reported in humans and animals following inhalation of HCFC-123. Exposure levels were not categorised in cases of human poisoning. No CNS effects were seen at 2500 ppm (15.6 mg/L) HCFC-123 in a behavioural study in rats.

CFCs and HCFCs are known to sensitise the heart to adrenalin-induced arrhythmias.[90] HCFC-123 caused cardiac sensitisation in dogs exposed to levels around 20,000 ppm (125 mg/L), whereas no effects were seen at 10,000 ppm (62.5 mg/L). Although no data were available on cardiac sensitisation effects for HCFC-123 in humans, such effects have been documented following exposure to other CFCs, including CFC-12, where sensitisation was reported at 10,000 ppm.[87]

In humans, liver toxicity, cardiac sensitisation and CNS depression are likely to be the critical effects following acute exposure to HCFC-123, although asphyxiation may also occur at very high levels.

Classification status

HCFC-123 does not meet the Approved Criteria[100] for acute lethal effects by oral, dermal or inhalation exposure. Inadequate data were available to classify HCFC-123 for Non-Lethal Irreversible Effects (hepatic) After Single Exposure (by inhalation) as the lowest dose tested was above the dose range for Harmful hazard classification and the reversibility of the lesions was not reported.

12.3.2 Irritant effects

Dermatological problems have been reported in humans exposed to other fluorocarbons.[89] However, no reports were available on the skin or eye irritation potential of HCFC-123 in humans.

Tests in rabbits and guinea pigs indicate that HCFC-123 is not a skin irritant. [12,64] HCFC-123 was a slight eye irritant in rabbits. [63]

Classification status

HCFC-123 does not meet the Approved Criteria[100] for Irritant Effects (skin and eyes).

12.3.3 Sensitising effects

No data exist on the skin or respiratory sensitisation potential of HCFC-123 in humans, although there is limited evidence of skin sensitisation for CFC-11 and CFC-12 used in deodorant sprays.[87] A study on skin sensitisation of HCFC-123, carried out in guinea pigs,[64] was considered negative under the conditions of the study. It is possible that the doses used may not have been sufficiently high to elicit a sensitisation response. However, sensitisation has

not been reported in other structural analogues of HCFC-123.[6,87] No studies were available on the sensitisation potential of HCFC-123 in animals by inhalation.

Classification status

HCFC-123 does not meet the Approved Criteria[100] for Sensitising Effects (skin).

12.3.4 Effects (other than carcinogenic and reproductive) from repeated exposure

There are no reports of adverse effects in humans following repeated or prolonged exposure to HCFC-123. In humans, repeated exposure to other CFCs and HCFCs have been associated with haematological effects, neurological disorders, liver damage, reproductive effects and coronary heart disease.

Neurological effects

Although behavioural effects and CNS effects have been seen in animals repeatedly exposed to HCFC-123, histological examination in rats of brain, spinal cord and nerve fibres indicates no neurotoxicity at the highest exposure (inhalation) level of 5000 ppm.[69]

A NOAEL for CNS (anaesthetic) effects in rats and dogs was determined at 1000 ppm (6.25 mg/L) from chronic and sub-chronic studies.

Liver effects

Human liver toxicity has been well documented for structural analogues of HCFC-123,[99] including halothane,[93] which has a similar metabolic, immunological and hepatotoxic profile to HCFC-123 in animal studies.

Adverse hepatic effects were seen in rats, guinea-pigs and dogs following repeated exposure (inhalation) to HCFC-123. The types of lesions observed varied between species and with duration of study. Generally, the lesions observed were hepatocyte enlargement and vacuolation (at 300 ppm) with necrosis and fatty change (at and above 1000 ppm). Such lesions were reported as reversible (30 days post-exposure) in a single 90-day study in rats exposed to 500–5000 ppm HCFC-123 and were not significantly increased at 300 ppm after 12 months in the two-year inhalation study. The NOAEL reported for hepatic effects in rats (28 weeks exposure in a two-generation reproductive toxicity study) was 100 ppm (0.63 mg/L).

Testicular effects

Adverse testicular effects were seen in sub-acute inhalation studies in rats (NOAEL = 10,000 ppm) but not in guinea pigs. The LOAEL determined from chronic exposure (inhalation) in rats is 300 ppm (1.9 mg/L).

Pancreatic effects

A statistically significant decrease in insulin levels was seen in a sub-acute study in rats exposed to approximately 18,000 ppm HCFC-123. This finding was considered to be a physiological response to decreased glucose levels rather than an indicator of diminished pancreatic function,[68] a finding supported by data from a 90-day study indicating a non statistical/biological change in rat insulin levels.[74] No pancreatic effects were seen in sub-acute inhalation studies in rats or guinea pigs, although pathological lesions were seen in rats exposed (oral) to HCFC-123a, the major impurity in HCFC-123 (see section 12.2). The NOAEL determined from chronic exposure (inhalation) in rats is 300 ppm (1.9 mg/L).

Classification status. HCFC-123 does not meet the Approved Criteria[100] for Severe Effects After Prolonged Exposure (by inhalation).

12.3.5 Reproductive effects

No data exist on the effects of HCFC-123 on male or female reproductive functions in humans.

Effects on fertility

In rats, exposure (inhalation) to HCFC-123 did not influence pre-mating interval, copulation index, pregnancy rate or pup sex ratio of the F_0 and F_1 generations, but was associated with decreased implantation sites among F_1 females at 1000 ppm, a level at which overt maternotoxicity was observed.[77]

Adverse effects on reproductive tissues, such as testicular Leydig (interstitial) cells have been seen in repeated dose studies at and above 300 ppm HCFC-123[50,65,68] although no histopathological effects on reproductive tissues were seen at 1000 ppm HCFC-123 after 39 weeks in a two-generation reprotoxicity study.[77]

Perturbations in serum sex hormone levels have also been reported in male rats and guinea pigs.[68] Effects on progesterone (F_1 generation only) and luteinising hormone (F_0 generation only) levels were seen in male rats at 100 ppm and 300 ppm respectively, with a NOAEL of 30 ppm.[77] As these effects were not consistent between generations, biological significance was considered questionable.

Classification status. HCFC-123 does not meet the EU Criteria for Effects On Male Or Female Fertility (by inhalation).

Effects on development

In rabbits, developmental effects (increased resorptions and foetal defects) were seen only at doses which caused maternotoxicity, that is, greater than 10,000 ppm.[75]

In rats, HCFC-123 caused reduced pup growth in the offspring of the F_1 generation at and above 30 ppm, and the F_0 generation, at and above 100 ppm. Sexual maturation was also slightly delayed in F_1 males (F_0 offspring) at and above 300 ppm. However, the group mean body weight at attainment of sexual maturity was similar to controls, suggesting differences in pup growth rates may account for this delay.[77]

Reduced pup growth was not considered to be a developmental effect as significant reduction in pup weight was not seen until seven to 14 days after birth. This effect may however be caused by HCFC-123 in breast milk (a lactational effect) as:

- the onset of reduced pup growth occurred during the period when exposure to HCFC-123 was restricted to parent dams;
- indicators of the integrity (quantity and quality) of milk, for example, CCK and milk fat, were normal during the suckling period; and
- maternal food intake during lactation was only decreased at and above 300 ppm HCFC-123. Information on the amount of HCFC-123 in breast milk or the pup milk intake during lactation was not available.

Classification status. HCFC-123 does not meet the European Union's Criteria for Developmental Toxicity. Inadequate data were available to classify HCFC-123 according to the European Union's Criteria for Effects During Lactation.

12.3.6 Genotoxicity

The genotoxic potential of HCFC-123 has been studied in a number of *in vitro* and *in vivo* bioassays. Most of these studies were designed to evaluate the genotoxic effects from exposure to HCFC-123 vapour.

HCFC-123 showed no evidence of mutagenicity with *in vitro* bacteria or yeast tests and *in vivo* mouse micronucleus test, and showed no evidence of inducing primary DNA damage by unscheduled DNA synthesis or cell transformation.

Evidence for clastogenicity, from *in vitro* and *in vivo* lymphocyte studies was conflicting.

Classification status

HCFC-123 does not meet the Approved Criteria[100] for Mutagenic Effects.

12.3.7 Carcinogenicity

No data exist for carcinogenicity in humans following exposure to HCFC-123. Although other structural analogues of HCFC-123 have been shown to cause tumours in animal studies, inadequate evidence exists for carcinogenicity in humans from epidemiological studies.[98]

Chronic exposure to HCFC-123 elicited benign tumours (liver, pancreas and testes) in rats at and above 300 ppm (1.9 mg/L).

As the available data indicate HCFC-123 is non-genotoxic, data relevant to characterising the mechanism for tumourigenicity in animals was reviewed in order to assess its relevance to humans.

Hepatic tumours

Two types of hepatic tumours were observed in the two-year inhalation study in rats—hepatocellular adenomas and cholangiofibromas.

Hepatocellular adenomas. HCFC-123, its major metabolite TFA and main impurity HCFC-123a have all been demonstrated to induce hepatic peroxisome proliferation.[68] As such, this mechanism has been proposed as the primary mechanism for hepatocellular tumour induction seen in rats exposed to HCFC-123.[68] Evidence indicates that this mechanism is species-specific: primates (including humans) and guinea pigs are not susceptible (in terms of peroxisome induction) to peroxisome proliferating substances.[104,105] As such, it has been proposed that peroxisome proliferators are unlikely to present a hepatocarcinogenic hazard to humans.[105]

Despite dose-related increases seen in hepatic peroxisome proliferation in sub-acute, sub-chronic and chronic studies, the existence of anomalies serve to question whether this mechanism *per se* fully accounts for the observed liver effects elicited by HCFC-123.

Firstly, in the two-year study a significant increase in liver adenomas was seen in female rats exposed to 300 ppm HCFC-123 without a concomitant increase in peroxisome proliferation at this exposure level.[50] However, a significant increase in peroxisome proliferation was seen at this concentration in female rats in a 90 day study by the same laboratory and as such this anomaly was considered by the study author to represent a biological variation in ß-oxidation potential. In addition, despite a dose related (significant) increase in peroxisome proliferation in male rats (in the two-year study) at 300 ppm and 1000 ppm, no increase was seen in liver adenomas at these exposure levels.

Secondly, HCFC-123 induced hepatic cell proliferation (CPI*), and decreased serum cholesterol and triglycerides in guinea pigs, despite the lack of peroxisome proliferation[68] potential seen in this species. Of these effects, only triglyceride perturbations were statistically significant. However, increases in CPI were comparable to increases in rats. In addition, hepatocellular lesions (fatty change and necrosis) were also seen in HCFC-123 exposed guinea pigs, although their relevance to potential neoplastic lesions is purely speculative.

Finally, HCFC-123 has a similar metabolic profile to halothane with respect to TFA formation, ß-oxidation potential and effects on serum lipids.[106] However, halothane did not induce tumours[98] in either rats or mice. This finding should not be regarded as strong evidence of a non-peroxisomal mechanism for HCFC-123 as some peroxisome proliferators are more potent carcinogens than others, despite inducing similar levels of peroxisome proliferation, and only limited data on carcinogenicity for halothane were available.[105]

Hepatocholangiofibromas. Benign cholangiofibromas (seen in female rats exposed to 5000 ppm) have generally not been reported for other peroxisome proliferating substances (exceptions being thioacetamide and ethionine[107]) and hence peroxisome proliferation does not appear to be an obvious mechanism for this tumour type.

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* CPI is a measure of mitogenic effect, that is, an increase in hepatic replicative DNA synthesis.

Hepatic cholangiocarcinomas (in addition to hepatocellular adenomas) have been reported in humans taking androgenic steroids, including oxymetholone, methyltestosterone and testosterone.[98] Perturbations in serum sex hormone levels (including testosterone) have been demonstrated in repeated dose animal studies with HCFC-123[68,77] Further evidence of a hormone mediated mechanism with respect to cholangiofibroma induction in rats is the fact that this tumour type was seen only in female animals.[50]

The induction of cholangiofibromas with HCFC-123 is directly related to the occurrence of cholangiofibrosis (also seen in females only at 5000 ppm) and biliary hyperplasia (significantly increased in females only at 5000 ppm HCFC-123). Indeed, evidence exists that cholangiofibrosis may give rise to cholangiofibromas and eventually to cholangiocarcinomas with some carcinogens.[108,109] It has been observed that cholangiofibromas and especially cholangiocarcinomas appear only at high doses of hepatocarcinogen and as such it has been speculated that these tumours are a response to cellular injury.[109]

The significance of the cholangiofibromas seen in rats has been questioned on statistical grounds. Although life table analysis of these tumours showed a non-significant result ($p = 0.063$), this value is close to the conventional cut off ($p = 0.05$) and as such biological significance can not be discounted. Using the Fischer's exact pairwise test for this tumour p (two-tailed) equals 0.0002, which is highly significant and consistent with a threshold effect rather than a linear dose-response effect.

Pancreatic tumours

HCFC-123 exposure was associated with a dose-related increase in benign acinar cell adenomas in male rats. It is reported that other hepatic peroxisome proliferators also induce pancreatic acinar cell adenomas.[110] A concomitant increase (dose-related) in acinar cell focal hyperplasia seen in male rats indicate a tenuous association of this tumour type with peroxisome proliferation as dose response correlations for focal hyperplasia and peroxisomal response in rodents are reportedly poor.[111] Indeed, a slight increase in pancreatic cell proliferation rate (CPI) was seen in rats exposed to HCFC-123 without an increase in pancreatic peroxisome proliferation.[68] In addition, the apparent lack of accumulation or covalent binding of HCFC-123 and metabolites in pancreatic tissue[43] indicates that tumourigenicity is unlikely to be associated with direct cellular interaction. Therefore, other mechanisms for tumour induction would appear to be involved.

Steroid hormones have been implicated as non-genotoxic factors which may play a role in exocrine pancreatic cancer.[112] Compound-related perturbations in levels of testosterone, oestradiol, luteinising hormone and progesterone have been reported in rats exposed to HCFC-123.[68,77] Of particular note—because it is known to inhibit acinar cell function—was an increase in the gastrointestinal hormone CCK seen in rats at around 18,000 ppm HCFC-123. CCK has been shown to stimulate pancreatic growth and acinar cell carcinogenesis in animals and has also been implicated in the aetiology of human pancreatic cancer.[112] However, serum CCK, testosterone, progesterone and oestradiol, were not increased after 22 weeks in rats exposed to 1000 ppm HCFC-123,[77] despite a significant increase in male acinar cell adenomas at this exposure level in the two-year bioassay.[50] In further support of a hormone mediated mechanism for pancreatic adenoma induction is the fact that male rats exhibited a much higher incidence of this tumour type than females, with a seven-fold differential at the highest exposure level.

Testicular tumours

Leydig (interstitial) cell tumours in rats have been reported for a large number of substances including hepatic peroxisome proliferators.[113] The limited evidence available indicates that hepatic peroxisome proliferating substances do not significantly effect Leydig cell peroxisome proliferation (despite known levels of peroxisomes in Leydig cells) or testicular cell

proliferation rate.[68,114] In addition, other factors such as the apparent lack of covalent binding of HCFC-123 and metabolites in testes[43] and the lack of a dose-response relationship (with HCFC-123 elicited Leydig cell tumours) indicates that direct cellular damage or peroxisome proliferation are unlikely to be primary mechanisms in tumour induction.

In male rats, HCFC-123 (exposure approximately 18,000 ppm) has been shown to cause perturbations in serum oestradiol, testosterone,[68] luteinising hormone (LH) and progesterone[77] in addition to necrosis of testicular germ cell epithelium and tubular atrophy.[68] Such effects indicate involvement of the pituitary-adrenal axis in testicular toxicity. Chemically induced elevated oestradiol and LH levels,[115,116] and oestrogenic treatments[117] have been associated with increased Leydig cell tumour incidence in rats.

Recent evidence indicates that endocrine disturbances and testicular tumours (seen in animals) may be linked to hepatic peroxisome proliferation[114] In the study by Warheit,[68] testicular effects were seen in rats but not guinea pigs exposed to HCFC-123, indicating that testicular toxicity may be related to hepatic peroxisome proliferation. However, insufficient data was available to establish a link between peroxisome proliferation and endocrine disturbances for HCFC-123 as levels of testosterone were increased in rats and decreased in guinea pigs. In addition levels of LH and oestradiol were not established in guinea pigs.

Overall assessment of carcinogenic hazard

Although it is considered likely that the benign hepatocellular adenomas seen in rats exposed to HCFC-123 are related to increases in hepatic peroxisome proliferation (a mechanism believed not to present a hepatocarcinogenic hazard to humans), anomalies exist with respect to this proposed mechanism, mainly due to the lack of concordance of tumour incidence with liver ß-oxidation activity at certain exposure levels.

The mechanistic significance of benign hepatocholangiofibromas in female rats is unclear as this tumour type is not usually associated with peroxisome proliferation or hormone perturbation. However, its biological significance is confirmed by pre-neoplastic lesions (cholangiofibrosis) seen at 12 months in the same study. There is limited evidence from animal studies[109] to suggest that this tumour type might only be relevant at high dose/exposure levels and statistical interpretation of the data support a threshold for effect (1000–5000 ppm).

Despite limited epidemiological evidence to suggest that the proposed hormonal mechanism (CCK stimulation of pancreas growth) is of questionable relevance for human pancreatic cancers[118] and despite the fact that acinar cell cancers are not common in humans (by far the greatest number of human pancreatic tumours are of the ductal type[112]), it must be assumed that, until more is known about the mechanism for acinar cell tumour induction in animals and humans (particularly the role of CCK), the pancreatic adenomas found in rats may have some predictive value for human carcinogenicity.

Benign Leydig cell (interstitial cell) adenomas are common in aging rats and strongly associated with senile endocrine disturbances. In contrast to the rat, Leydig cell tumours in men are extremely rare, representing less than three per cent of all testicular neoplasms.[119] The rarity of this tumour type in humans as compared to its high spontaneous and chemically induced incidence in rodents, in addition to recent evidence indicating that endocrine disturbances and testicular tumours seen in animals may be linked to hepatic peroxisome proliferation,[114] serves to question the relevance of HCFC-123-induced Leydig cell adenomas in humans.

For all three tissues in which tumours occur, the cell type (except cholangiocellular tissue) has been a site of tumourigenic activity for other peroxisome proliferators, including hypolipidaemic drugs.[110] As this triad of tumour types have not been reported in epidemiological data on hypolipidaemic drugs (classic peroxisome proliferating substances), it has been hypothesised that hepatic, testicular and pancreatic tumours seen in rodents are not relevant to humans. However, such a conclusion should be viewed with caution as

epidemiological data on hypolipidaemic drugs only exist for clofibrate and fenofibrate, neither of which produce testicular or pancreatic tumours in animal studies. In addition, such studies are considered inconclusive due to the short period of exposure and follow-up.[120]

Overall, indications are that the primary mechanism(s) of tumourigenicity for HCFC-123 is non-genotoxic (epigenic) and that hormonal perturbations and peroxisome proliferation may be involved to some degree. In fact, these mechanisms may be interrelated as recent research indicates a link with hepatic peroxisome proliferation and hormonal perturbations. In further support of such an association is the recent discovery of an oestrogen-like hormone receptor in peroxisome mediated hepatic carcinogenicity.[105] Such a mechanism might account for the sex differences* and the lack of target organ specificity† with respect to HCFC-123 elicited tumours.

In summary, until further data become available regarding the mechanism of HCFC-123 induced tumours, particularly with respect to cholangiofibroma and pancreatic adenoma induction, it must be concluded that findings in rats may have some relevance for humans.

Classification status. HCFC-123 meets the Approved Criteria[100] for Carcinogenic Effects (Category 3[b]) and should be classified with risk phrase R40—Possible Risk Of Irreversible Effects. It should be noted that, according to the Approved Criteria,[100] this classification is provisional and further studies are necessary before a final decision can be made.

* Design elementDesign elementDesign elementDesign elementDesign elementDesign elementDesign elementDesign elementDesign elementDesign elementSex differences in peroxisome

proliferation with HCFC-123 do not account for this observation.

† Non-genotoxic carcinogens tend to be organ, species and sex specific.

13. Human health risk characterisation

In order to assess the health risks associated with the use of HCFC-123 it is necessary to integrate information on human exposure with human health hazards. This process, referred to as 'risk characterisation', provides the basis for evaluating occupational health and safety risk management strategies, including the setting of exposure standards.

13.1 Critical effects and exposures

13.1.1 Acute effects

Effects identified for acute exposure to HCFC-123 are eye irritation, liver toxicity, CNS depression, cardiac sensitisation and asphyxiation. The major route of exposure for these effects (except eye irritation) is inhalation.

Critical effects associated with acute HCFC-123 exposure are liver toxicity, CNS depression and cardiac sensitisation, all of which have been seen in humans from exposure to structural analogues of HCFC-123.

In a single acute inhalation study carried out in guinea pigs, liver necrosis was seen at the lowest test exposure of 1000 ppm HCFC-123. Lesions in this study were similar to those seen in guinea pigs but not rats (exposed to around 9000 ppm and 18,000 ppm HCFC-123 respectively) in a 28 day study. A similar hepatotoxicity profile to HCFC-123[68] was seen in rats and guinea pigs from acute exposure to halothane (see Section 12.1.1.1). Although there is evidence to suggest that HCFC-123 may exhibit a similar acute toxicological profile to halothane in humans, it should be noted that the incidence[60] of halothane elicited hepatitis in humans is around one in 10,000 for the severe necrotic form, and around 20% for the mild form at anaesthetic concentrations at and above 10,000 ppm. By analogy to halothane, humans would be expected to be significantly less sensitive to HCFC-123 elicited hepatic effects seen in animals.

The most sensitive study for CNS effects (carried out in rats) demonstrated a no effect level of 2500 ppm HCFC-123. There are no data to suggest that humans are likely to be more or less sensitive than rats with respect to CNS effects.

Although no data are available on HCFC-123 exposure levels associated with cardiac sensitisation in humans, a no effect level for cardiac sensitisation in dogs was determined at 10,000 ppm HCFC-123. Available evidence[121] indicates that cardiotoxic levels obtained from dog studies are likely to be conservative with respect to extrapolation to humans.

All critical effects reported from acute exposure to HCFC-123 are essentially reversible in nature, and evidence from studies in humans and animals with halothane suggests that humans would be less sensitive to HCFC-123 elicited hepatotoxicity than animals.[60,93] However, based on the available data, it would seem prudent to assume that acute inhalational exposure to HCFC-123 above 1000 ppm (6.3 g/m^3) may present a human health risk.

13.1.2 Chronic effects

Critical effects identified from repeated HCFC-123 exposure in animals were seen in liver, pancreas and testes. Retarded pup growth and sexual maturation occurred in a reproductive toxicity study. The major route of exposure for these effects is inhalation.

Liver effects have been seen in rats, guinea pigs and dogs and have been reported in humans for other halogenated ethanes, including the HCFC-123 analogue, halothane. Therefore,

hepatotoxicity would appear to be the adverse effect of most relevance to humans and also represents the most sensitive effect with respect to detection of chronic tissue damage. The lowest dose causing liver damage (histological evidence) in repeated dose studies was 300 ppm, with a NOAEL of 100 ppm.

Benign liver tumours (in rats) seen at the lowest dose tested (LOAEL = 300 ppm) following chronic exposure to HCFC-123, may well be a secondary consequence of the hepatocellular effects seen at this exposure level. Indeed, there is evidence for peroxisome proliferating substances, that both toxic and proliferative phenomena (for example, CPI) occur in the interval between liver enlargement and tumour production.[122] It appears valid to assume a threshold exists for tumourigenicity for HCFC-123, as evidence indicates that tumour induction in all three target organs is associated with a non-genotoxic mechanism.

The NOAEL from repeat-dose animal bioassays (inhalation) is 100 ppm HCFC-123. Although this level of exposure was not tested in the two-year chronic rat study, data from other studies indicate that this level of exposure may also represent a NOAEL for tumourigenicity. Such data include the findings that:

- little hepatic protein binding was seen at 100 ppm in rats;[45]
- changes indicative of peroxisome proliferation and hormone perturbation were not significant at this exposure level;[77] and
- no significant pathological changes were seen at 300 ppm after 12 months in the two-year study.

13.2 Occupational health risks

In Australia, occupational exposure to HCFC-123 is limited to workers engaged in the transport, handling, storage and filling of refrigerant or extinguishant containers, workers involved in chiller and extinguishant system installation, maintenance and testing and repair, and firefighters. Occupational health risks for all workers potentially exposed to HCFC-123 refrigerant or extinguishant can be divided into acute and chronic risks.

13.2.1 Acute health risks

Refrigerant exposure

Although breathing zone levels of several hundred parts per million HCFC-123 have been measured following spills, risks of critical health effects from acute HCFC-123 exposure (CNS depression, liver toxicity and cardiac sensitisation) are considered to be low during normal transport, handling and use scenarios, including chiller maintenance. Similarly, risks of asphyxiation from acute exposure to HCFC-123 are considered even lower and would only exist following a catastrophic leakage of chiller refrigerant or where refrigerant leakage was allowed to accumulate in a confined space or low lying areas, for example, pits.

Extinguishant exposure

Although information on exposure to HCFC-123 during installation and testing of HCFC extinguishant blends was not available for assessment, exposures and hence acute health risks are expected to be low. Similarly exposures during normal transport, handling (including filling operations) are also expected to be low.

Apart from the remote possibility of occupants remaining in the hazard zone during fixed extinguishant discharge, limited human exposure to total flooding extinguishants would be expected, due to their automated mode of discharge and intended discharge into non occupied areas. However, the design level of HCFC-blend extinguishant in such systems may lead to 5000 ppm HCFC-123 in an enclosed unventilated area, which may present an acute health risk to workers remaining in the hazard zone. Concomitant exposure to other HCFCs in the blend may present an increased risk due to additive effects.

The potential for exposure to HCFC-123 from discharge of portable extinguishers is much greater than from total flooding systems due to the manual mode of operation. Apart from failure of SCBA respirators, risks to professional firefighters would be expected to be minimal due to the deployment of full protective equipment. However, risks to other workers without personal protective equipment using such extinguishants would be considerably higher, particularly where the extinguishant is discharged into a confined working area. Although monitoring data indicates that levels of HCFC-123 from portables containing HCFC blends are unlikely to present a health risk *per se*, concomitant exposure to other HCFCs in the extinguishant blend may increase this risk due to the additive effects of other ingredients, particularly, CFCs and HCFCs.

In the overall assessment of risk, consideration should be given to confined spaces and duration of exposure.

Sensitive populations

There is limited evidence to suggest that some workers may be at greater risk from acute exposure to HCFC-123 than others[89]. Individuals with pre-existing cardiovascular disease or individuals using medications containing adrenalin or catecholamines (sympathomimetic medications) may be more sensitive to cardiac effects elicited by HCFC-123.

13.2.2 Chronic health risks

Refrigerant exposure

Exposures from drum leakage and spills will generally be infrequent. Therefore, the risk of chronic health effects from normal transport and handling is considered negligible.

The population at risk from chronic exposure to HCFC-123 are chiller maintenance technicians. The potential for chronic exposure of maintenance technicians to HCFC-123 refrigerant is dependent on the number of hours spent at chiller installations running on HCFC-123 and the types of maintenance activities carried out. Results from personal monitoring studies indicate that the TWA exposure during a normal working shift is generally 1–5 ppm, even where peak levels in excess of 100 ppm are encountered* during the working shift.

In assessing the risk of chronic effects in workers, the approach used is that of determining the 'margin of safety', that is, chronic N(L)OAEL divided by the measured TWA occupational exposure. The NOAEL determined for chronic effects in animals is 100 ppm (see section 13.1.2) and levels of exposure are 1–5 ppm (TWA). Therefore, the 'margin of safety' is 20–100 for chronic occupational effects. This range of margin is considered sufficient when taking into consideration other interrelated factors such as inter- and intraspecies differences and the confidence and adequacy of the animal database. Therefore, the risk of chronic health effects in chiller maintenance technicians from exposure to HCFC-123 is considered to be low.

Extinguishant exposure

Exposures from cylinder leakage and spills will generally be infrequent. Therefore, the risk of chronic health effects from normal transport and handling (including filling operations) is considered negligible. Similarly, exposure to HCFC-123 during extinguishant installation and testing is also likely to be infrequent, taking into account the specialist use of HCFC-blend extinguishants. However, should these extinguishants be used on a much larger scale, the potential risk to maintenance workers should be further investigated by characterising the duration and extent of worker exposure.

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* Such levels do not usually last for more than a few minutes and would be not be expected to be encountered more than 3 times during a normal working shift (6-8 hours).

Despite the potential for high level exposures to HCFC-123 during extinguishant discharge, occupational exposure to either streaming or total flooding agents would be expected to be infrequent. In addition, modern SCBA equipment used by professional firefighters affords a high level of protection (protection factor* of at least 10,000[123]). The removal of facepieces following fire extinction may result in exposure to residual HCFC-123.

In view of the low frequency of discharges of HCFC-blend extinguishants, the risk of chronic health effects from HCFC-123, in both professional firefighters and other workers using extinguishants, is considered to be extremely low.

13.3 Health risks from exposure to products of combustion

In addition to risks from exposure to HCFC-123, a potential also exists for health risks from exposure to products of combustion (POCs). This is particularly relevant for firefighters using extinguishants containing HCFC-123.

For HCFC-123, POCs are reported to include phosgene, hydrogen chloride and hydrogen fluoride. No data were available on levels of phosgene from extinguishant pyrolysis. Levels of hydrogen chloride and hydrogen fluoride around their exposure standard levels were measured in a study with the streaming agent Halotron-I. Products resulting from reaction of the extinguishant with combusting materials may present an additional hazard.

The nature and severity of potential health effects from the above pyrolysis reactions will be unpredictable because of the potentially wide variation in the concentration of HCFC-123 in extinguishant blends, the amount discharged, the type and size of fire.

13.4 Public health risks

Given that HCFC-123 is enclosed within sealed systems during its working life as a refrigerant or fire extinguishant, exposure to the public is unlikely and health risks are low. Significant short-term exposure of the public to HCFC-123 could arise from a transport accident, given the high vapour pressure of the chemical.

Emissions of HCFC-123 do occur during maintenance of chiller systems, however they are usually low. Even large scale leakage is unlikely to present a public hazard as refrigerant is likely to be confined to air conditioning plant room which is usually situated in an area to which there is restricted public access. Catastrophic accidents have occurred in other nations where most of the refrigerant charge is liberated. However, it has been estimated that such an incident would occur less than once per year per 2000 installed chillers. Used or surplus HCFC-123 will not be intentionally released into the atmosphere or otherwise disposed of in Australia, and hence exposure from environmental sources is unlikely.

Smaller amounts of HCFC-123 are used in the fire protection industry as streaming and total flooding agents. Fire extinguishant blends currently in use in Australia contain 5–55% HCFC-123. Under normal conditions, no public exposure to HCFC-123 containing extinguishants should occur (see section 8.4). However, acute health risks could arise from:

- activation of a fire extinguishing system within a building from which the occupants had not been evacuated;
- use of a hand held fire extinguisher in a confined space; and
- entering an inadequately ventilated hazard area following discharge.

Transport accidents, large scale chiller leakage and indoor extinguishant discharges are expected to be rare events and would probably result in a short duration of exposure. Hence, potential public health risks from HCFC-123 exposure are considered to be extremely low.

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* The US NIOSH recommends a protection factor (PF) of 10,000 for the pressure-demand, SCBA respirators used by fire fighters.

14. OHS risk management

The key elements in the management of occupational health and safety (OHS) risks from exposure to a hazardous substance include:

- workplace control measures;
- emergency procedures;
- hazard communication and training;
- exposure standards and air monitoring; and
- health surveillance.

In this section, measures currently employed and/or recommended to reduce occupational health and safety risks associated with the handling and use of HCFC-123 have been assessed. The information reviewed includes national and international standards and codes of practice as well as training material, guidance documents, labels and MSDS developed by manufacturers and users.

14.1 Workplace control measures

HCFC-123 is classified as a hazardous substance in accordance with the National Commission's Approved Criteria.[100] Under the National Commission's *National Model Regulations and Code of Practice to Control Workplace Hazardous Substances*,[124] control measures to reduce exposure must be implemented to minimise risks to health and safety. In particular, controls should be implemented to minimise inhalation exposure to HCFC-123 vapour.

In general, the control of worker exposure to any hazardous substance should be achieved through the following hierarchy of control strategies:

- elimination;
- substitution;
- isolation;
- engineering controls/equipment design;
- safe work practices; and
- personal protective equipment.

Control measures are not mutually exclusive and effective control usually requires a combination of these measures.

It is not within the scope of this report to document all assessed control measures. However, all measures made available for assessment were evaluated in order to identify the essential elements of the above control strategies.

14.1.1 Elimination and substitution

Refrigerant

In the air conditioning industry HCFC-123 is currently being used as an interim replacement for the refrigerant CFC-11, which is being phased out due to its high ozone depleting potential (ODP) under the Montreal Protocol. Because HCFC-123 is also an ozone-depleting substance (low ODP), it is to be phased out under the Montreal Protocol by 2030 or earlier if a more suitable, long-term replacement is found.

Currently, HCFC-123 is the only suitable 'drop-in'* alternative to CFC-11 use in low pressure centrifugal chillers, based on a number of criteria which include thermodynamic properties, flammability, compatibility with lubricants and other materials used to fabricate and service refrigeration systems. Based mainly on environmental grounds, its use as an interim replacement for CFC-11 has been endorsed by the Australian EPA and the US EPA.

Due to lack of human data, it is unclear whether HCFC-123 is less hazardous than CFC-11 based on health effects. In general, substitution requires great care as other refrigerants may not necessarily offer a greater degree of safety and indeed many refrigerants in current use present additional hazards.[125,126]

Extinguishant

In the firefighting industry, HCFC-123 blends (NAF S-III and NAF P-III) are currently being used as interim replacements for Halons 1301 and 1211, the use of which are being phased out according to the Montreal Protocol.

With regard to toxicity, it is reported that NAF S-III is more toxic than Halon 1301 with respect to lethality in animal bioassays but less toxic with respect to cardiac effects.[127] No data on comparative toxicity were available for NAF P-III and Halon 1211.

It should be emphasised that other so called 'inert' extinguishants are extremely hazardous, for example CO_2 (asphyxiation and CNS depressant effects), at the concentrations required for fire protection. Alternatives to HCFC extinguishant blends should be considered carefully to ensure that risks to health and safety are not increased.

14.1.2 Isolation

Refrigerant

HCFC-123 is isolated by virtue of its containment within the sealed chiller system where relief points are vented to atmosphere. Isolation of the refrigerant is also maintained during chiller maintenance activities by the use of portable refrigerant recovery devices.

Extinguishant

Extinguishants are contained in pressurised cylinders which are closed systems and as such are isolated from the workplace. Total flooding (fixed) systems are further isolated from the workplace in that extinguishant cylinders are located away from work areas. In addition, measures are usually taken to confine extinguishant discharge to a particular 'hazard area', thus preventing exposure of personnel located in other work areas.

14.1.3 Engineering controls, safe work practices and personal protective equipment

Sources of occupational exposure have been identified and assessed (section 8). Thus further options, such as engineering controls, safe work practices and personal protective equipment should be considered to reduce such exposures. In addition, equipment design and specification is of particular importance in controlling exposure to refrigerants and extinguishants. With regard to reducing health risks from HCFC-123 exposure, control measures should focus on reducing exposure by inhalation.

Refrigerant

Control measures introduced to protect workers from adverse health effects from HCFC-123 refrigerant need to address hazards from chronic exposure to low levels of refrigerant in addition to hazards from acute high level exposures. Current control measures employed in the air conditioning industry would appear to be sufficient to maintain TWA levels (eight hours)

Design element* Suitable for direct replacement of CFC-11 pending retrofit of chiller, for example, gasket/seal change.

below 5 ppm HCFC-123. However, peak levels in excess of 100 ppm have been recorded during certain chiller maintenance activities. In general, such excursion levels can be reduced by paying particular attention to control measures aimed at ensuring efficient refrigerant recovery during transfer and adherence to safe work practices during maintenance and repair procedures, particularly during leak test operations.

A number of control measures were identified as integral to reducing occupational health risks during refrigerant handling and use, and these are listed in Appendix 2. The majority of the control measures are embodied in the following codes and standards, which currently comprise the fundamental reference documentation used by chiller maintenance technicians in Australia:

- *Safety Code for Mechanical Refrigeration* (ASHRAE 1994).[16]
- The *Australian Refrigeration and Air Conditioning Code of Good Practice* (AFCAM 1992).[40]
- Australian Standard AS 1677—*Refrigerating Systems* (1986)*.[15]

The Safety Code for Mechanical Refrigeration (ASHRAE 1994).[16] Developed by the American Society of Heating, Refrigeration and Air Conditioning Engineers (ASHRAE) in conjunction with the American National Standards Institute (ANSI), ASHRAE Standard 15 provides information relating to requirements for equipment design, installation, operation and maintenance of air conditioning systems. Some aspects of refrigerant hazards are also addressed, including HCFC-123. Coverage of engineering controls and equipment design is fairly extensive, particularly with respect to pressure relief devices and mechanical ventilation. Safe working practices and personal protective equipment are dealt with in less detail.

The Australian Refrigeration and Air Conditioning Code of Good Practice (AFCAM 1992).[40] Developed by Australian Association of Fluorocarbon Consumers and Manufacturers (AFCAM) and approved by the EPA, Code HB40 provides information on control measures for ozone depleting refrigerants.† This code is not exhaustive and does not constitute a technical design document and as such the authors recommend that it be used in conjunction with other existing codes and standards. The code covers engineering controls and equipment design, installation and routine servicing protocols (including leak testing), requirements for refrigerant recovery and disposal, and to a lesser extent, refrigerant handling and storage.

Australian Standard AS 1677—Refrigerating Systems (1986).[15] Developed by the Standards Association of Australia, Australian Standard 1677 addresses the requirements for equipment design and installation of refrigerating systems. With regard to control measures, this standard deals with refrigerant use, equipment specification and design (including requirements for ventilation, refrigerant detectors and pressure-relief devices), materials specification and use of personal protective equipment.

This standard is currently being reviewed with the intention of updating information on 'alternative' refrigerants (including HCFC-123) and incorporating technical changes to chiller systems that have taken place over the last decade. It is reported that the updated standard will take into account relevant features from standards produced by ASHRAE and the ISO.

Overall remarks. Not withstanding the different requirements, aims and scope of the above documents, specific areas of risk management (including control measures) were identified as either not being addressed or lacking details in some or all of the documents. In summary these are:

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* This standard is currently being reviewed and will take into account ASHRAE standards and the International Organization for Standardization (ISO). It is also intended that the update be a joint Australia/New Zealand standard.

† Compliance with this code is a feature of ozone protection legislation of most Australian States and Territories.

- safety requirements/precautions;
- procedures for refrigerant transfer and refrigerant/water leak testing;
- specifications/requirements for purging equipment;
- criteria and testing specifications for monitoring equipment, alarms and mechanical ventilation;
- restrictions/requirements (including incompatible materials) for HCFC-123 retrofits;
- use of personal protective equipment (other than SCBA); and
- details of emergency procedures and training requirements.

Extinguishant

Control measures introduced to protect workers from adverse health effects from HCFC-123 in fire extinguishants need to address hazards from acute high level exposures, as chronic exposure to HCFC-123 is unlikely. Such exposures are unlikely to result during transport, handling, filling and installation/testing operations.

Firefighters and emergency personnel represent the population at most risk from exposure to HCFC-123 from portable extinguishants. Control measures introduced to reduce exposure to professional firefighters rely mainly on personal protective equipment (the selection and specification of which is dealt with by the appropriate authorities). However, other workers using portable extinguishers will be reliant on hazard communication, for example, training and labels. Engineering controls aimed at reducing HCFC-123 exposures to workers from total flooding systems are pre-discharge alarms, safety interlocks and controlling the discharge , that is, compliance with design concentration. As with portable extinguishers hazard communication, including warning signs and training/drills will help minimise risks of exposure.

A number of control measures were identified as integral to reducing occupational health risks during extinguishant (total flooding and streaming agents) handling and use, and these are listed in Appendix 3. The control measures in Appendix 3 are embodied in the following codes/standards, which currently comprise the fundamental reference documentation for HCFC blend fire extinguishants used in Australia:

- US Standard on Clean Agent Fire Extinguishing Systems.[127]
- Australian/New Zealand Standard AS/NZS 4214.5—*Gaseous Fire Extinguishing Systems—NAF S-III (HCFC Blend A) Total Flooding Systems*.[128]
- Australian/New Zealand Standard AS/NZS 4214.1—*General Requirements for Gaseous Fire Extinguishing Systems*.[129]
- Australian Standard/New Zealand Standard AS/NZS 1851.12—*Maintenance of Fire Protection Equipment—Gaseous Fire Extinguishing Systems*.[130]
- Australian Standard AS 1841.7—*Portable Fire Extinguishers—Vapourizing-Liquid Type*.[131]
- The FPIAA *Code of Practice for Design, Installation, Inspection and Testing of Gaseous Fire Extinguishants*.[41]

US Standard on Clean Agent Fire Extinguishing Systems.[127] Developed by the US National Fire Protection Association, NFPA 2001 provides information on new total flooding agents (including NAF S-III) developed to replace Halon 1301. This standard addresses the design, installation, testing, maintenance and operation of total flooding systems and hazards from exposure to replacement extinguishants and their combustion products. With regard to control measures, this standard addresses extinguishant use and limitations; safety requirements; extinguishant storage; equipment specification and design (including detection,

actuation, alarm and control systems); pressure relief venting; requirements for maintenance and testing.

Australian Standard/New Zealand Standard—Gaseous Fire Extinguishing Systems—NAF S-III (HCFC Blend A)—Total Flooding Systems.[128] Developed by the Standards Associations of Australia and New Zealand, this standard addresses the requirements for equipment design and installation and commissioning of gaseous extinguishant (fixed) systems and extinguishant identification, labelling and hazards, including combustion products. Maintenance requirements are the subject of AS/NZS 1851.12 (1995) (see below). With regard to control measures, this standard deals with extinguishant use and limitations, safety requirements/precautions, extinguishant storage, equipment specification and design, requirements for pressure relief venting and procedures and requirements for testing.

Australian Standard/New Zealand Standard—General Requirements for Gaseous Fire Extinguishing Systems.[129] Developed by the Standards Associations of Australia and New Zealand, this standard addresses the general requirements for gaseous extinguishant (fixed) systems and extinguishant agents and covers similar information as AS/NZS 4214.5 (1995)[128] (see above) with the exception of the inclusion of control and actuation systems in this code.

Australian Standard/New Zealand Standard—Maintenance of Fire Protection Equipment—Gaseous Fire Extinguishing Systems.[130] Developed by the Standards Associations of Australia and New Zealand, this standard addresses the maintenance requirements for gaseous fire extinguishing (fixed) systems and contains information on installation, inspection and testing. With regard to control measures, this standard deals exclusively with procedures for testing.

Australian Standard—Portable Fire Extinguishers—Vapourizing-liquid Type.[131] Developed by the Standards Association of Australia, this standard addresses the general requirements for vaporising-liquid portable fire extinguishers. This standard has recently been amended to include new replacement (for halons) extinguishants. It does not specifically address HCFC-123 Blend C (NAF P-III). With regard to control measures, this standard deals with extinguishant specification, discharge fittings and testing methods.

The FPIAA Code of Practice for Design, Installation, Inspection and Testing of Gaseous Fire Extinguishants.[41] Developed by the FPIAA this code provides information on controlling emissions of ozone depleting extinguishants. The code covers engineering controls and equipment design, installation and routine inspection and testing protocols.

Overall remarks. Not withstanding the different requirements, aims and scope of the above documents, specific areas of risk management (including control measures) were identified as either not being addressed or lacking details in some or all of the documents. In summary these are:

- safety requirements/precautions;
- restrictions/requirements (including incompatible materials) for retrofitting extinguishants with blends containing HCFC-123;
- requirements for extinguishant disposal; and
- training requirements.

14.2 Emergency procedures

For any hazardous chemical, an emergency response plan is an essential component of OHS risk management. In the event of a substantial leak, spill, release or fire, a written procedure is necessary for workers and emergency services.

14.2.1 Refrigerant

Apart from guidelines for emergency discharge of refrigerants (ASHRAE 1994),[16] emergency procedures were not submitted for assessment. Key elements of an emergency plan should include:

- emergency shutdown procedures, displayed in a suitably conspicuous location;
- emergency contact number for the chiller maintenance company;
- respiratory protection (including SCBA) in accordance with AS 1715[132] and AS 1716[133] and other personal protective equipment to be available and clearly labelled (AS 1319[134]) at storage areas and outside equipment rooms;
- first aid procedures for acute health effects;
- an evacuation plan for building occupants; and
- clean-up procedures and waste disposal arrangements.

Clean-up and first aid procedures should be recorded on an MSDS,[138] which should be readily available to workers and emergency services. As HCFC-123 is not scheduled by the Australian Code for the Transport and Handling of Dangerous Goods[135] (ADG Code) there are no guidelines for accidental exposure during transportation.

14.2.2 Extinguishant

An emergency response plan was not submitted for assessment. Both NAF S-III and NAF P-III are regulated by the ADG Code[135] and a separate emergency response plan is required for transportation.

Transport and handling

The Hazchem emergency action code for NAF S-III specified by the label in AS/NZS 4214.5[128] recommends the use of water fog for dispersal/dilution of spillages together with the use of full protective clothing.

According to the ADG Code,[135] the most appropriate emergency procedure guide for the two major ingredients (>90%) of HCFC Blend A (NAF S-III)* and the two major ingredients (>40%) of HCFC Blend C (NAF P-III)† is 2C2.

Clean-up and first aid procedures should also be available on the MSDS[138] which should be readily available to workers and emergency services.

Discharge, testing and filling of extinguishant systems

For fire situations suitable safeguards should be provided to ensure prompt evacuation from and prevent entry into hazardous atmospheres and also to provide the means for prompt rescue of any trapped personnel. Similarly an emergency response plan should cover accidental discharge during testing and filling procedures. The elements that should form the basis for appropriate action in response to discharge of HCFC-123 extinguishants include:

- an evacuation plan for building occupants, for example, conducting fire drills;
- first aid procedures;
- respiratory protection,‡ including SCBA;§
- emergency contact telephone numbers; and
- clean-up procedures.

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* HCFC-22 and HCFC-124.

† HFC-134a and HCFC-124.

‡ In accordance with Australian Standard AS1715 and Australian Standard 1716.

§ It is recommended that reference be made to Commonwealth Fire Board, *Fire Safety Circular*, no. 88—'Self-Contained Breathing Apparatus'.

Emergency procedures for professional firefighters are well developed and assessment of such is not within the scope of this report. Specific information on the hazards of HCFC-123 containing extinguishants should be made available to firefighters. In addition to the manufacturers' MSDS, current information on extinguishant hazards is available from the Commonwealth Fire Board.[136]

14.3 Hazard communication

14.3.1 Education and training

Education and training form the basis for management of OHS risks. Guidelines for the induction and training of workers potentially exposed to hazardous substances are provided in the National Commission's *National Model Regulations and Code of Practice for the Control Workplace Hazardous Substances*,[124] which lists the key components of a good induction and training program. In addition, the ANZECC *Revised Strategy for Ozone Protection*[2] calls for training of all persons involved in the use of ozone-depleting substances. In particular, training should cover the health hazards associated with both acute and chronic exposure to HCFC-123, include instruction on the use of recommended personal protective equipment—particularly in the fitting and use of respirators—and provide information on clean-up and disposal.

Refrigerant use

Training of chiller maintenance technicians should consist of supplementing existing information on refrigeration hazards with information specific to HCFC-123. Technicians are trained in refrigeration mechanics with CFC accreditation where applicable.

A considerable amount of guidance material has been prepared for the safe handling and use of HCFC-123 in air conditioning applications. In general, available training material provided for chiller maintenance technicians appears to be commensurate with the health risks associated with acute exposure to HCFC-123, but fails to provide sufficient information on potential chronic health hazards. As such the importance of maintaining HCFC-123 levels as low as is practicable may be understated.

Extinguishant use

Training of professional firefighters should consist of supplementing existing information on extinguishant hazards with information specific to HCFC-123. With regard to use of portable extinguishants by other workers, it is imperative that employers provide adequate training for HCFC-123-blend extinguishers, particularly with respect to their use in confined areas. Apart from extinguishant system testing procedures, no formal training material was provided for assessment.

With respect to training of installation mechanics, accreditation (where required by State legislation) can be arranged through the FPIAA.[41]

Although the available information on the safety requirements and specifications for extinguishant systems appears adequate, information on the hazards from exposure to HCFC-123-blend extinguishants is lacking.

14.3.2 Material Safety Data Sheets and labelling

Material Safety Data Sheets

MSDS are the primary source of information for workers employed in the handling, use, storage and disposal of hazardous chemicals and must be made available to all employees potentially exposed to HCFC-123 in the workplace in accordance with the National Commission's *National Model Regulations for the Control of Workplace Hazardous Substances*.[124]

Five MSDS for HCFC-123 and two MSDS for mixtures containing HCFC-123 (extinguishants) were submitted for assessment.

To evaluate these MSDS, a prescribed set of criteria from a recognised study were used.[137] These criteria were based on information requirements set out in the National Commission's *National Code of Practice for the Preparation of Material Safety Data Sheets*.[138]

MSDS were scored for availability and quality of data only. Analysis focused on the content of the MSDS and not their format. Scorings for individual MSDS are presented in Table 14.

Table 14: Evaluation of MSDS made available for assessment

MSDS	Company details (out of 5)	Identification (out of 28)	Health hazard information (out of 34)	Precautions for use (out of 16)	Safe handling and use (out of 12)	Total score (out of 92)
A*	3	22	19	8	9	61 (66%)
B*	5	20	22	8	6	61 (66%)
C*	5	20	23	11	8	67 (73%)
D*	1	18	6	0	3	28 (30%)
E*	5	16	15	4	5	45 (49%)
F†	4	22	19	10	4	59 (64%)
G†	4	23	19	8	4	58 (63%)

* MSDS for HCFC-123 refrigerant.

† MSDS for extinguishants containing HCFC-123 (HCFC Blends A and C).

A qualitative assessment for the above scores can be obtained for each MSDS using the following prescribed scale:[137]

Total score	Adequacy	Meaning
0–40%	Inadequate	Unacceptable. Should not be used
41–60%	Poor	Only to be used as an interim measure
61–80%	Good	Adequate
81–100%	Very good	Nearly complete/complete

Although the majority of the MSDS submitted for assessment were rated as 'adequate' according to this scale, none were considered 'nearly complete'.

In general, company details and substance identification data were adequate. Information on health hazard, safe handling and use was more variable, both with respect to availability and quality of data. None of the MSDS contained a statement of the hazards of HCFC-123 according to the National Commission's Approved Criteria.[100] In general, chronic health effects were not adequately addressed and information was misleading with respect to critical effects and hazardous exposure levels. Recommendations for treating spills and methods for disposal were particularly poor and, in general, very little consideration was given to potential environmental contamination and effects.

Most MSDS for HCFC-123 refrigerant were compiled overseas and generally did not contain information specific for use in Australia, such as emergency contact numbers telephone in Australia, relevant Australian standards and codes, the status of Australian exposure standards, and ADG Code[135] classification and SUSDP scheduling.[139] With respect to the last three information items, the MSDS should state whether or not the relevant information is available.

A sample MSDS for HCFC-123 refrigerant,* prepared in accordance with the National Commission's *National Code of Practice for the Preparation of Material Safety Data Sheets*,[138] is provided at Appendix 1. This sample MSDS was compiled from the information made available for assessment and is intended for guidance purposes only. Under the National Commission's *National Model Regulations for the Control of Workplace Hazardous Substances*,[124] manufacturers and importers are responsible for preparing† MSDS and ensuring information is up to date.

Labels

In accordance with the National Commission's *National Model Regulations for the Control of Workplace Hazardous Substances*,[124] all containers of hazardous substances supplied to, used in, or handled in the workplace should be appropriately labelled to allow that substance to be used safely.

Two labels for HCFC-123 and two proposed labels for fixed and portable extinguishants containing HCFC-123 were submitted for assessment. Labels were assessed for requirements under the National Commission *National Code of Practice for the Labelling of Workplace Hazardous Substances*.[140] This assessment took the form of a qualitative appraisal with respect to the inclusion of the following categories of information:

- substance identification;
- hazard category/signal word;
- ADG Code[135] classification;
- risk information (or phrase);
- safety information (or phrase);
- first aid information (or phrase);
- information on spills/leaks; and
- firefighting precautions.

Neither of the labels for HCFC-123 (refrigerant) included the signal words 'Hazardous' or 'Harmful'. Only one of the labels included information on health risks, first aid and spills/leaks, and neither contained precautions for firefighting.

Neither of the labels for extinguishants included the signal words 'Hazardous' or 'Harmful'. The label for the fixed extinguishant, prepared according to AS/NZS 4214.1,[129] complied only with substance identification and ADG Code[135] classification requirements and referred to the MSDS for safe use information. The label for the portable extinguisher, prepared according to AS 1841.1,[141] did not comply with any of the above categories of information. In particular, it should be noted that HCFC-123 is a Type 1 Ingredient according to the National Commission's *National Code of Practice for the Labelling of Workplace Substances*[140] and, as such, is subject to full disclosure on the label when present as an ingredient in a mixture above 1% w/w. In addition, the extinguisher rating, prepared in accordance with AS 1850,[142] did not include its B Fire Test rating.

14.4 Exposure standards

14.4.1 Atmospheric monitoring

Air monitoring is necessary to obtain a quantitative estimate of exposure for the purpose of determining the effectiveness of control measures. Continuous monitoring of workroom air at

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* Some of the information in this MSDS may also be appropriate for extinguishants containing HCFC-123- blends.

† It is recommended that the preparation of an MSDS is carried out by a suitably informed and qualified person.

chiller installations, using an automated detection system, is recommended by Australian Standard AS 1677[15] and ASHRAE Standard 15[16] and is currently reported to be standard practice for HCFC-123. Detection systems are usually adjusted to activate both an alarm and mechanical ventilation at preset trigger concentrations.

This type of monitoring not only provides an instant warning of excursions above a set airborne level of HCFC-123, but also provides a continuous record of TWA exposure levels for each working day. The main problem with this type of monitoring system is lack of sensitivity, as other chlorinated compounds (including CFC-11) have been known to interfere with detection, particularly at low exposure levels, that is, less than 10 ppm.

It is important to ensure that the positioning of detectors is appropriate for assessing actual worker exposures encountered during maintenance operations. Therefore, detectors should be located in areas where refrigerant vapour leaks are most likely and should be positioned to account for air flow patterns in the equipment room. There exists a need for routine personal monitoring to validate the accuracy of automated monitors and the siting of detectors.

The usefulness of routine monitoring during maintenance/installation of systems using HCFC-blend extinguishants is difficult to evaluate as exposure levels and duration have not been characterised.

14.4.2 Industry-set exposure limits

Refrigerant

In June 1991, following the publication of preliminary findings from the PAFT chronic oncogenicity/toxicity study, the industry-set AEL-TWA for HCFC-123 in workroom air was reduced, at the recommendation of Du Pont Ltd, from 100 ppm to 10 ppm. In September 1993 following publication of the final study report from PAFT together with results from a follow-up metabolism/mechanistic study, Du Pont[17] increased the AEL-TWA from 10 ppm (62.5 mg/m^3) to 30 ppm (187 mg/m^3).

Other industry-set workplace exposure levels for HCFC-123 include an EEL, currently set at 1000 ppm with a ceiling limit of 2500 ppm. The Emergency Exposure Limit (EEL) is defined as the maximum concentration to which a worker can be exposed for a one hour period, with a one minute ceiling limit in the event of an emergency such as a spill.

Extinguishant

There are no industry-set exposure limits for atmospheric levels of HCFC-123 arising from the use of HCFC-blend fire extinguishants. However, according to Australian/New Zealand Standard AS/NZS 4214.5 (1995),[128] NAF S-III total flooding systems are not recommended for use at a design concentration greater than 10_ per cent in 'normally occupied areas'. This concentration is claimed to be based on health-based studies, although these were not cited in the Standard and were unavailable for assessment. Such a concentration of extinguishant would lead to an exposure of approximately 0.5 per cent HCFC-123 (5000 ppm).

14.4.3 Regulatory standards

There is no Australian occupational exposure standard for HCFC-123. Similarly, international exposure standards do not exist for this chemical.[143] The German Commission for the Investigation of Health Hazards of Chemical Compounds in the Work Area have recently classified HCFC-123 as a Group IIIB carcinogen (that is, suspected of having carcinogenic potential) and, therefore, a maximum workplace concentration (MAK value) was not established.[144] It is understood that the Workplace Environmental Exposure Level (WEEL) Committee of the American Industrial Hygiene Association is in the process of developing workplace standards for a number of HCFCs .[145]

The setting of an eight hour TWA occupational exposure standard would provide guidance for industry in determining the adequacy of control measures. The setting of a STEL is not considered appropriate for HCFC-123.

14.5 Health surveillance

There are no formal requirements for health surveillance programs for workers exposed to HCFC-123. HCFC-123 is not listed on the National Commission's Schedule of Substances Requiring Health Surveillance (Schedule 3) in the *Model Regulations for the Control of Workplace Hazardous Substances*.[124]

In accordance with the National Commission's *National Model Regulations for the Control of Workplace Hazardous Substances*,[124] employers have a responsibility to provide health surveillance in those workplaces where the workplace assessment has shown that exposure to a hazardous substance may lead to an identifiable substance-related disease or adverse health effect.

The risk assessment for HCFC-123 indicates that under 'anticipated conditions' of use, risks of adverse health effects for workers involved in firefighting and in chiller maintenance are likely to be low. In addition, atmospheric monitoring is considered sufficient to evaluate exposure to HCFC-123 to chiller technicians. Therefore routine health surveillance is not indicated at present.

15. Environmental risk assessment

15.1 Environmental fate

15.1.1 Aquatic fate

Significant amounts of HCFC-123 are not expected to enter aquatic environments because of limited solubility and high volatility. Spills to water would largely evaporate as HCFC-123 is not readily biodegradable. Oxygen consumption during a 28-day closed bottle test (OECD Test Guideline No 301D) amounted to 24% of theoretical at a concentration of 12.5 mg/L. The test substance also proved resistant to chemical degradation, with chemical oxygen demand (acid dichromate at 150ºC for two hours) being only 14% and four per cent of theoretical at concentrations of 243 and 567 mg/L respectively.[146]

Like other halogenated solvents, HCFC-123 has the potential to contaminate groundwater. However, HCFC-123 is reluctant to dissolve, notwithstanding moderate solubility, and degases readily from solution even at concentrations well below the solubility limit, as was evident in aquatic toxicity testing (see below). Furthermore, the isomer HCFC-123a has been shown to undergo reductive dechlorination under the influence of bacteria in methanogenic landfill leachate.[147] Thus anaerobic biodegradation pathways should exist for HCFC-123, although they are unlikely to represent a significant degradation mechanism because of limited exposure of anaerobic environments to the volatile halocarbon.

While HCFC-123 itself is expected to be mainly associated with the atmosphere, hydrophilic substances which precipitate in rain, such as TFA, are formed from its degradation. No biodegradation was observed when the sodium salt of TFA was subjected to the closed bottle test (OECD Test Guideline 301D) even though the test was continued for 77 days.[148] While biodegradation was not observed in these laboratory tests, recent studies[149] demonstrate that trace amounts of TFA can be degraded by reductive defluorination under anoxic conditions and by decarboxylation under oxic conditions, implying that significant microbial sinks exist in nature for the elimination of TFA from the environment. However, the rate and significance of these processes remain uncertain.

TFA will be deposited on both land and water, but is expected to become associated mainly with the aquatic compartment as the sodium salt underwent minimal sorption (average zero per cent from duplicate tests using OECD Test Guideline 106 in three different soils[150]).

15.1.2 Atmospheric fate

Because of its volatility, any HCFC-123 released to the environment will partition almost entirely to the atmosphere, where its main mode of degradation will be reaction with tropospheric hydroxyl radicals. It has been estimated that 88 per cent of emissions will be so degraded,[151] leading to an estimated atmospheric lifetime at steady state of 1.4 years.[14] This compares with 50 years for CFC-11.[14]

Mechanistic studies[152] on hydrogen abstraction from HCFC-123 used chlorine rather than hydroxyl radicals because of their greater ease of laboratory generation. The only product detected, in 98% yield, was trifluoroacetyl chloride. A minor component was thought to be chlorodifluoroacetyl fluoride, formed from the isomer HCFC-123a. Following hydrogen abstraction, the pentahaloalkyl radical reacts with atmospheric oxygen to form the peroxyalkyl radical, which reacts further to the corresponding alkoxy radical. Chlorine elimination generates trifluoroacetyl chloride.

Trifluoroacetyl chloride is expected to be removed from the troposphere by dissolution in cloud water, hydrolysis to TFA and precipitation in rain. Alternatively, further photolysis in the upper troposphere leads to carbonyl fluoride, which can photolyse further to hydrogen fluoride in the stratosphere. Model simulations[153] indicate that formation and precipitation of TFA is the dominant removal mechanism, although photolysis to carbonyl fluoride in the upper troposphere is also significant.

Trifluoroacetyl chloride may also be transported to the stratosphere under turbulent conditions. Its behaviour in the stratosphere will be similar to that for carbonyl halides, being removed mainly by photolysis. However, the available evidence[154] suggests that the formation of fully halogenated substances, such as CFC-11, from photolysis of triflouracetyl chloride is sufficiently low that the ODP of the parent compound, HCFC-123, will be increased by less than 0.01.

Carbonyl fluoride does not react with hydroxyl radicals or undergo photochemical transformation at significant rates in the troposphere. Its fate is somewhat speculative as its Henry's law solubility and reactive sticking coefficient (a measure of the reaction probability on aqueous surfaces) are unknown. However, by using data for phosgene, a tropospheric lifetime of 17 days may be estimated for carbonyl fluoride with respect to incorporation and hydrolysis in clouds.[155] Dry deposition may also be important. Tropospheric loss mechanisms may be inferred from the observation of carbonyl fluoride in the stratosphere, but not in the troposphere.[156] However, such conclusions are tentative as stratospheric sources of carbonyl fluoride include the common CFCs, CFC-11 and CFC-12.

15.2 Environmental effects

15.2.1 Aquatic organisms

HCFC-123 appears to be slightly toxic to practically non-toxic to fish. No mortality occurred in fathead minnows exposed for 96 hours to solutions of HCFC-123 (350 mg/L nominal, 76 mg/L measured, isomeric ratio of 4:1 from inspection of HRGC chromatograms) in a flow-through system. Fish were anaesthetised by exposure to HCFC-123, becoming immobilised within minutes on static exposure to 700 mg/L (nominal) but regaining full activity 12–14 hours later as the halocarbon degassed from solution. However, when fish were maintained in the stock solution at this same nominal concentration for six hours, recovery did not occur and all fish died. Concentrations to which fish were exposed are unclear as solubility in the diluter stock reservoir was visibly incomplete, and HCFC-123 degassed readily from test solutions, despite the nominal concentrations being well within the stated solubility limit.[157]

The effects of HCFC-123 on rainbow trout were investigated under semi-static conditions, with test media renewed at 24-hour intervals. Measured concentrations were close to nominal except for the highest concentration tested of 133 mg/L in which dissolution was visibly incomplete and the mean measured concentration was 68 per cent of nominal. All fish died within 24 hours at this concentration. Results are expressed as mean measured concentrations. A no-effect concentration could not be obtained as fish exhibited lethargic behaviour and darkened pigmentation even at the lowest concentration of 15 mg/L.[158]

The first of the two cladoceran tests used static conditions, with endpoints expressed as mean measured concentrations, which were significantly lower than nominal at test initiation but increased during the test.[159] Measured concentrations were consistently 25 per cent or less of nominal in the second static test on *Daphnia magna*. Anaesthetic effects were again observed.[160] Results in both tests are indicative of slight toxicity.

An algal growth inhibition test was conducted in sealed vessels under static conditions with concentrations measured at 0, 48 and 96 hours. As in the other tests, HCFC-123 proved reluctant to dissolve, and measured concentrations increased during the first 48 hours due to

slow dissolution and then declined because of volatilisation. The EC_{50} (67.8 mg/L) based on biomass and mean measured concentrations indicates HCFC-123 to be slightly toxic to algae.[161]

Results of the studies in aquatic organisms are summarised in Table 15.

Table 15: Summary of effects of HCFC-123 in aquatic organisms

Test	Species	Results and references
Acute toxicity (96 hr)	Fathead minnow	LC_{50} > 350 mg/L[157]
Acute toxicity (96 hr)	Rainbow trout	LC_{50} = 55 mg/L[158]
Immobilisation (48 hr)	*Daphnia magna*	EC_{50} = 17.3 mg/L[159]
Immobilisation (48 hr)	*Daphnia magna*	EC_{50} = 45.8 mg/L[160]
Algal growth inhibition (96 hr)	*Selenastrum capricornutum*	EC_{50} = 67.8 mg/L[161]

Chronic effects on aquatic organisms would not be expected as HCFC-123 is clearly non-persistent in water, even at concentrations below the solubility limit.

15.2.2 Atmospheric effects

Halocarbon refrigerants can affect the atmosphere. The dominant concern associated with chlorine or bromine containing refrigerants and extinguishants is that they can transport these halogens to the stratosphere where they catalyse the destruction of ozone.

Because of their high tropospheric stability, fully halogenated CFC refrigerants are being phased out in favour of HCFC refrigerants as an interim measure while ozone benign replacements are developed, for example, HFCs. HCFC-123 is one of these transitional refrigerants. Model calculations[162] indicate that the ODP of HCFC-123 is around two per cent of that for CFC-11 and CFC-12, which have ODPs of about one. Numerous studies confirm these findings.

Whereas HCFC-123 is removed predominantly in the troposphere, there is some degradation and release of chlorine in the stratosphere by reaction with hydroxyl radicals and photolysis. Computer modelling studies undertaken to date indicate that only one to two per cent of HCFC-123 would reach the stratosphere. While further research in this area may be forthcoming, and should be monitored, it appears unlikely that the ODP of HCFC-123 will alter significantly from the currently estimated value (0.02 relative to CFC-11).

Like other halocarbons, HCFC-123 contributes to the global warming potential (GWP) of the atmosphere. However, its atmospheric lifetime is short at less than two years, and its GWP is only two per cent of that for CFC-11 and less than one per cent of that for CFC-12.[163] CFC-11 has the shortest lifetime and lowest GWP of the common CFCs. Numerous studies confirm these findings.

15.3 Hazard evaluation

HCFC-123 does not represent a direct ecotoxicological hazard as both exposure and toxicity are low. Data on HCFC-123 and other HCFCs that have been reviewed by the US EPA generally support the contention that these chemicals exhibit a low level of ecotoxicity.[164] However, HCFC-123 may exhibit biological effects indirectly by impacting on the atmosphere, particularly stratospheric ozone. The stratospheric ozone layer reduces the amount of harmful ultraviolet radiation that reaches the Earth's surface. While the ODP is reduced by a factor of 50 relative to CFC-11, it remains finite. Accordingly, HCFC-123 is only considered acceptable for use in refrigeration equipment as an interim replacement for fully halogenated CFCs.

Similarly, the use of blends containing HCFC-123 in the fire protection industry (to replace Halons 1211 and 1301) is only considered acceptable as an interim measure pending development of ozone benign alternatives. However, the interim transition represents a major hazard reduction, as Halons 1211 and 1301 have ODPs of five and 12–13 respectively.[14] In addition, atmospheric lifetimes are approximately 20 and 65 years respectively.[14]

Greenhouse concerns are less significant than ODP concerns for halons because of the relatively short atmospheric lifetimes. However, some easing of GWP can be expected from the transition to the HCFC blends in view of the shorter lifetimes of their component gases of:

- HCFC-123—1.4 years;
- HCFC-124—5.9 years;
- HCFC-22—13.3 years; and
- HFC-134a—14.0 years.[14]

Degradation products of HCFC-123 are not expected to present a hazard to the environment. The persistence of the degradation product TFA raises concerns for its accumulation in the environment, possibly within a few decades in certain wetlands where evaporation is high and water seepage limited. The recent discovery of aerobic and anaerobic sinks for this TFA is promising, but further research in this area will need to be monitored.

It has been estimated recently that by 2010 the global average TFA concentration in rainwater will be 0.016 micrograms/L, 15 per cent of which will be due to atmospheric degradation of HCFC-123, the other 85 per cent due to degradation of HCFC-124 and HFC-134a. This level of TFA is three orders of magnitude below toxic thresholds of the most sensitive species yet addressed. However, under high evaporation conditions TFA levels in some wetlands could reach 100 mg/L within a few decades, assuming no loss by degradation or water seepage.[165,166] The effects of TFA at such levels are unknown. While there is no immediate prospect of such levels being reached in Australia, further research in this area should be monitored.

15.4 Risk management

Adherence to the *Australian Refrigeration and Air Conditioning Code of Good Practice*[40] is expected to minimise environmental emissions of HCFC-123 arising from current use, handling and disposal of refrigerant. Australia's ratification of the Copenhagen Amendment to the Montreal Protocol will require that current uses of HCFCs are controlled prior to phase out.[3]

Extinguishant use entails inevitable atmospheric release. However, State legislation prohibits discharge of halons from firefighting systems during testing and training, and similar measures are expected with respect to HCFCs. Adherence to the FPIAA's *Code of Practice for Design, Installation, Inspection and Testing of Gaseous Fire Extinguishants*[41] is expected to minimise environmental emissions of HCFC-123 arising from extinguishant testing.

To ensure an orderly phase out, the Commonwealth proposes controls on the importation and manufacture of HCFCs at a level that will meet the needs of existing owners of HCFC-based equipment, but will not encourage the use of HCFCs where alternative technologies are available. The controls will be administered under the Commonwealth *Ozone Protection Act (1989)*. Two yearly licences to import and manufacture HCFCs will be issued and an administrative fee of A$10,000 will be charged. In addition, an activity fee of A$2000 per ODP tonne of HCFCs imported or manufactured will be placed in a trust fund to be created which will be used to improve public awareness of the phase out and alternatives.

An Australian phase-out timetable for HCFCs from 1996 to 2030 has been proposed. The phase out will discriminate against consumption of those HCFCs which contribute most to ozone depletion by imposing an activity fee based on the ODP of individual HCFCs.

The proposed phase-out timetable meets Australia's current obligations under the Montreal Protocol and will be responsive to future changes to it. Regulations will gradually reduce the quantity of HCFCs imported and manufactured until 2015, with a small quantity available for the maintenance of long-life commercial air conditioning equipment until 2030.

If total consumption does not exceed annual targets set by the Commonwealth Minister for the Environment, industry may be allowed to self-regulate. Annual targets will be set at least two years ahead by regulations. Industry believes that the proposed Australian phase-out timetable is realistic and have hailed the scheme as innovative.

The policy was endorsed in its entirety by Commonwealth Cabinet on 24 October 1994. Amendments to the *Ozone Protection Act (1989)* were passed by Parliament in October 1995.

The policy for control of HCFC emissions in Australia proposes the extension of some existing controls on CFCs and halons to include the control of future emissions of HCFCs. States and Territories recommend that:

- the sale of HCFCs should be restricted to registered persons;
- service personnel for HCFC equipment need to have some formal training in reducing emissions of HCFCs;
- service personnel should work in accordance with appropriate codes of practice;
- unnecessary emissions of HCFCs should be banned;
- sales of HCFCs should be recorded and reported; and
- controls should be reviewed in 2000.

The proposed controls substantially exceed Australia's international obligations but industry agrees that they provide sufficient HCFCs to meet Australia's current and future needs in a regulatory framework that discourages new or unnecessary uses of HCFCs.

Although non-government organisations prefer that HCFCs not be used at all, they recognise that existing equipment has to be phased out without delaying the transition away from CFCs. Government environment departments, industry and non-government organisations are keen to ensure that current emission controls on CFCs and halons are extended to HCFCs.

Ozone depleting refrigerants must not be released to the atmosphere. It is intended that under Commonwealth legislation (to be introduced by January 1996), that manufacturers or importers of HCFC-123 will be required to accept recovered HCFC-123 and be responsible for its storage, recycling or destruction. A number of initiatives have been implemented to assist in the recycling of CFCs and halons in Australia such as the establishment of the Halon Bank by DASCEM.

16. Summary and conclusions

In Australia, HCFC-123 is currently being used as a replacement for CFC refrigerants in the air conditioning industry and in HCFC blends as replacements (in both portable and fixed extinguisher systems) for halons in the fire protection industry. As with CFCs, HCFCs are being phased out under the *Ozone Protection Act 1989* (Cwlth) due to their ozone depleting potential.

The main sources of occupational and environmental exposure to HCFC-123 are release during chiller maintenance and firefighting.

Data on human health effects from HCFC-123 exposure are limited. However, adequate toxicity data exist from animal studies which, when considered with available human health effects information on structural analogues of HCFC-123, provide a basis for characterising human health risks from acute and chronic exposure to HCFC-123.

Acute effects from inhalation of HCFC-123 are CNS depression, cardiac sensitisation and asphyxiation and possible liver damage. In animals, the most sensitive acute effect is hepatotoxicity which was seen in guinea pigs at 1000 ppm, the lowest dose tested. Data on structural analogues indicate that humans are likely to be less sensitive than guinea pigs with respect to acute liver toxicity. Occupational exposure to acutely toxic levels of HCFC-123, would not be expected for chiller maintenance workers, as monitoring data indicate that peak levels do not usually exceed a few hundred parts per million. Levels of HCFC-123 (in the breathing zone) have been measured around 1000 ppm from indoor discharge of portable fire extinguishers. Although such a level of exposure is unlikely to present a health risk, exposure to other HCFC ingredients will increase the risk.

Health risks for professional firefighters are low due to deployment of personal protective equipment, however, the risk of acute effects may be significant for other workers using portable extinguishers, particularly where discharge takes place in confined work areas. Occupational exposure to extinguishant from fixed (total flooding) systems is not expected to occur under normal discharge conditions. Additional health risks may arise from acute exposure to toxic substances (including phosgene and hydrogen fluoride) formed from both extinguishant combustion and reaction of extinguishant with burning materials.

Chronic effects from inhalation of HCFC-123 are possible damage to liver, pancreas and testes, including a potential carcinogenic hazard in these organs. In view of the available mechanistic and genotoxicity data, a threshold approach was considered appropriate for characterising chronic health risks from exposure to HCFC-123. Animal studies indicate that the NOAEL for chronic effects is 100 ppm HCFC-123. Chiller maintenance workers, although potentially exposed on a routine basis are unlikely to be exposed to levels (airborne) in excess of 5 ppm (TWA) and hence the risk of chronic health effects is considered low.

Similarly, chronic exposure to HCFC-123 extinguishant blends is likely to be minimal due to: (a) deployment of PPE by professional firefighters; and (b) the infrequency of exposure to extinguishant discharges for other worker populations, and hence the risk of chronic effects is likely to be negligible.

Although it has been demonstrated that compliance with existing control measures as described in the relevant codes and standards for the air conditioning industry results in TWA HCFC-123 (airborne) exposure levels of less than 5 ppm and generally less than 1 ppm, peak levels in excess of 100 ppm may be encountered during certain maintenance operations. Emissions of HCFC-123 could be controlled further by paying particular attention to engineering controls and safe work practices recommended for refrigerant transfer and leak testing operations.

Adherence to relevant codes and standards for both fixed and portable extinguisher systems will also contribute significantly to controlling inadvertent emissions and accidental exposures.

In general, the Codes and Standards reviewed for both refrigerants and extinguishants contain sufficient information on engineering controls and safe work practices. Labels and MSDS were generally below National Commission requirements. Labels in particular were lacking adequate risk, safe use and first aid information. It is recommended that an occupational exposure standard (TWA) for HCFC-123 be developed by the National Commission.

HCFC-123 is unlikely to present a public health hazard, except as a consequence of a catastrophic accident (for example, a major chiller failure) or exposure during extinguishant discharge. The likelihood of such events is very small and the scale and duration of any resultant public exposure is expected to be low.

HCFC-123 is not directly toxic to flora and fauna. Indirect biological effects are possible due to the contribution of HCFC-123, albeit small, to ozone depletion. A possibility exists that the degradation product TFA may accumulate within a few decades to potentially toxic levels in certain wetlands. Recent findings suggest that TFA degrades in aerobic and anaerobic environments, but further research on this aspect should be monitored.

17. Recommendations

17.1 Classification

In accordance with the National Commission's *Approved Criteria for Classifying Hazardous Substances,*[100] HCFC-123 is considered to be a 'Hazardous' substance.

With respect to the available health effects data and in accordance with the health effects criteria detailed in the Approved Criteria,[100] HCFC-123 should be classified as:

- CARCINOGEN—CATEGORY 3

HCFC-123 falls into sub-category 3(b), signifying that further studies are necessary before a final decision on carcinogenic status can be made.

Products or preparations containing more than 1% by weight HCFC-123 should also be classified as 'Hazardous' or 'Harmful'. However, products containing other hazardous chemicals (for example, fire extinguishant blends) should be classified taking into account the health effects of all ingredients.

17.2 Provision of information

As HCFC-123 is a hazardous substance, employers and suppliers should be aware of their obligations to provide information about the hazards of the chemical, such as MSDS and labels. Details of these obligations, consistent with employers' general duty of care, are provided in the National Commission's *National Model Regulations to Control Workplace Hazardous Substances*.[124]

17.2.1 Material Safety Data Sheets

The National Commission's *National Code of Practice for the Preparation of Material Safety Data Sheets*[138] provides guidance for the preparation of MSDS.

A survey of the MSDS for HCFC-123 and extinguishant containing HCFC-123 products indicated that some were below the standard considered adequate under this code of practice. The following important items were not included in the majority of MSDS:

- a 'statement of hazardous nature', that is, the hazard classification according to the Approved Criteria[100] or the word 'hazardous';
- information on potential chronic health effects. Animal data should be summarised and the species, route of exposure and exposure levels stated;
- summary of the health effects of potential pyrolysis products of HCFC-123 containing extinguishants;
- information on the use and disposal of the substance, including any restrictions according to the *Ozone Protection Act (1989)* (Cwlth);
- the current status of the Australian exposure standard; ADG Code[135] classification and SUSDP scheduling[139] and details of relevant Australian standards and codes.

It is recommended that manufacturers and importers review and upgrade the MSDS in accordance with the National Commission's *National Code of Practice for the Preparation of Material Safety Data Sheets*[138] and ensure that the above items are addressed. A 'sample' MSDS for HCFC-123 refrigerant is provided at Appendix 1 for guidance.

17.2.2 Labels

The National Commission's *National Code of Practice for the Labelling of Workplace Substances* [140] provides guidance for the labelling of workplace hazardous substances.

It is recommended that labels be reviewed and upgraded to include, risk and safety phrases, first aid procedures, emergency procedures and conform to ingredient disclosure requirements—that is, HCFC-123 is a 'Type I' hazardous ingredient and as such should be disclosed on the label when present in a mixture above 1% w/w. Consistent with its classification, the following risk and safety phrases are recommended for HCFC-123:

Risk phrases	
R40	Possible risk of irreversible effects
Safety phrases	
S3/9	Keep in a cool, well ventilated place.
S23	Do not breath vapour.
S35	This material and its container must be disposed of in a safe way.
S36	Wear suitable protective clothing.
S41	In the case of fire and/or explosion, do not breathe fumes.

HCFC-blend extinguishants containing other hazardous ingredients should be classified and labelled accordingly. Risk phrase R40 will apply to all extinguishant blends containing HCFC-123 above 1% w/w. Appropriate safety phrases should be selected from the National Commission's *National Code of Practice for the Labelling of Workplace Substances.*[140]

Labels for portable fire extinguishers containing HCFC-123 should take into account the requirements of the National Commission's *National Code of Practice for the Labelling of Workplace Substances.*[140] Collaboration with the Fire Protection Group of Australia Standards is encouraged with respect to this issue.

Labels for portable fire extinguishers (containing HCFC-123) should contain a prominent warning about using the extinguisher in a confined space and include the appropriate test ratings, that is, Classes A–F according to AS 1850.[142]

17.2.3 Training and education

Guidelines for the induction and training of workers potentially exposed to hazardous substances are provided in the National Commission's *National Model Regulations and Code of Practice for the Control of Workplace Hazardous Substances.*[124]

Workers potentially exposed to HCFC-123 need to be trained in safe work practices to be followed in the handling, storage, transportation and disposal of the chemical.

For chiller maintenance technicians, training provided at induction should include relevant information from the *Australian Refrigeration and Air Conditioning Code of Good Practice*,[40] the MSDS and Australian Standard 1677—*Refrigerating Systems*,[15] and should be reinforced at regular intervals. In particular, training should provide information on acute and chronic effects from exposure to HCFC-123 and should address appropriate control and safety measures required to minimise both occupational and environmental exposure.

For extinguishant maintenance workers, training provided at induction should include relevant information from appropriate Australian Standards (including AS/NZS 1851.12[130]) and the FPIAA Code of Practice.[41]

For personnel working in areas protected by portable HCFC-blend extinguishants, employers should ensure that adequate training is provided on the safe use of these extinguishants, which should include adequate information on acute health hazards (including first aid) and appropriate warning and instruction on extinguishant discharges in confined work areas.

17.3 Occupational control measures

Under the National Commission's *National Model Regulations and Code of Practice to Control Workplace Hazardous Substances*,[124] control measures must be implemented to minimise health risks during handling and use of hazardous substances. With respect to HCFC-123, control measures should be implemented to minimise incidental and accidental exposure to refrigerant and extinguishant vapours.

With regard to the use of HCFC-123 as a *refrigerant* it is recommended that:

- particular attention should be given to engineering control measures and safe work practices aimed at reducing HCFC-123 loss during refrigerant transfer and leak test operations;
- refrigerant and inert gas (usually N_2) mixtures (used in pressure test and leak test operations) should be recovered;
- leak testing should be conducted at least quarterly;
- re-seatable bursting/rupture discs (piped to the low pressure side of the system) should be installed;
- the use of high efficiency purge equipment and purge filter reprocessing (to recover or recycle HCFC-123) be encouraged;
- retrofitting existing chiller systems to use HCFC-123 should only be carried out after consultation with equipment and component manufacturers;
- mechanical ventilation should be installed in machine rooms where chillers are operating on HCFC-123 refrigerant; and
- where a maintenance technician is required to work at an installation on their own, a personal 'motion detector' alarm should be worn.

With regard to the use of HCFC-123 as an *extinguishant* it is recommended that:

- both fixed systems and portable extinguishers containing HCFC-123 should be regularly (at least annually) inspected and tested for proper operation and the inspection report (with recommendations) should be filed with the owner of the equipment;
- extinguishant release mechanisms should be locked (by key) during maintenance and testing of total flooding (fixed) systems;
- a non-combustible, non-toxic trace gas (with low odour threshold) should be added to portable extinguishers containing HCFC-123 to aid in leak detection;
- employers utilising portable extinguishers containing HCFC-123 should be required to provide employees with adequate training in their use; and
- the sales literature, instructions for use and label of portable fire extinguishers containing HCFC-123 should instruct the operator to evacuate any area into which the extinguishant has been discharged and to delay re-entry until the area has been thoroughly ventilated.

17.4 Exposure standard

It is recommended that an occupational exposure standard for HCFC-123 be developed by the National Commission.

From the information made available for assessment it is recommended that the TWA exposure standard is based on the NOAEL for liver effects, determined at 100 ppm (0.6 g/m^3) HCFC-123 in repeat dose animal studies. This is considered a reliable NOAEL, derived from a well conducted two-generation reproduction study, and supported by other mechanistic and toxicity studies.

There is no indication that a STEL or 'skin notation' should apply.

17.5 Health surveillance

It is considered that HCFC-123 is unlikely to adversely affect the health of workers under the present conditions of use. In addition, air monitoring techniques are considered to provide an accurate estimate of exposure.

Therefore, it is recommended that HCFC-123 not be considered for addition to Schedule 3 of the National Commission's *National Model Regulations for the Control of Workplace Hazardous Substances*.[124] Under regulations introduced in Commonwealth, State or Territory government jurisdictions, in accordance with these model regulations, employers will need to provide health surveillance in workplaces where assessment shows that exposure to HCFC-123 may result in a substance-related health effect.

17.6 Revision of codes of practice and Australian Standards

In order to improve the usefulness of the *Australian Refrigeration and Air Conditioning Code of Good Practice*[40] and the *Australian Code of Practice for Design, Installation, Inspection and Testing of Gaseous Fire Extinguishants*,[41] it is recommended that consideration be given to revising these documents to provide more complete information on occupational health and safety. Such information may include: health hazards; precautions for use, for example, specifications for personal protective equipment and safe handling information, for example, requirements for storage and disposal of refrigerant and extinguishant products.

Until Australian Standard 1677—*Refrigerating Systems*[15] has been updated,* it is recommended that the US ASHRAE *Safety Code for Mechanical Refrigeration*[16] be used in conjunction with the abovementioned Australian codes.

Based on its health effects, it is recommended that HCFC-123 be classified as a Group 2 Refrigerant for the purposes of updating Australian Standard 1677—*Refrigerating Systems*.[15]

It is recommended that future revisions of the Australian Standards for portable extinguishers (AS 1841.1[141]) and gaseous (fixed) extinguishers (AS/NZS 4214.5[128]) take into account the National Commission's *National Code of Practice for the Labelling of Workplace Substances*.[140]

17.7 Transport

It is recommended that the Federal Office of Road Safety's Advisory Committee for the Transport of Dangerous Goods (ACTDG) consider HCFC-123 for classification as a Class 9 Dangerous Good in view of the following hazardous properties:

- ozone depleting potential;
- potential acute and chronic health effects; and
- toxic pyrolysis products.

17.8 Environmental protection

Use of HCFC-123 to replace CFCs in cooling applications is recommended on environmental grounds, since the ODP and GWP of the replacement substance are typically some 50 times lower than those for CFCs.

Similarly, the use of extinguishant blends containing HCFC-123 to replace halons in certain firefighting applications is recommended because of the major reduction in ODP.

Users should be aware that HCFC-123 is not environmentally innocuous, and that its use will only be acceptable as an interim measure pending development of alternatives with lower ozone

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* Australian Standard AS1677 is currently being revised and will take into account certain requirements of ASHRAE standards and the ISO including requirements for the newer alternative refrigerants.

depletion potential. Australia's ratification of the Copenhagen amendment to the Montreal Protocol requires that domestic consumption of HCFCs be frozen in 1996, followed by reductions in use of 35% by 2004, 65% by 2010, 90% by 2015, 99.5% by 2020 and total phase-out by 2030.

In view of the phase-out schedule required by the Copenhagen Amendment to the Montreal Protocol, manufacturers of equipment requiring HCFCs, including HCFC-123, should investigate options for converting to other forms of refrigeration and fire protection technology.

Manufacturers, distributors and users must minimise atmospheric emissions of HCFC-123 by adhering to the *Australian Refrigeration and Air Conditioning Code of Good Practice*,[40] and the FPIAA's Code of Practice.[41]

Existing legislative controls on halons, including requirements for their recovery and safe disposal, should be extended to HCFCs.

17.9 Further studies

17.9.1 Toxicological studies

Mechanisms of carcinogenicity

Ideally, further research should concentrate on establishing the relevance of the compound related benign tumours to humans, particularly cholangiofibromas and pancreatic adenomas. The available mechanistic data indicate that the rat may not be the most suitable animal model for characterising potential carcinogenic effects of HCFC-123 in humans. For pancreatic tumour studies, the BOP hamster model has been considered more relevant (to humans), because of tumour type similarities and with respect to peroxisome proliferation, the guinea pig is considered a more suitable model for humans. While it is appreciated that life-time studies in these species may not be a viable option for a number of reasons, for example, HCFC-123 is only being used as an interim alternative to CFCs, it is recommended that efforts are made to further elucidate the mechanisms of HCFC-123-induced tumours in rats, in an attempt to characterise potential human hazards. Further studies might include:

- the relationship of hormone perturbation to hepatic peroxisome proliferation; and
- the relevance of hormone perturbation to pancreatic adenoma and cholangiofibroma induction.

Reproductive effects

Experimental evidence from a two-generation reproductive toxicity study in rats indicate that reduced weight gain and delayed sexual maturation in offspring may result from HCFC-123 transfer through breast milk, that is, a lactational effect. This could be investigated further by:

- establishing whether this effect is due to a reduced intake of breast milk by pups in exposed groups; and
- analysing breast milk to establish whether HCFC-123 is present in potentially toxic levels.

17.9.2 Monitoring studies

It is recommended that monitoring studies be carried out to establish potential airborne levels of total HCFCs from discharge of HCFC blends from portable (hand-held) extinguishers (3–5 kg), particularly in confined working areas.

Quantitative information on yields of thermal degradation products of HCFC-123 and HCFC-blend extinguishants under high temperature conditions would assist in characterising the acute health risk or hazard during exposure.

18. Secondary notification

Under the *Industrial Chemicals (Notification and Assessment) Act 1989* (Cwlth), secondary notification of HCFC-123 shall be required if any of the circumstances under subsection 64(2) of the Act arise.

Appendix 1

Sample Material Safety Data Sheet for HCFC-123

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HCFC-123 is classified as Hazardous according to the National Occupational health and Safety Commission's *Approved Criteria for Classifying Hazardous Substances* [NOHSC:1008(1994)].

Company details

Company name	
Address	
	State Postcode
Telephone number	Emergency telephone number
Facsimile number	Telex number

Identification

Product name	2,2-dichloro-1,1,1-trifluoroethane
Other names	HCFC-123
Manufacturer's product code	
UN Number	Not allocated
Dangerous goods class and subsidiary risk	Not allocated
~~Hazchem~~ code	Not allocated
Poisons Schedule number	None allocated
Use	As a refrigerant

Physical description and properties

Appearance
Colourless liquid (at 25 °C)

Boiling point → Freezing point
27.6 °C (at 760 mm Hg) → −107 °C

Vapour pressure
670 mm Hg (at 25 °C)

Specific Gravity
1.46 (at 25 °C)

Flashpoint
Does not ignite

Flammability limits
Non-flammable

Solubility in water
2.1 g/L (at 25 °C)

Other properties

Odour: Slight ethereal odour

pH: Neutral

Evaporation Rate: < 1 (CCl_4 = 1.0)

Partition Coefficient: Log $P_{o/w}$ = 2.3 – 2.9

Ingredients

Chemical entity	CAS Number	Proportion
HCFC-123	306-83-2	
Impurities		

Health hazard information

HEALTH EFFECTS

Acute

Inhalation: At high concentrations may cause central nervous system and cardiac (sensitisation) effects and liver damage.

Eye: Slight irritation to eyes in animal studies.

Skin: Not irritating to skin in animal studies.

Swallowed: Low acute oral toxicity in animal studies.

Other: At very high concentrations may cause asphyxiation.

Chronic

Inhalation: No human evidence. Repeated or prolonged exposure caused liver damage and an increase of benign tumours in animal studies.

Contraindications

Individuals with pre-existing cardiovascular system disease may be predisposed to adverse health effects caused by acute exposure.

Workers who are taking sympathomimetic medication should be warned about potential cardiovascular effects from excessive exposure to HCFC-123.

FIRST AID

(Show this MSDS to medical doctor if consulted)

Swallowed: If swallowed no specific intervention is indicated. DO NOT INDUCE VOMITING. Drinking water may be beneficial. Consult a physician if necessary.

Eye: In case of contact with eyes, rinse with plenty of water.

Skin: In case of skin contact wash area with water.

Inhaled: If exposed to high concentrations remove to fresh air. Keep patient calm. If breathing is difficult give oxygen. Give artificial respiration if patient not breathing.

First Aid Facilities

Advice to doctor

No specific antidote. Treat symptomatically.

Use of adrenalin or other catecholamines may be contraindicated. Ventricular arrhythmias may be better treated with beta-blocking agents.

Precautions for use

EXPOSURE STANDARDS

National (Worksafe): Not allocated

International: Not allocated

ENGINEERING CONTROLS

Enclosure of process materials & isolation of reaction vessels with proper design of filling heads should be implemented to limit exposure during manufacture and packaging.

Appropriate fittings should be used for opening /decanting containers.

When opening/decanting/transferring HCFC-123 indoors, local exhaust ventilation should be used.

Approved low-pressure refrigerant recovery/recycle equipment should be used.

Chiller pressure relief devices (refer to AS 1210 & AS 1677) should be installed and vented to location outside equipment room.

Automated HCFC-123 detector (interlocked with alarm) should be installed at chiller installation site.

PERSONAL PROTECTION

Under normal maintenance conditions no respiratory protection is required.

Respiratory protection (including SCBA) to be *readily available* at chiller installations, storage and filling areas (refer to AS1319; AS 1715 and AS 1716).

Personal protective equipment to be selected in accordance with appropriate Australian Standards.

Where a technician is required to work at an installation unassisted, PPE should include a personal 'motion detector/alarm'.

FLAMMABILITY

HCFC-123 is not flammable under conditions of use. Materials with similar chemical structure have been shown to be combustible at low pressure when mixed with air (>60% by volume).

Safe handling information

STORAGE AND TRANSPORT

Quantities of HCFC-123 stored at chiller installation to be limited to reasonable requirements.

Containers should be stored away from direct sunlight and kept below specified temperature (TO BE SPECIFIED).

Containers should be kept away from incompatible materials (TO BE SPECIFIED).

Empty containers to be stored outside chiller installation or in a well ventilated location inside.

SPILLS AND DISPOSAL

Evacuate area of spill and ventilate by natural or mechanical means, taking care to ventilate low level confined areas.

Contain spill with sand, earth, sawdust or other absorbent material and transfer to steel drum(s) for recovery/disposal.

Product and container to be recovered/held for recycling/reprocessing or disposal in an approved manner (TO BE SPECIFIED).

FIRE/EXPLOSION HAZARD

Negligible fire hazard when exposed to heat or flame. May decompose in a fire producing toxic vapours of chlorine; hydrogen chloride, hydrogen fluoride, dichloroethylene and phosgene. DO NOT BREATH FUMES.

Heated containers may generate explosive pressures. Heated containers should be removed (provided they can be moved safely) from hazard area and cooled with water.

No 'Hazchem Code' allocated.

Potentially dangerous interaction may occur with certain materials (TO BE SPECIFIED).

Other information

Use/importation information

In Australia, the importation and use of HCFC-123 is restricted according to the *Ozone Protection Act (1989)*, which is implemented by the Environment Protection Agency (EPA).

Animal toxicity data

Acute *Oral* (ALD) 9000 mg/kg body weight (rat)

Acute *Dermal* (LD_{50}) => 2000 mg/kg body weight (rat & rabbit)

Acute *Inhalation* ($LC_{50[4hr]}$) => 32,000 ppm (rat)

Acute *Inhalation* (liver damage -- LOAEL) = 1000 ppm (guinea pig)

Acute *Inhalation* (cardiac sensitisation -- NOAEL) = 10,300 ppm (dog)

Acute *Inhalation* (anaesthetic effects -- NOEL) = 2,500 ppm (rat)

HCFC-123 does NOT appear to be genotoxic

Chronic Inhalation (tumourigenicity -- LOAEL) = 300 ppm (rat)

Chronic Inhalation (liver effects -- NOAEL) = 100 ppm (rat)

Use/importation information

In Australia, the importation and use of HCFC-123 is restricted according to the *Ozone Protection Act (1989)*, which is implemented by the Environment Protection Agency (EPA).

Animal toxicity data

Acute *Oral* (ALD) 9000 mg/kg body weight (rat)

Acute *Dermal* (LD_{50}) = > 2000 mg/kg body weight (rat & rabbit)

Acute *Inhalation* ($LC_{50\,[4hr]}$) = > 32,000 ppm (rat)

Acute *Inhalation* (liver damage - LOAEL) = 1000 ppm (guinea pig)

Acute *Inhalation* (cardiac sensitisation - NOAEL) = 10,300 ppm (dog)

Acute *Inhalation* (anaesthetic effects - NOEL) = 2,500 ppm (rat)

HCFC-123 does NOT appear to be genotoxic

Chronic Inhalation (tumourigenicity - LOAEL) = 300 ppm (rat)

Chronic Inhalation (liver effects - NOAEL) = 100 ppm (rat)

Other information

ENVIRONMENTAL DATA

Mobility

HCFC-123 is moderately mobile in soils (soil organic adsorption coefficient = 430) and may contaminate ground water. Spills should be cleaned up immediately.

Persistence

HCFC-123 is not readily biodegradable. It will evaporate quickly from surface water (half-life about 4 hr) but may persist in ground water.

Bioconcentration

HCFC-123 has a low potential for bioaccumulation (estimated bioconcentration factors (range 10-33).

Aquatic toxicity

HCFC-123 is slightly toxic to aquatic organisms:

Acute (96hr) LC_{50} > 350 mg/L (Fathead minnow)

Acute (96hr) LC_{50} = 55 mg/L (Rainbow trout)

Acute (48hr) immobilisation EC_{50} = 17.3 – 45.8 mg/L (Daphnia magna)

96 hr growth inhibition EC_{50} = 67.8 mg/L (Selenastrum capricornutum)

Ozone depletion

HCFC-123 has an Ozone Depleting Potential (ODP) of 0.02. It is an interim replacement for CFCs, being scheduled for phase out by 2030 under the Copenhagen Amendment to the Montreal Protocol on Substances that Deplete the Ozone Layer.

Further Information

Association of Fluorocarbon Consumers and Manufacturers, Australian Refrigeration and Air Conditioning Code of Good Practice, HB40-1992, 24 pp., Canberra, 1992.

National Industrial Chemicals Notification & Assessment Scheme, Full Public Report Priority Existing Chemical No. 4 HCFC-123, AGPS, Canberra, 1996.

Standards Australia, 'Australian Standard AS1677 - Refrigerating Systems', Sydney, 1986.

American Society of Heating, Refrigerating and Air Conditioning Engineers, 'ASHRAE Standard 15-1994 - Safety Code for Mechanical Refrigeration', Atlanta, 1994.

Contact point

Contact name	Telephone number
Position title	
Address	
State	Postcode / Country

Control measures for managing risks of exposure to HCFC-123 refrigerant

A2.1 Engineering controls and equipment design

- Containers (drums) to withstand specified temperature and pressure.
- Appropriate fittings (valve) to refrigerant container during opening.
- Use of approved low-pressure refrigerant recovery/recycle equipment.*†
- Appropriate fittings/connections (for example, hoses‡ and vent lines) for refrigerant container during transfer procedures.
- All chiller materials (hoses, gaskets, motor insulation etc.,) to be compatible§ with HCFC-123.
- Where refrigerant cylinders are manifolded together, single direction flow valves to be used to prevent gravity overfill of cylinders (AS 2030.1).
- Installation of mechanical ventilation** at chiller site and refrigerant storage site.
- Appropriate location and air flow for mechanical ventilation system (AS 1677).
- Use of a high efficiency purge unit†† (in accordance with AFCAM Code of Practice HB-40,1992) for all new and retrofitted chillers.
- Installation of purge monitor (to indicate purging time) (AFCAM 1992).
- Installation of automated gas bubble (non-condensables) sensor (with alarm) in liquid line of chiller.
- Installation of automated refrigerant sensor/detector (with alarm) at chiller site (AS 1677) (with periodic testing).
- Location of sensor/detector(s) in area(s) where refrigerant vapour leaks are most likely, accounting for air flow patterns in equipment room.
- Use of suitably constructed chiller pressure vessels (AS 1210).
- Where pressurisation is used to prevent ingress of air during shutdown of low pressure chillers, a high pressure limit switch should be installed.
- Installation of pressure relief devices (AS 1210 and AS 1677) vented to location outside equipment room.

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* The Australian Code (AFCAM 1992) requires that both refrigerant liquid and vapour be recovered, with pressure reduced to 3 kPa.

† To avoid mixing of refrigerants it may be necessary to use dedicated equipment. No Australian Standard developed—ARI Standard 740 (1991) currently used in air-conditioning industry.

‡ No Australian Standard developed—ARI Standard 720 (1988) currently used in air-conditioning industry.

§ HCFC-123 attacks the elastomers present in seals and gaskets used in chillers operating on other refrigerants including CFC-11.

** Interlocked with automated refrigerant detector (AS 1677).

†† No Australian Standard developed—ARI Standard 580 (1993) currently used in air-conditioning industry.

- Isolation/stop valves fitted at appropriate locations on compressor, condenser and evaporator (AS 1210).
- Stop valves connecting refrigerant-containing parts to atmosphere to be capped or locked closed when not in use.

A2.2 Safe work practices

- Initial opening of sealed refrigerant containers to be carried out outdoors if possible.
- Proper resealing of refrigerant containers.
- Storage of refrigerant containers below specified temperature.
- Storage of refrigerant containers away from incompatible materials.
- Storage of empty refrigerant containers outside of chiller room (if feasible) away from building ventilation air intakes.
- Quantities of refrigerant stored at chiller installation (indoors) to be limited to reasonable requirements (20% of refrigerant charge) (AS1677).
- Quantity of refrigerant (in chiller) required for duty to be kept to a minimum (for example, as computed or as determined by sight glass).
- Prompt clean up of leaks and spills—procedure to be pre-planned.
- Occupancy of chiller installation restricted to personnel with authorised access.
- Entry to plant room carried out under supervision following alarm actuation.
- Care should be taken when working (for extended periods) underneath the chiller as higher concentrations of HCFC-123 vapour are likely to occur at floor level.
- Recovered refrigerant charge to be metered (weight or volume) to ensure maximum recovery.
- Recovery cylinders to be used only as designated (by colour coding, labelling etc) and dedicated to HCFC-123 (AS 2030.1).
- Retrofitting a system for HCFC-123 to be carried out after consultation with equipment/component manufacturers (AFCAM Code of Practice HB-40,1992).
- Regular monitoring of the chiller integrity by purge system monitoring and regular leak testing*.
- Leak testing of connecting pipework to be carried out before charging of refrigerant systems.
- Correct procedures for refrigerant leak testing (AS1677).
- Refrigerant and inert gas (usually N2) mixtures (used in pressure test and leak test operations) to be recovered or as a minimum not to be exhausted into plant room.
- The labelling, colour coding and nameplates for a retrofitted system to be changed to identify new refrigerant and/or lubricant (AS1319)
- Containers to be properly labelled (NOHSC:2012,1994).
- Correct procedures (in compliance with Federal and/or State regulations) for the disposal transportation and storage of HCFC-123 contaminated oil, oil filters and filter drier cores.
- Refrigerant to be held for reprocessing or disposal in an approved manner (in accordance with appropriate government legislation).
- MSDS to be available at storage facility and chiller installation (NOHSC:2011, 1994).

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* At least every three months according to AFCAM Code of Practice (AFCAM 1992).

A2.3 Personal protective equipment

- Appropriate gloves (AS 2161), safety glasses (AS 1336 and AS 1337) and safety shoes (AS/NZS 2210.2) to be used when handling refrigerant containers.
- Respiratory protection (including SCBA) to be available at storage facility and outside chiller room (AS1319, AS1715 and AS1716).
- A personal 'motion detector' alarm has also been proposed as a requisite part of ppe. Such an alarm will sound if a worker is immobilised for a preset period of time.

A2.4 Note

It should be emphasised that the above is not a listing of each and every control measure relevant to the handling and use of HCFC blend extinguishants, but comprises the most significant initiatives from information provided for assessment. Relevant Australian Codes/Standards are quoted in parentheses.

Control measures for managing risks of exposure to extinguishants containing HCFC-123*

A3.1 Engineering controls and equipment design

- Extinguishant cylinders to withstand specified pressure (AS 1210 and AS 2030.1).
- Containers to have a reliable means of indicating pressure of contents.
- Appropriate fittings/connections for extinguishant transfer/filling operations (AS 2030.1).
- Specification for both portable extinguishers and fixed systems to meet the Building Code of Australia and a 'compliance certificate' to be obtained from appropriate local government authority.
- Correct specification (AS/NZS 4214.5) for fixed extinguishant 'distribution system' (for example, piping, valves†, spans and joints and pressure relief devices).
- Compatible system components (for example, piping, valves, pressure relief switches and gauges) for retrofitted extinguishing systems.
- All components to comply with appropriate Australian Standards and to be listed by the Commonwealth Scientific Services Laboratory (FPIAA 1995).
- Appropriate design, installation and commissioning of detection systems (AS 1603.4; AS 1670).
- Extinguishant discharge (for total flooding (fixed) systems) to be completed in specified time (AS/NZS 4214.5).
- Installation of automated mechanical ventilation system (with fixed extinguishant systems) for prompt ventilation after discharge.
- Concentration of discharged extinguishant (for total flooding (fixed) systems) not to exceed specified limits (AS/NZS 4214.5).
- Extinguishant discharge to comply with distribution and holding requirements (AS/NZS 4214.5).
- Quantity of extinguishant in system (i.e., primary agent supply) to be the least amount required for the largest single fire hazard protected (FPIAA 1995).
- Provision for isolation or shut down of air handling system for 'protected enclosure' (FPIAA 1995).
- Precautions (for example, sealed openings or automatic closures) should be taken to prevent loss of discharged extinguishant to adjacent work areas.
- Factors resulting in unwanted discharge during testing/service to be thoroughly evaluated and corrected‡.

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* NAF S-III(HCFC Blend A) and NAF P-III (HCFC Blend C) are currently the only such extinguishants used in Australia.

† Some HCFC extinguishants may not be compatible with the elastomers used in halon system valves.

‡ Equipment lockout or service disconnects can be instrumental in preventing false discharges during testing/service.

- Adherence to 'protected enclosure requirements' (AS/NZS 4214.5).

A3.2 Safe work practices

- Cylinders to be inspected in accordance with government requirements and standards.
- Correct procedure* to be followed for filling of extinguishant cylinders (AS 2030.1).
- Extinguishant cylinders to be charged to correct filling ratio/density (AS/NZS 4214.1 and AS 1841.1).
- Storage of extinguishant containers below specified temperature.
- Storage of extinguishant containers away from incompatible substances.
- Prompt clean-up of leaks and spills—procedure to be pre-planned.
- Disposal of extinguishant to be carried out in accordance with appropriate government legislation.
- Maintenance of fire protection equipment according to appropriate standards (AS/NZS 1851.12)
- Extinguishant discharge test carried out according to specified protocol (AS/NZS 4214.1; AS 1841.7; AS/NZS 1851.12; FPIAA 1995).
- Commissioning tests for installed systems to be carried out in the presence of occupational safety officer(s) (AS/NZS 4214.1).
- Certification of testing to be provided by installation contractor (AS/NZS 4214.5).
- Retrofitting of existing fire extinguishing equipment with HCFC-123 containing agents should be approved by the appropriate authority.
- Cylinders to be properly marked/labelled (NOHSC:2012, 1994; AS 1841.1; AS/NZS 4214.1; FPIAA 1995).
- MSDS to be available at storage facility (NOHSC 1994).

Personal protective equipment

- Appropriate gloves (AS 2161), safety glasses (AS 1336 and AS 1337) and safety shoes (AS/NZS 2210.2) to be used when handling and/or filling extinguishant containers.
- Respiratory protection (including self-contained breathing apparatus) to be available at storage facility/filling site. (AS1319, AS1715 and AS1716).
- Appropriate equipment for firefighters (including AS1715, AS 2375, AS 4067).

Note

It should be emphasised that the above is not a listing of each and every control measure relevant to the handling and use of HCFC blend extinguishants, but comprises the most significant initiatives from information provided for assessment. Relevant Australian Codes/Standards are quoted in parentheses.

* In accordance with manufacturers recommendations.

Chemical names, abbreviations and synonyms

CFC	chlorofluorocarbon
CFC-11	trichlorofluoromethane
CFC-12	dichlorodifluoromethane
CFC-113	1,1,2-trichloro-1,2,2-trifluoroethane
CFC-114	1,2-dichloro-1,1,2,2-tetrafluoroethane
CFC-115	chloropentafluoroethane
CFC-114b1	1-chloro-2-bromotetrafluoroethane
CFC-216	dichlorohexafluoropropane
CFC-500	CFC-12 (73.8%); HCFC-152a (26.2%)
CFC-502	CFC-115 (51.2%); CFC-12 (48.8%)
CFC-1112a	1,1-dichloro-2,2-difluoroethene
CFC-1113	1-chloro-1,2,2-trifluoroethene
CFC-1317mx	chloroheptafluorobutene
Cl2	chlorine
F2	fluorine
FC-218	octafluoropropane
FIC	fluoroiodocarbon
Halon 1211	bromochlorodifluoromethane
Halon 1301	bromotrifluoromethane
Halothane	see HCFC-123b1
Halotron-1	HCFC-123 (93%) (plus proprietary additive)
HCFC	hydrochlorofluorocarbon
HCFC-22	chlorodifluoromethane
HCFC-121	1,1,2,2-tetrachloro-1-fluoroethane
HCFC-123	2,2-dichloro-1,1,1-trifluoroethane
HCFC-123a	1,2-dichloro-1,1,2-trifluoroethane
HCFC-123b	1,1-dichloro-1,2,2-trifluoroethane
HCFC-123b1	1,1,1-trifluoro-2-bromo-2-chloroethane
HCFC-124	1-chloro-1,2,2,2-tetrafluoroethane
HCFC-124a	1-chloro-1,1,2,2-tetrafluoroethane
HCFC-133a	1-chloro-2,2,2-trifluoroethane
HCFC-142b	1-chloro-1,1-difluoroethane
HCFC-152a	1,1-difluoroethane
HCFC Blend A	see NAF S-III
HCFC Blend C	see NAF P-III

HCFC-Blend D	see Halotron-1
HCI	hydrochloric acid
HF	hydrofluoric acid
HFC	hydrofluorocarbon
HFC-32	difluoromethane
HFC-143a	1,1,1-trifluoroethane
HFC-134a	1,1,1,2-tetrafluoroethane
HFC-227ea	1,1,1,2,3,3,3-heptafluoropropane
NAF P-III	HCFC-123 (55%); HCFC-124 (31%); HFC-134a (10%); 4-isopropenyl-1-methylcyclohexene (4%)
NAF S-III	HCFC-22 (82%); HCFC-124 (9.5%); HCFC-123 (4.75%); 4-isopropenyl-1-methylcyclohexene (3.75%)
R-22	see HCFC-22
TFA	trifluoroacetic acid
TFC	trifluoroacetyl chloride
WY-14643	4-chloro-6-(2,3-dimethylphenyl)amino-2-pyrimidinylthioacetic acid

Acronyms and Abbreviations

ACF	Australian Conservation Foundation
ACGIH	American Conference of Governmental Industrial Hygienists
ACTDG	Advisory Committee for the Transport of Dangerous Goods
ADG	Australian Dangerous Goods
AEL	allowable exposure limit
AFCAM	Association of Fluorocarbon Consumers and Manufacturers
AFEAS	Alternative Fluorocarbon Environmental Acceptability Study
AICS	Australian Inventory of Chemical Substances
ALD	Approximate lethal dose
ALP	alkaline phosphatase
ALT	alanine transaminase
ANSI	American National Standards Institute
ANZECC	Australian and New Zealand Environment and Conservation Council
ARI	American Air Conditioning and Refrigeration Institute
AS	Australian Standard
AS/NZS	Australian/New Zealand Standard
ASHRAE	American Society of Heating, Refrigeration and Air Conditioning Engineers
AST	aspartate transaminase
BAT	Biologischer Arbeitsstoff Toleranz–Wert (Biological Tolerance Value)
CAS	Chemical Abstracts Services
CCK	cholecystokinin
CFC	chlorofluorocarbon
CNS	central nervous system
COPA	Commonwealth Ozone Protection Act
CPI	cell proliferation index
DASCEM	Department of Administrative Services Centre for Environmental Management
DFG	Deutche Forschungsgemeinschaft
DNA	deoxyribonucleic acid
ECETOC	European Centre for Ecotoxicology and Toxicology of Chemicals
EEL	emergency exposure limit
EPA	Environment Protection Agency
EPG	Emergency Procedure Guide
EU	European Union (formerly called the EEC)
FID	flame ionisation detection
FPIAA	Fire Protection Industry Association of Australia
GC	gas chromatography
GC-MS	gas chromatography—mass spectrometry

GWP	global warming potential
HCFC	hydrochlorofluorocarbon
HSDB	Hazardous Substances Database
ICDH	isocitrate dehydrogenase
IPCS	International Programme on Chemical Safety
IR	infrared
IRPTC	International Register for Potentially Toxic Chemicals
ISO	International Organization for Standardization
JETOC	Japan Chemical Industry Ecology—Toxicology and Information Center
LH	luteinising Hormone
LHRH	luteinising Hormone Release Hormone
LOAEL	lowest observed adverse effect level
LOEL	lowest observed effect level
MAK	Maximale Arbeitsplatz Konzentration (Maximum Workplace Concentration)
MSDS	Material Safety Data Sheet
NFPA	National Fire Protection Association (US)
NICNAS	National Industrial Chemicals Notification and Assessment Scheme
NIOSH	National Institute of Occupational Safety and Health
NOAEL	no observed adverse effect level
NOEL	no observed effect level
NOHSC	National Occupational Health and Safety Commission
ODP	ozone depleting potential
OECD	Organisation for Economic Cooperation and Development
PPE	personal protective equipment
PAFT	Program for Alternative Fluorocarbon Toxicity Testing
POCs	products of combustion
QSAR	Quantitative Structure Activity Relationships
RTECS	Register of Toxic Effects of Chemical Substances
SCBA	self contained breathing apparatus
SNAP	Significant New Alternatives Program
STEL	short term exposure limit
TWA	time weighted average
UNEP	United Nations Environment Programme
UDS	unscheduled DNA synthesis
US EPA	United States Environmental Protection Agency
WEEL	

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