Toxicity of Possible Impurities and By-products in Fluorocarbon Products

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CONTENTS

EXECUTIVE SUMMARY

This report has been produced to accompany the ongoing series of reviews on fluorocarbons under the ECETOC Joint Assessment of Commodity Chemicals (JACC) programme. It presents the available data on the physico-chemical properties and a critical evaluation of the toxicity of 30 (halogenated) hydrocarbons that may be found as impurities or by-products in hydrofluorocarbon and hydrochlorofluorocarbon products. Most of the commercial fluorocarbons are not toxic (many are used as refrigerants), but the presence of a highly toxic compound, even at a modest level, could alter their toxicity.

Typically, the parent substances are produced to high levels of purity (≥ 99%). Therefore, the presence of low levels of impurities will not be a concern regarding REACH approval. However, the identification of potential impurities that could be carcinogens, mutagens or reproductive toxicants (CMRs) will enable producers to set maximum levels and minimise these impurities in their commercial products. This will thus avoid the need to register these impurities. Products having higher levels of CMRs will require separate registration in addition to the requirements for the higher purity materials.

Looking over the list of 30 chemical substances covered in this report, there appear both saturated and unsaturated compounds with a short carbon chain (C1 to C4). Larger molecules are easily removed in the product purification steps. As most of the substances are not commercial products, generally there is little toxicology information available on them. Also in some cases, reports of acute lethal concentrations vary widely and one must suspect that the purity of some of the materials may not have been known.

A list of impurities or by-products reviewed by other organisations is provided.

1. SUMMARY AND CONCLUSIONS

This report contains brief summaries on the physico-chemical properties and toxicity of 30 halogenated hydrocarbons that can be found as impurities in various commercial hydrofluorocarbons (HFCs) and hydrochlorofluorocarbons (HCFCs) [a]. (A list of impurities or by-products reviewed by other organisations is provided.) As many of the commercial substances are not very toxic they have high occupational exposure levels (OELs). If a highly toxic impurity were present even at a modest level, e.g. 0.1%, it could influence the toxicity profile of the parent substance. For example, the OEL for dichlorodifluoromethane (CFC-12) [b] is 1,000 ppm as an 8-hour time-weighted-average. If a sample of CFC-12 contained 0.1% of dichloroacetylene, at 1,000 ppm for CFC-12, the level of exposure to dichloroacetylene would be 1 ppm. This is 10 times the maximum recommended OEL in the UK and the USA. It is also 100 times the maximum level generally recommended for an impurity with that OEL. (To avoid additive effects, the maximum levels for impurities are generally set at 1/10 the recommended maximum for the same material if pure.) A method to calculate the maximum recommended guidance levels has been published (Millischer *et al*, 2007).

The chemicals covered in this report include saturated (and unsaturated) compounds. Some are methanes while others are ethanes, propanes or butanes (ethenes, propenes or butenes). It is unlikely to find larger molecules as they are easily removed during production in the purification steps. As most of these substances are not commercial products, generally there is very little toxicological information available on them. Also in some cases, reports of acute lethal concentrations (ALCs) vary widely and it must be assumed that the purity of some of the materials may not have been known.

Some generalisations, however, can be made. Those substances with a double bond tend to be more toxic than the saturated substances. Dichloroacetylene falls into this category of unsaturated compounds. It is a highly toxic chemical that also causes kidney cancer. These unsaturated substances may also form cysteine conjugates that are highly toxic to the kidney. The following chemicals have reported median lethal concentrations (LC_{50}s) of less than 100 ppm for studies ranging from 15 minutes to 4 hours: CFC-1112a, FC-C318, CFC-1316, CFC-1326mxz, and HCFC-1353b. Others like CFC-1111, HFC-1122, HCFC-1131a, CFC-1113, FC-1225zc and HCFC-1327mzy have higher median lethal levels, up in the range of 200 to 5,000 ppm. These are still renal toxicants. A few like HCFC-1122a, HFC-1243zf and HFC-1123 show very little acute toxicity. Most of these materials are mutagenic in at least one assay. Only HFC-1243zf and CFC-1113 have data showing a lack of mutagenic activity.

[a] A list of special abbreviations is given at Appendix A
[b] The naming and numbering convention is explained in Appendix B

Saturated compounds, where there is the possibility of generating monofluoroacetic acid (a potent Krebs cycle poison), are highly toxic, while the structural isomers are not. For example, HCFC-142a, HCFC-151 and HFC-152 all have LC_{50}s of less than 100 ppm while HCFC-142b (ECETOC, 1990), HCFC-151a (this report) and HFC-152a (ECETOC, 2004a) have LC_{50}s of over 30,000 ppm. While the perfluorobutenes are highly toxic, both CFC-C316cbb and FC-C318 have LC_{50}s greater than 50,000 ppm. HFC-41 and HFC-32 (ECETOC, 2008) also have LC_{50}s greater than 100,000 ppm and are not mutagenic, while HCFC-31 has an LC_{50} of 45,000 ppm but is highly mutagenic and carcinogenic.

While these are generalities and, as can be seen, have many exceptions, the key to understanding if a fluorinated hydrocarbon is likely to be highly toxic is to try to understand the metabolic pathway. If it can form monofluoroacetic acid, it will be toxic. If it can form a cysteine conjugate, it has a high probability of being a renal toxicant. It is difficult to predict mutagenicity; some of the unsaturated compounds are mutagenic while others are not. There are no data to allow any conclusions to be drawn regarding carcinogenicity or reproductive toxicity.

Typically, the parent substances are produced to very high levels of purity (≥ 99%). Therefore, the presence of low levels of these impurities will not be a concern regarding approval under the EU regulation on the registration, evaluation and authorisation of chemicals (REACH). However, the identification of potential impurities that could be carcinogens, mutagens or reproductive toxicants (CMRs) will enable producers to define maximum acceptable contaminant levels and adapt their processes to minimise these impurities in the commercial products. This will thus avoid the need to register these impurities. Products having higher levels of CMRs will require separate registration in addition to the requirements for the higher purity materials.

2. INTRODUCTION

Since 1989 ECETOC has published a series of Joint Assessment of Commodity Chemicals (JACC) reports on fluorinated chlorofluorocarbon (CFC) alternates (see listing on the back cover of this report). All these fluorinated CFC alternates, although relatively pure (generally the purity level of the substance is higher than 99%) may contain small amounts of a diversity of halogenated impurities. These impurities may originate from the raw materials used and from chemical intermediates or by-products formed during the production processes. They are fluoro-, chloro-, chlorofluoro- or even bromofluoro- alkanes or alkenes with a short carbon chain ranging from C1 to C4.

Some of these impurities, especially those that are unsaturated, are known to present critical toxic properties such as high acute toxicity, genotoxicity, reproductive toxicity or carcinogenicity. The toxicological data on these substances are often limited and unpublished. Consequently, ECETOC felt that it would be useful to gather all the toxicity data available on the most frequently occurring impurities.

It should be stressed that most of these impurities, especially where they are by-products, are non-commercial molecules that have never been produced on an industrial scale. They have been identified analytically and then synthesised on a laboratory scale for studying their diverse properties (including sometimes toxicity screening).

To address these issues, the Task Force formed by ECETOC was assigned the following terms of reference:

- Collect and assess all available toxicity and human health-related information on (un-) saturated fluoroalkyl compounds that are a potential cause of concern as impurities, by-products or decomposition products in HFCs and HCFCs.
- Prepare a Technical Report in the form of individual datasheets as for glycol ethers (ECETOC, 1995 [a]).

A number of the compounds have been internationally reviewed. When this is the case, the compound has only been referenced in this report in a tabular form together with the official OELs (Section 4, Table 7 and 8). If they exist, official OEL values are also cited at the end of individual profiles. Internal industry OELs are not reported but the data profiles would help in setting/revising such internal industry hygiene standards.

[a] Updated by ECETOC, 2005a

An initial evaluation of the environmental impact of the impurities was deemed worthwhile, but beyond the scope of the Task Force. Methods for monitoring of environmental levels for many of these materials have been developed, and while beyond the scope of this review, three current references are provided (Fraser *et al*, 1998; Sturrock *et al*, 2001; Yokouchi *et al*, 2005).

In this report, the individual toxicity profiles are presented in Section 3 in the order of the numbers contained in the usual names, without regard to the alphabetical prefix. Thus HFC-161 comes before FC-C316, for example.

The basic physico-chemical properties of each compound usually refer to European standard conditions (20°C and 1,013 hPa), unless stated otherwise. If available, the specific gravity or relative density (D_4^{20}) is stated, i.e. the density of a compound (usually measured at 20°C) compared to that of water at 4°C (= 1,000 kg/m^3). Vapour density is sometimes given, relative to that of air (= 1).

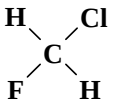
Conversion factors for concentrations in air are given at 25°C. The generic formula is given in Appendix C. In this report, converted values are given in parentheses. Concentrations originally reported as percentages are given here in ppm (1% = 10,000 ppm).

3. SUBSTANCE PROFILES

3.1 Substance profile: HCFC-31

3.1.1 Identity

Name:	Chlorofluoromethane
IUPAC name:	Methane, chlorofluoro-
CAS registry number:	593-70-4
Molecular formula:	CH_2ClF
Molecular mass:	68.5
Chemical structure:	



3.1.2 Physico-chemical properties

Melting point:	–133°C
Boiling point:	–9.1°C
Vapour pressure:	No data
Solubility in water:	No data
Conversion factors:	1 ppm = 2.800 mg/m^3; 1 mg/m^3 = 0.357 ppm

3.1.3 Toxicological data

3.1.3.1 Acute Toxicity

Oral

No data are available (HCFC-31 is a gas under normal conditions).

Inhalation

In rats exposed for a single 6-hour period, HCFC-31 was not lethal up to 20,000 ppm (56,000 mg/m^3). Signs of CNS depression were observed in rats exposed at this concentration (Coate, 1976a). Concentration-related lethality was observed in rats exposed to concentrations from 26,400 to 83,800 ppm HCFC-31 (73,900 - 234,600 mg/m^3) for 4 hours; the LC_{50} was calculated to be 45,000 ppm (126,000 mg/m^3). Histopathological examination revealed kidney

nephrosis, oedema of testis and epididymis, and liver necrosis in rats exposed to concentrations of 27,200 ppm (76,200 mg/m^3) and above (Kelly, 1974).

HCFC-31 was lethal to one of 2 monkeys, 4 days after exposure to 10,000 ppm (28,000 mg/m^3) for 6 hours. Signs of CNS depression were observed (Coate, 1976a).

One of 3 guinea pigs survived exposure to 57,000 ppm HCFC-31 (160,000 mg/m^3) for 6 to 7 hours (Benning, 1934).

3.1.3.2 Irritation and sensitisation

No data are available.

3.1.3.3 Repeated dose toxicity

Subacute toxicity

Ten male Charles River CD rats were exposed (6 h/d, 5 d/wk) by inhalation to 10,000 ppm HCFC-31 (28,000 mg/m^3), the only concentration tested, for 2 weeks, followed by a 14-day observation period. A group of 10 male rats exposed to air only served as controls. Five rats from each group were killed immediately following the last exposure and the 5 remaining rats from each group were killed after the 14-day recovery period. Immediately following exposure, there was evidence of thymic atrophy, increased medullary haematopoiesis and congestion, kidney nephrosis (acute degenerative change, tubular epithelial hyperplasia and tubular dilatation), adrenal cortical necrosis and epididymal spermatic granuloma. After the 14-day recovery period, there were regenerative changes in the bone marrow and thymus. Extra-medullary haematopoiesis was observed in the liver and spleen and there was evidence of sinusoidal haemorrhage and haemosiderin-laden macrophages in the lymph nodes. Progressive aspermatogenesis in the testicular tubules was prominent. The effects on the kidney tubular epithelium were still present, but less evident than immediately following exposure (Moore and Trochimowicz, 1976; Trochimowicz *et al*, 1977).

Sprague-Dawley rats (15/sex/group) were exposed (6 h/d, 5 d/wk) to 0, 416, 970 or 4,900 ppm HCFC-31 (0, 1,165, 2,720, 13,700 mg/m^3) for 20 days. There were no changes of behaviour, body-weight gain, haematology, clinical chemistry or organ weights in any exposed group. Minimal to slight hypo-spermatogenesis was observed in those exposed to 4,900 ppm (Coate, 1976b).

Cynomolgus monkeys (*Macaca fascicularis*) (4/sex/group) were exposed (6 h/d, 5 d/wk) to 0, 416, 970 or 4,900 ppm HCFC-31 (0, 1,165, 2,720, 13,700 mg/m^3) for four weeks. One animal in the 416 ppm group died from pneumonia and nephropathy. At 4,900 ppm, six animals died or were killed moribund. In that group, severe epistaxis, abnormal haematological profile (decreased red blood cell count, haemoglobin and haematocrit values) and hepatotoxicity were observed. The presence of an intercurrent infectious disease rendered interpretation of the data difficult (Coate, 1976c).

A guinea pig was killed following two exposures to 57,000 ppm HCFC-31 (160,000 mg/m^3) for seven hours. Autopsy showed lung and liver damage (Benning, 1934).

Subchronic toxicity

Sprague-Dawley rats (35 males/group) were exposed (6 h/d, 5 d/wk) to 0, 100, 500 or 1,000 ppm HCFC-31 (0, 280, 1,400, 2,800 mg/m^3) for 13 weeks followed by 30 days recovery. There were no significant changes in body-weight gain, clinical observations, haematology, clinical chemistry or urine analysis in any of the exposed groups. Increased urinary fluoride levels were seen in all exposed groups. Mean relative spleen weight was significantly lower than the control values in all exposed groups and relative testis weight was lower in rats exposed to 1,000 ppm. Interim histological examination after 30 and 60 days of exposure did not show any alteration but, after 90 days of exposure, hypo-spermatogenesis was observed in 9 out of 20 rats exposed to 1,000 ppm. This effect was still present and reportedly more severe (5/5 rats) at the end of the recovery period (Coate, 1977a).

3.1.3.4 Genetic toxicity

Yeast

HCFC-31 showed no mutagenic activity when tested in *Saccharomyces cerevisiae* exposed to 50,000 ppm (140,000 mg/m^3) for up to 1 hour (Brusick and Weir, 1976).

Bacteria

HCFC-31 was mutagenic in the Ames test using *Salmonella typhimurium* TA1535 and TA100 with metabolic activation, incubated at a concentration of 10,000 ppm (28,000 mg/m^3) (Longstaff *et al*, 1984).

HCFC-31 was tested in the Ames test using *Salmonella typhimurium* TA1535, TA1537, TA1538, TA98 and TA100 at an unspecified concentration, with exposures of 5 and 24 hours duration, both with and without metabolic activation. HCFC-31 was mutagenic in *Salmonella typhimurium* TA1535 and TA100 in both the absence and presence of metabolic activation under both test conditions. No activity was seen in strains TA1537, TA1538 or TA98 (Brusick and Weir, 1976).

HCFC-31 was tested in the Ames test using *Salmonella typhimurium* TA1535, TA1537, TA98 and TA100 at concentrations of 150,000 and 200,000 ppm (420,000, 560,000 mg/m^3) without metabolic activation, and at 200,000 and 400,000 ppm (560,000, 1,120,000 mg/m^3) with metabolic activation. HCFC-31 was strongly mutagenic in *Salmonella typhimurium* TA1535 and TA100 in both the absence and presence of metabolic activation at all concentrations tested. No activity was seen in strains TA1537 or TA98 (Barsky and Butterworth, 1976a). The mutagenic activity of HCFC-31 in *Salmonella typhimurium* TA1535 and TA100 was confirmed in both the absence and presence of metabolic activation at concentrations of 1,000, 5,000, 10,000 and 50,000 ppm (2,800, 14,000, 28,000, 140,000 mg/m^3). The inactivity in strains TA1537 and TA98 was also confirmed (Russell and Krahn, 1980). HCFC-31 was also shown to be mutagenic in the Ames test using *Salmonella typhimurium* strain TA100 at concentrations of 25,000, 50,000 and 100,000 ppm (70,000, 140,000, 280,000 mg/m^3), both with and without metabolic activation. The response was shown to be due to bacterial metabolism of the test compound, in common with a structural analogue, dichloromethane (Green, 1983).

The mutagenicity of HCFC-31 and other dihalomethanes has been studied in *Salmonella typhimurium* strain TA1535 that had been transformed to express either rat or human glutathione S-transferase enzymes (rat GST 5-5 and human GST T1) or a bacterial dichloromethane dehalogenase (DM11). HCFC-31 did not cause as large an increase in the number of revertants when compared to other dihalomethanes (e.g. dichloromethane) (Wheeler *et al*, 2001).

Mammalian cells

When HCFC-31 was tested on Chinese hamster ovary cells (HGPRT locus), it showed mutagenic activity both in the absence and presence of metabolic activation at all concentrations tested from 100,000 to 670,000 ppm (280,000 to 1,880,000 mg/m^3) (Krahn, 1979; McCoody and Krahn, 1981; Krahn *et al*, 1982).

Germinal cells *in vivo*

HCFC-31 was tested in a dominant lethal assay in male Sprague-Dawley rats exposed (6 h/d, 5d/wk) at concentrations of 100, 500 and 1,000 ppm (280, 1,400, 2,800 mg/m^3) for 10 weeks.

HCFC-31 showed mutagenic activity at 1,000 ppm as evidenced by a significant increase in the number of dead implants (Coate, 1977b).

Chromosomal aberration *in vivo*

A cytogenetic assay in male (Sprague-Dawley) rats exposed (6 h/d, 5 d/wk) to 1,000 ppm HCFC-31 (2,800 mg/m^3) for 13 weeks did not show any increase in the frequency of chromosomal aberration rate (Coate *et al*, 1979).

Cell transformation

HCFC-31 increased the number of cell transformations in a Styles test using baby hamster kidney fibroblasts (BHK21) in the presence of metabolic activity (Longstaff *et al*, 1984).

DNA damage

The DNA damaging potential of HCFC-31 in hepatocytes derived from the rat, the mouse and humans has been studied in the Comet assay. This test detects a range of DNA damage including single strand breaks, double strand breaks, repair sites and alkali labile sites. Dose-related increases in tail moments reached statistical significance in cultures of hepatocytes from both the rat and mouse exposed to high concentrations of HCFC-31 (25,000 and 100,000 ppm [70,000, 280,000 mg/m^3] and above for the rat and mouse, respectively). No significant differences were seen in the magnitude of the responses obtained in DNA derived from rat or mouse hepatocytes (Mainwaring, 2007).

The Comet assay was also performed using human hepatocytes derived from 6 subjects in three separate experiments. In one experiment, a statistically significant increase in mean tail moment was seen in hepatocytes exposed to 500,000 ppm HCFC-31 (1,400,000 mg/m^3), but not at concentrations of 100,000 ppm and below ($\leq$ 280,000 mg/m^3). In a second experiment, a statistically significant increase in mean tail moment was seen in hepatocytes exposed to 100,000 ppm HCFC-31, but not at lower concentrations or at concentrations of 250,000 or 500,000 ppm. In a third experiment, no statistically significant increase in mean tail moment was seen in hepatocytes exposed to HCFC-31 at concentrations of 100,000 ppm and above. Hepatocytes in all three experiments responded as expected to a positive control substance, N-methyl-N'-nitro-N-nitrosoguanidine (MNNG). The magnitude of the response to HCFC-31 in human hepatocytes was generally less than in hepatocytes derived from either rats or mice (Mainwaring, 2007).

3.1.3.5 Chronic toxicity and carcinogenicity

Rats receiving (5 d/wk) 300 mg HCFC-31/kgbw/d (chemical dissolved in corn oil) by gavage for 52 weeks and then examined for tumours until week 125 had a high incidence of malignant tumours (squamous cell carcinoma and fibro-sarcoma) of the stomach with peritoneal and pulmonary metastasis; early mortality occurred in rats with stomach fibro-sarcoma (Longstaff *et al*, 1984).

IARC has classified HCFC-31 in group 3 (not classifiable as to its carcinogenicity to humans) because of limited evidence in animals (IARC, 1999a). The German MAK [a] Commission recommends category 2, i.e. HCFC-31 is to be considered as a human carcinogen based on sufficient evidence either from long-term animal experiments or from animal and/or *in vitro*, and epidemiological and/or toxicokinetic data (DFG, 2008).

3.1.3.6 Reproductive and developmental toxicity

Fertility

Male Sprague-Dawley rats exposed (6 h/d, 5 d/wk) by inhalation to 1,000 ppm (2,800 mg/m^3), the highest concentration tested, for 10 weeks had a decreased fertilisation rate of females as observed during the dominant lethal assay (Coate, 1977b).

Developmental toxicity

Female Sprague-Dawley rats were exposed (6 h/d, 5 d/wk) to 100, 500 or 1,000 ppm (280, 1,400, 2,800 mg/m^3) during the sensitive part of gestation (day 6 - 15). There were no teratogenic or embryo- or foetotoxic effects except for a slight increase in extra ribs at 500 and 1,000 ppm (Coate, 1977a).

3.1.3.7 Kinetics and metabolism

The blood to air partition coefficient for HCFC-31 has been determined and found to be approximately 4.4 (Mainwaring *et al*, 2006).

[a] Maximale Arbeitsplatzkonzentration

There are two possible routes of metabolism of HCFC-31: Either conjugation with glutathione and formation of formaldehyde and, subsequently, CO_2 or oxidation by cytochrome P450 and formation of carbon monoxide and CO_2 (analogy with Cl_2CH_2) (Green, 1983; Gargas *et al*, 1986). Metabolism via a glutathione S-transferase (GST) mediated conjugation is thought to be a predominant route of metabolism of dihalomethanes, in general. The reaction is catalysed by mammalian theta class glutathione transferases (rat GST 5-5 and human GST T1) and by a group of bacterial dehalogenases, with the subsequent generation of formaldehyde. HCFC-31 has been shown to be conjugated by the theta family of glutathione S-transferases (GST), albeit less efficiently than other dihalomethanes, generating metabolites that are potentially DNA reactive. This activity was demonstrated by a concentration-dependent increase in mutation rates in *Salmonella typhimurium* expressing rat GST 5-5, the bacterial enzyme DM11, but not human GST T1 (Wheeler *et al*, 2001).

Theta-GSTs have been shown to have differential expression across species and thus the toxicity of HCFC-31 may correlate with this metabolism. An inter-species comparison of the metabolism of HCFC-31 by the glutathione-dependent pathway to formaldehyde has been conducted *in vitro* using liver cytosol fractions derived from the rat, the mouse and three individual samples of human liver. The assays were performed using a saturated solution of HCFC-31 and gave activities of 75.2 and 21.5 nmol/min/mg protein for the mouse and rat, respectively. The rate in human liver cytosol was found to be much lower at between 2.0 and 3.2 nmol/min/mg protein. Comparison of these results with those obtained for dichloromethane demonstrates that the metabolism of HCFC-31 follows a similar species-dependent trend, with the mouse having the greatest metabolic activity of the three species examined. These findings imply that reactive metabolites formed by this reaction will have greatest significance in the mouse, less in the rat and much less in humans.

The metabolism of HCFC-31 was also compared in fractions of rat glandular and fore-stomach cytosol, using the same conditions as for the liver. The rates were 3.6 and 4.9 nmol/min/mg protein, respectively. Thus there was no significant difference in the rates of metabolism of HCFC-31 in different parts of the stomach. This finding, along with the observed species differences in the metabolism of HCFC-31, suggest that humans may be less sensitive to the DNA-damaging, and thus carcinogenic, effects of HCFC-31 than the rat (Mainwaring *et al*, 2006; Mainwaring, 2007).

3.1.3.8 Cardiac sensitisation

Twelve dogs were exposed for 5 minutes to concentrations of 25,000, 37,500, 50,000 or 100,000 ppm HCFC-31 (70,000, 105,000, 140,000, 280,000 mg/m^3). Cardiac sensitisation to

exogenous adrenaline was observed in 1/12 dogs at 50,000 ppm and in 6/12 dogs at 100,000 ppm (Mullin and Trochimowicz, 1973).

3.1.3.9 Neurological data

CNS depression was seen following short-term exposure (Section 3.1.3.1).

3.1.4 Human data

No data are available.

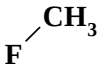
3.1.4.1 Occupational exposure limit value

Switzerland: 8-h TWA 0.5 ppm (1.4 mg/m^3), carcinogenic (Suva, 2007).

3.2 Substance profile: HFC-41

3.2.1 Identity

Name:	Methyl fluoride
IUPAC name:	Fluoride, methyl-
CAS registry number:	593-53-3
Molecular formula:	CH_3F
Molecular mass:	34.0
Chemical structure:	



3.2.2 Physico-chemical properties

Melting point:	No data
Boiling point:	–78°C
Vapour pressure:	No data
Solubility in water:	No data
Conversion factors:	1 ppm = 1.390 mg/m^3; 1 mg/m^3 = 0.720 ppm

3.2.3 Toxicological data

3.2.3.1 Acute Toxicity

Oral

No data are available.

Dermal

No data are available.

Inhalation

The median lethal dose was found to be in excess of 138,000 ppm (192,000 mg/m^3) in the rat (Parr-Dobrzanski, 1993a).

3.2.3.2 Irritation and sensitisation

Skin irritation

No data are available.

Eye irritation

No data are available.

Sensitisation

No data are available.

3.2.3.3 Repeated dose toxicity

Subacute toxicity

Alpk:APfSD rats (5/sex/group) were exposed (6 h/d) to HFC-41 at measured concentrations of 0, 4,450 or 44,600 ppm (0, 6,190, 62,000 mg/m^3) for 10 consecutive days. No effects were observed at 4,450 ppm. Both male and female rats exposed to 44,600 ppm showed lesions characterised as epithelial degeneration of the anterior part of the nasal cavity. An increase in urinary fluoride levels was also observed in both sexes exposed to 44,600 ppm. The no observed adverse effect level (NOAEL) for the study was considered to be 4,450 ppm (Rattray, 1996).

Subchronic toxicity

No data are available.

3.2.3.4 Genetic toxicity

Bacteria

HFC-41 was found to be mutagenic in the Ames assay using *Salmonella typhimurium* and *Escherichia coli* strains, both in the presence and absence of metabolic activation (rat liver S9 [a]). The most consistent positive response was seen in *Escherichia coli* strain WP2P (Elliot *et al*, 1992, 1993, 1994).

Mammalian cells *in vivo*

Male CD-1 mice were exposed (whole body) to a target concentration of 150,000 ppm HFC-41 (achieved mean concentration of 121,300 ppm) (209,000, 168,600 mg/m^3) for 5 hours. Bone marrow smears were taken 24 and 48 hours after exposure and examined for changes in the number of micronucleated polychromatic erythrocytes. No statistically or biologically significant increases in the incidence of micronucleated cells were observed. In addition, there was no difference in the percentage of polychromatic erythrocytes between the exposed rats and control rats exposed to air alone. It was concluded that HFC-41 was not clastogenic in the mouse micronucleus assay (Elliot *et al*, 1995a).

[a] Supernatant of centrifuged 9,000 × g liver homogenate, containing the microsome and cytosol fractions usually derived from rats previously treated with microsomal enzyme inducing compounds such as phenobarbital or Aroclor.

In conclusion, HFC-41 shows mutagenic potential *in vitro*, but is not mutagenic *in vivo* in a mouse liver micronucleus assay. The possibility that HFC-41 might express its mutagenic potential *in vivo* as a direct acting mutagen in dividing cells, for example in the nasal epithelium, cannot be excluded.

3.2.3.5 Chronic toxicity and carcinogenicity

No data are available.

3.2.3.6 Reproductive and developmental toxicity

No data are available.

3.2.3.7 Kinetics and metabolism

No data are available.

3.2.3.8 Cardiac sensitisation

No data are available.

3.2.3.9 Neurological data

No data are available.

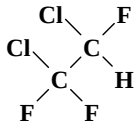
3.2.4 Human data

HFC-41 has been reported to cause anaesthesia at 0.14 atm (140,000 ppm) (195,000 mg/m^3) (Miller *et al*, 1965).

3.3 Substance profile: HCFC-123a

3.3.1 Identity

Name:	Dichlorotrifluoroethane
IUPAC name:	Ethane, 1,2-dichloro-1,1,2-trifluoro-
CAS registry number:	354-23-4
Molecular formula:	$C_2HCl_2F_3$
Molecular mass:	152.9
Chemical structure:	



3.3.2 Physico-chemical properties

Melting point:	–78°C (DuPont, no date)
Boiling point:	28°C (DuPont, no date)
Relative density D_4^{25}:	1.50 (DuPont, no date)
Vapour pressure:	1,020 hPa (DuPont, no date)
Solubility in water:	No data
Conversion factors:	1 ppm = 6.249 mg/m^3; 1 mg/m^3 = 0.160 ppm

3.3.3 Toxicological data

3.3.3.1 Acute toxicity

Oral

Charles River COBS rats (2/sex/group) were dosed by gavage with HCFC-123a at doses from 900 to 3,038 mg/kgbw, and observed for 14 days. No animals died at 1,125 mg/kgbw or below. Two of four animals died at 1,350 and 2,025 mg/kgbw. The median lethal dose (LD_{50}) was 1,750 mg/kgbw (Kretchmar, 1972).

Dermal

HCFC-123a was applied to the skin of New Zealand white rabbits at a dose of 2,000 mg/kgbw for 24 hours. There were no deaths or signs of toxicity during dosing or for up to 14 days after

treatment. The animals showed signs of irritation at the site of the application. The LD_{50} was > 2,000 mg/kgbw (Kretchmar, 1972).

Inhalation

Sprague-Dawley rats (5/sex/group) were exposed to 21,400 or 31,800 ppm HCFC-123a (133,700, 198,700 mg/m^3) (nominal concentrations) for 4 hours. The animals were then observed for 14 days. There were no deaths or effects on body weight. At 31,800 ppm, the animals exhibited deep narcosis. They recovered promptly (within minutes) after the exposure was terminated (Elliot, 1972).

Two dogs (breed not specified) were exposed to 140,000 ppm HCFC-123a (875,000 mg/m^3). Anaesthesia was induced rapidly and smoothly. Once induced, this anaesthesia could be maintained at 70,000 ppm HCFC-123a (437,000 mg/m^3). There was no indication of respiratory depression during induction; however, a severe drop in blood pressure was noted in all animals. When the anaesthesia was continued for 5 minutes and then terminated the dogs recovered rapidly and were walking within 12 minutes (Burn *et al*, 1959). Exposure of dogs and cats (breed not specified) to levels of 40,000 ppm (250,000 mg/m^3) and higher, occasionally led to the development of reversible cardiac arrhythmias (Burn *et al*, 1959).

3.3.3.2 Irritation and sensitisation

Skin irritation

When 0.5 ml of HCFC-123a was placed on the back of 6 New Zealand rabbits for 24 hours, barely perceptible erythema was noted. Based on this study HCFC-123a would be considered minimally irritating (Draize score 0.4 out of 8.0) (Kretchmar, 1972).

Eye irritation

The potential for HCFC-123a to cause eye irritation was evaluated using 6 New Zealand rabbits. Instillation of 0.5 ml of the test material into one eye resulted in mild transient eye irritation, which remained present for 24 hours post treatment, but had resolved by 72 hours post treatment (Kretchmar, 1972).

Sensitisation

No data are available.

3.3.3.3 Repeated dose toxicity

Rats (5/group; strain and sex not stated) exposed (1 h/d) to 40,000 or 60,000 ppm HCFC-123a (250,000, 375,000 mg/m^3) for 5 days exhibited anaesthesia, but no signs of toxicity (Burn *et al*, 1959).

Exposure (6 h/d, 5 d/wk) of male ChR-CD rats at 9,386 ppm HCFC-123a (58,650 mg/m^3) for 2 weeks resulted in increased urinary fluoride, and decreased haematocrit and blood urea nitrogen levels. All effects were reversible within two weeks after exposure. Histopathological examination of tissues from the exposed rats did not reveal evidence of treatment-related effects (Sarver and Trochimowicz, 1977).

One group of 17 male Crl:CD BR rats were exposed (6 h/d) to HCFC-123a for 21 days over a 26-day period. The initial exposure level was 20,000 ppm (125,000 mg/m^3), however after signs of severe toxicity were seen in both this group and a second group being exposed to the same level of HCFC-123, the exposure levels were lowered and the resulting average exposure level was 18,500 ppm (115,600 mg/m^3). A similar sized air exposed control group was included. Rats exposed to HCFC-123a became anaesthetised 30 to 60 minutes into the exposure. The effect was reversible within minutes after the end of each exposure. The HCFC-123a exposed rats had significant increases in mean and absolute liver weights and minimal to mild diffuse hepatocellular hypertrophy. The rate of hepatic peroxisomal β-oxidation was also increased compared to control levels. Serum triglyceride, glucose and insulin levels were decreased. The decrease in insulin, however, was attributed to the lower glucose levels. It was not seen as a direct effect of the HCFC-123a (Warheit, 1993).

3.3.3.4 Genetic toxicity

HCFC-123a was not mutagenic in the *Salmonella typhimurium* mutation assay at exposure levels of 50,000 or 150,000 ppm (312,000 or 937,000 mg/m^3), with or without S9 metabolic activation (Barsky and Butterworth, 1976b).

HCFC-123a did not induce sex-linked recessive lethal mutations in *Drosophila melanogaster* exposed to 30,000 ppm (187,500 mg/m^3) (Davis, 1982).

Rats were given a single 6-hour exposure to HCFC-123a at 10,000, 15,500 or 25,000 ppm (62,500, 96,900, 156,200 mg/m^3). Following the exposure, the liver hepatocytes were examined for evidence of unscheduled DNA synthesis. No such effects were observed (Kennely and Barber, 1993).

3.3.3.5 Chronic toxicity and carcinogenicity

No data are available.

3.3.3.6 Reproductive and developmental toxicity

No data are available.

3.3.3.7 Kinetics and metabolism

HCFC-123a was metabolised by rat, mouse and human microsomes to yield fluoride and chlorodifluoroacetic acid. Metabolism was induced in the presence of inducers of cytochrome P450 2E1, suggesting that this enzyme is responsible (Dekant *et al*, 1995a,b).

3.3.3.8 Cardiac sensitisation

Exposure of dogs and cats (breed not specified) to 40,000 ppm HCFC-123a (250,000 mg/m^3) and higher, occasionally lead to the development of reversible cardiac arrhythmias (Burn *et al*, 1959).

3.3.3.9 Neurological data

No data are available.

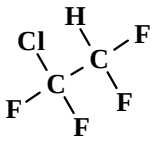
3.3.4 Human data

No data are available.

3.4 Substance profile: HCFC-124a

3.4.1 Identity

Name:	Chlorotetrafluoroethane
IUPAC name:	Ethane, 1-chloro-1,1,2,2-tetrafluoro-
CAS registry number:	354-25-6
EC number:	206-552-0
Molecular formula:	C_2HCLF_4
Molecular mass:	136.5
Chemical structure:	



3.4.2 Physico-chemical properties

Melting point:	–117°C
Boiling point:	–10.2°C
Relative density D_4^{20}:	1.379
Vapour pressure:	No data
Solubility in water:	No data
Conversion factors:	1 ppm = 5.579 mg/m^3; 1 mg/m^3 = 0.179 ppm

3.4.3 Toxicological data

3.4.3.1 Acute Toxicity

No data are available on oral or dermal toxicity.

Inhalation

Two guinea pigs (strain and sex not stated) were exposed by inhalation to 25,000 or 200,000 ppm HCFC-124a (140,000 or 1,120,000 mg/m^3) for 2 hours. Following 1.5 hours of exposure to 25,000 ppm, animals appeared nervous as judged by an increased respiration rate. No gross pathological effects were noted. After 10 minutes at 200,000 ppm, animals appeared nervous and respiration rate increased. Anaesthetic-like effects became more severe until the animals were

immobile after 1.5 hours of exposure. The ALC was greater than 200,000 ppm (> 1,120,000 mg/m^3) (Benning *et al*, 1938).

Male guinea pigs were exposed to 30,000 ppm HCFC-124a (167,400 mg/m^3) for 6 hours. No signs of toxicity were observed. Slight lung congestion was noted as well as fluid in the bronchial region (DuPont, 1945).

3.4.3.2 Irritation and sensitisation

No data are available.

3.4.3.3 Repeated dose toxicity

Subacute toxicity

Two guinea pigs (strain and sex not stated) were exposed (7 h/d) to 8,700 or 29,100 ppm HCFC-124a (48,500, 162,300 mg/m^3) for 6 days. Animals were observed during a 37-day recovery period. Pathological examination did not reveal any abnormal effects not present in the control animals (Benning *et al*, 1938).

Subchronic toxicity

No data are available.

3.4.3.4 Genetic toxicity

No data are available.

3.4.3.5 Chronic toxicity and carcinogenicity

No data are available.

3.4.3.6 Reproductive and developmental toxicity

No data are available.

3.4.3.7 Kinetics and metabolism

No data are available.

3.4.3.8 Cardiac sensitisation

No data are available.

3.4.3.9 Neurological data

No data are available.

3.4.4 Human data

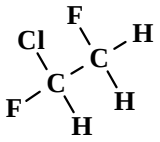
No data are available.

3.5 Substance profile: HCFC-142a

3.5.1 Identity

Name:	1-Chloro-1,2-difluoroethane
IUPAC name:	Ethane, 1-chloro-1,2-difluoro-
CAS registry number:	338-64-7
Molecular formula:	$C_2H_3ClF_2$
Molecular mass:	100.5

Chemical structure:



3.5.2 Physico-chemical properties

Melting point:	No data
Boiling point:	No data
Vapour pressure:	No data
Solubility in water:	No data
Conversion factors:	1 ppm = 4.108 mg/m^3; 1 mg/m^3 = 0.243 ppm

3.5.3 Toxicological data

3.5.3.1 Acute Toxicity

No data are available on oral or dermal toxicity.

Inhalation

Four-hour exposure to 8, 15, 40 or 238 ppm HCFC-142a (32.9, 61.6, 164, 978 mg/m^3) caused mortality in 0/3, 3/3, 3/3 and 3/3 rats, respectively (Keller *et al*, 1996). The high mortality results from the metabolism of HCFC-142a into fluoroacetic acid, a potent Krebs cycle poison (Section 3.5.3.7).

3.5.3.2 Irritation and sensitisation

Skin irritation

No data are available.

Eye irritation

No data are available.

Sensitisation

No data are available.

3.5.3.3 Repeated dose toxicity

Subacute toxicity

No data are available.

Subchronic toxicity

No data are available.

3.5.3.4 Genetic toxicity

No data are available.

3.5.3.5 Chronic toxicity and carcinogenicity

No data are available.

3.5.3.6 Reproductive and developmental toxicity

No data are available.

3.5.3.7 Kinetics and metabolism

Male CD rats were exposed by inhalation to 0 or 700 ppm HCFC-142a (0, 2,880 mg/m^3) for 4 hours. Significant (11-fold) elevations of serum and heart citrate concentrations were observed compared to controls. Fluoroacetate and fluorocitrate were found in the kidneys, and fluoroacetate in the urine of exposed animals. Fluoride ion was detected in the serum of exposed animals. HFC-142a toxicity was likely to occur via CYP 2E1 metabolism as pre-treatment with SKF-525A, disulfiram or DMSO interfered with, prevented or delayed toxicity associated with the fluoroacetate metabolite. There was evidence that formation of fluoroacetate occurred via an aldehyde or acyl fluoride. The data were consistent with the postulated metabolic pathway using the cytochrome P450 oxidation (Keller et al, 1996):

$$FCH2–CH2Cl \rightarrow [FCH2–CHClOH] \rightarrow FCH2–COOH \quad \text{(Eq. 1)}$$

The metabolic formation of fluoroacetate is responsible for the blocking of the Krebs cycle (which leads to the increase of fluorocitrate) and for the high acute toxicity level and the clinical symptoms that are the same as those observed in the case of direct intoxication by sodium fluoroacetate.

3.5.3.8 Cardiac sensitisation

No data are available.

3.5.3.9 Neurological data

No data are available.

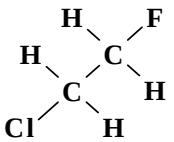
3.5.4 Human data

No data are available.

3.6 Substance profile: HCFC-151

3.6.1 Identity

Name:	1-Chloro-2-fluoroethane
IUPAC name:	Ethane, 1-chloro-2-fluoro-
CAS registry number:	762-50-5
Molecular formula:	C_2H_4ClF
Molecular mass:	82.5
Chemical structure:	



3.6.2 Physico-chemical properties

Melting point:	No data
Boiling point:	59°C
Vapour pressure:	No data
Solubility in water:	No data
Conversion factors:	1 ppm = 3.372 mg/m^3; 1 mg/m^3 = 0.297 ppm

3.6.3 Toxicological data

3.6.3.1 Acute Toxicity

No data are available on oral or dermal toxicity.

Inhalation

Male CD rats (3/group) were exposed to 7, 13, 45 or 136 ppm HCFC-151 (23.6, 43.8, 152, 459 mg/m^3) for 4 hours. There were 0, 3, 2 and 3 deaths, respectively, at these concentrations. The 4-hour LC_{50} value was 13 ppm. Within 30 minutes of the beginning of the exposure, rats showed signs of fluoroacetate intoxication such as lethargy, hunched posture and convulsions (Keller *et al*, 1996).

In guinea-pigs, the 10-minute lowest lethal concentration (LC_{Lo}) was 30 ppm (100 mg/m^3) (NDRC cited by RTECS, 2000a).

3.6.3.2 Irritation and sensitisation

No data are available.

3.6.3.3 Repeated dose toxicity

No data are available.

3.6.3.4 Genetic toxicity

HCFC-151 was evaluated for mutagenic activity in the Ames test at concentrations of 0, 10,000, 25,000, 50,000, 75,000 or 100,000 ppm (0, 33,700, 84,300, 169,000, 253,000, 337,000 mg/m^3). There was no genotoxic effect in *Salmonella typhimurium* strain TA98, TA100, TA102 or TA1537 with or without metabolic activation. In TA1535, HCFC-151 induced a dose-related mutagenic effect from concentrations of 50,000 ppm and above. The effect was more marked in the presence of metabolic activation (Déchariaux, 1996).

3.6.3.5 Chronic toxicity and carcinogenicity

No data are available.

3.6.3.6 Reproductive and developmental toxicity

No data are available.

3.6.3.7 Kinetics and metabolism

Single exposure of male CD rats by inhalation to 700 ppm HCFC-151 (2,360 mg/m^3) for 4 hours induced a significant increase of fluorocitrate in serum and in heart (Section 3.6.3.1). The data were consistent with the postulated metabolic pathway using the cytochrome P450 oxidation (Keller et al, 1996):

$$FCH2–CH2Cl \rightarrow [FCH2–CHClOH] \rightarrow FCH2–COOH \quad \text{(Eq. 1)}$$

The metabolic formation of fluoroacetate is responsible for the blocking of the Krebs cycle (which leads to the increase of fluorocitrate) and for the high acute toxicity level and the clinical symptoms that are the same as those observed in the case of direct intoxication by sodium fluoroacetate.

In vitro exposure of rat hepatocyte primary cultures to vapour of HCFC-151 for 4 days induced moderate peroxisome proliferation as assessed by a dose-related increase in palmitoyl-coA-oxidase activity from 25,000 ppm (84,300 mg/m^3) and upwards (Gouy *et al*, 1996).

3.6.3.8 Cardiac sensitisation

No data are available.

3.6.3.9 Neurological data

No data are available.

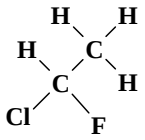
3.6.4 Human data

No data are available.

3.7 Substance profile: HCFC-151a

3.7.1 Identity

Name:	1-Chloro-1-fluoroethane
IUPAC name:	Ethane, 1-chloro-1-fluoro-
CAS registry number:	1615-75-4
Molecular formula:	C_2H_4ClF
Molecular mass:	82.5
Chemical structure:	



3.7.2 Physico-chemical properties

Melting point:	No data
Boiling point:	16.1°C
Vapour pressure:	No data
Solubility in water:	No data
Conversion factors:	1 ppm = 3.372 mg/m^3; 1 mg/m^3 = 0.297 ppm

3.7.3 Toxicological data

3.7.3.1 Acute Toxicity

No data are available on oral or dermal toxicity.

Inhalation

Sprague-Dawley-CD rats (5 males and 5 females) were exposed snout-only to HCFC-151a at the maximum sustainable chamber concentration of 116,000 mg/m^3 (34,000 ppm) (measured) for 4 hours. There were no deaths during the following 14 days of observation. Slight ataxia was noted in all animals on their removal from the exposure tubes (Cracknell, 1991).

In the mouse, a 2-hour LC_{50} of 125,000 mg/m^3 HCFC-151a (37,000 ppm) has been reported (Izmerov *et al*, 1982 cited by RTECS, 2000b).

3.7.3.2 Irritation and sensitisation

No data are available.

3.7.3.3 Repeated dose toxicity

No data are available.

3.7.3.4 Genetic toxicity

HCFC-151a induced gene mutations in *Salmonella typhimurium* TA100 and TA1535, with and without rat S9 metabolic activation. Marked dose-related effects were seen following exposure at vapour concentrations of 25,000 ppm and above (≥ 84,300 mg/m^3) (May, 1990).

In a human lymphocyte chromosome aberration assay without metabolic activation (rat liver S9), HCFC-151a showed clear evidence of clastogenic activity at vapour concentrations of 50,000 ppm and above (≥ 169,000 mg/m^3) in air. In the presence of rat liver S9, HCFC-151a was not clastogenic (Dance, 1990).

HCFC-151a did not induce micronucleated polychromatic erythrocytes (PCEs) in the bone marrow of CD-1 mice (5 - 10 males/group) exposed by inhalation to 0, 5,600, 21,000 or

34,000 ppm HCFC-151a (0, 18,900, 70,800, 115,000 mg/m^3) for 6 hours. Bone marrow smears were prepared 24 and 48 hours post exposure (Cox, 1999).

3.7.3.5 Chronic toxicity and carcinogenicity

No data are available.

3.7.3.6 Reproductive and developmental toxicity

No data are available.

3.7.3.7 Kinetics and metabolism

HCFC-151a has been shown to undergo oxidative dechlorination by rat liver microsomes *in vitro*. Metabolites formed from this dehalogenation have not been identified (Van Dyke, 1977).

3.7.3.8 Cardiac sensitisation

No data are available.

3.7.3.9 Neurological data

No data are available.

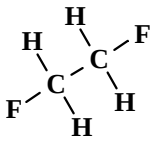
3.7.4 Human data

No data are available.

3.8 Substance profile: HFC-152

3.8.1 Identity

Name: 1,2-Difluoroethane
IUPAC name: Ethane, 1,2-difluoro-
CAS registry number: 624-72-6
Molecular formula: $C_2H_4F_2$
Molecular mass: 66.1
Chemical structure:



3.8.2 Physico-chemical properties

Melting point: –160.2°C
Boiling point: 30.7°C
Relative density D_4^{19}: 0.913
Vapour pressure: 616 mm Hg (821 hPa) at 25°C (Yaws, 1994 cited by HSDB, 2003)
Solubility in water: 2,319 mg/l[a] at 25°C
Partition coefficient, log K_{ow} 1.21 (calculated following Meylan and Howard, 1995) (octanol/water) at 20°C
Conversion factors: 1 ppm = 2.702 mg/m^3; 1 mg/m^3 = 0.370 ppm

3.8.3 Toxicological data

3.8.3.1 Acute Toxicity

No data are available on oral or dermal toxicity.

Inhalation

All four male rats exposed to HFC-152 at concentrations of 75 ppm and above (≥ 203 mg/m³) for 4 hours died within 24 hours. Rats exposed to 25 ppm (67.6 mg/m³) for 4 hours had ruffled fur, narrowly open eyes and hunched posture during the exposure and 24 hours post exposure. Rats

[a] Reported as 2,312 mg/kg; density of water at 25°C is 0.997044 g/ml

did not eat for approximately 28 hours after the exposure had ended but appeared normal 2 days post exposure. No toxicity was observed at 15 ppm (40.5 mg/m³) (Reinhardt, 1991).

Four male CD rats were exposed by inhalation to HFC-152 at 24, 100 or 116 ppm (64.8, 270, 313 (mg/m³). HFC-152 caused mortality in 0/4, 2/4 and 4/4 rats, respectively (Keller *et al*, 1996).

3.8.3.2 Irritation and sensitisation

No data are available.

3.8.3.3 Repeated dose toxicity

Subacute toxicity

Two male mice (strain not stated) were exposed (20 min/d) by inhalation to 3,000 ppm (8,100 mg/m^3) HFC-152 for 5 days. The 3,000 ppm exposure was stopped after 3 days because one of the mice died. The remaining mouse died 10 days later. One of 2 mice exposed (20 min/d) by inhalation to 1,000 ppm (2,700 mg/m^3) for 5 days displayed occasional convulsions and died 4 days after the last exposure. Neurotoxic effects were also reported (Section 3.8.3.9) (Reinhardt, 1992a).

Subchronic toxicity

No data are available.

3.8.3.4 Genetic toxicity

No data are available.

3.8.3.5 Chronic toxicity and carcinogenicity

No data are available.

3.8.3.6 Reproductive and developmental toxicity

No data are available.

3.8.3.7 Kinetics and metabolism

Male CD rats were exposed by inhalation to HFC-152 for 4 hours. Significant elevations of serum and heart citrate concentrations were observed (2- to 4-fold). Serum citrate levels increased proportionately with doses up to 1,000 ppm (2,700 mg/m^3). Heart citrate levels were also increased in a dose-dependent manner up to 1,000 ppm. Fluoroacetate and fluorocitrate were found in the kidneys, and fluoroacetate in the urine of exposed animals. Fluoride ion was detected in the serum of exposed animals. HFC-152 toxicity was considered likely to occur via CYP 2E1 metabolism as pre-treatment with SKF-525A, disulfiram or DMSO interfered with, prevented or delayed toxicity associated with the fluoroacetate metabolite. There was evidence that formation of fluoroacetate occurred via an aldehyde or acyl fluoride (Keller *et al*, 1996).

3.8.3.8 Cardiac sensitisation

No data are available.

3.8.3.9 Neurological data

Two male mice (strain not stated) exposed (20 min/d) to 1,000 ppm HFC-152 (2,700 mg/m^3) for 5 days appeared sluggish with slow, rhythmic walking 30 minutes after the first exposure. Both mice showed symptoms of ataxia, impaired motor abilities, and tremors. One mouse demonstrated frequent episodes of circling behaviour. Two mice exposed (20 min/d) by inhalation for 5 days to 500 ppm (1,350 mg/m^3) demonstrated episodes of staggering and convulsions during days 4 and 5 of exposure. The mice were slightly lethargic for 1 day following exposure, but then appeared normal (Reinhardt, 1992a).

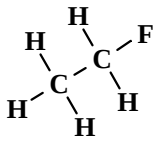
3.8.4 Human data

No data are available.

3.9 Substance profile: HFC-161

3.9.1 Identity

Name:	Fluoroethane
IUPAC name:	Ethane, fluoro-
CAS registry number:	353-36-6
Molecular formula:	C_2H_5F
Molecular mass:	48.1
Chemical structure:	



3.9.2 Physico-chemical properties

Melting point:	–143.2°C
Boiling point:	–37°C
Vapour pressure:	6,842 mm Hg (9,122 hPa) at 25°C
Relative density D_4^{25}:	0.7062
Solubility in water:	2,158 mg/l at 25°C
Conversion factors:	1 ppm = 1.966 mg/m^3; 1 mg/m^3 = 0.509 ppm

3.9.3 Toxicological data

3.9.3.1 Acute Toxicity

No data are available on oral or dermal toxicity.

Inhalation

No acute lethality was observed in rats exposed to HFC-161 at 100,000 ppm (197,000 mg/m^3) for 4 hours in a closed, recirculating chamber. Higher concentrations were not tested and pathology evaluations were not conducted (Keller, 1992).

Following exposure of 6 Sherman rats to HFC-161, the 4-hour ALC was reported to be 256,000 ppm (503,000 mg/m^3). Clinical observations were noted on all animals and gross pathological examinations were conducted on animals that died during the study to ensure deaths

did not result from infection or other factors not related to the chemical exposure (Carpenter *et al*, 1949).

In a review of existing and alternative refrigerants, HFC-161 was listed, in error, as having a high toxicity (McLinden and Didion, 1988). Based on inquiry and supporting documentation (Bingham, 1993), the authors acknowledged that HFC-161 should have been listed as having a low toxicity (McLinden and Didion, 1993).

3.9.3.2 Irritation and sensitisation

No data are available.

3.9.3.3 Repeated dose toxicity

No data are available.

3.9.3.4 Genetic toxicity

No data are available.

3.9.3.5 Chronic toxicity and carcinogenicity

No data are available.

3.9.3.6 Reproductive and developmental toxicity

No data are available.

3.9.3.7 Kinetics and metabolism

The extent HFC-161 metabolism in rats was small and fluoroacetate was not a major metabolite. Metabolism was presumed via defluorination to acetaldehyde. Urinary fluoride levels were increased 10- to 20-fold over control levels in rats exposed (6 h/d) to 49,000 ppm (96,300 mg/m^3) HFC-161 for 5 days (Keller, 1994).

HFC-161 had a blood-air partition coefficient of 1.3 (Keller, 1992).

3.9.3.8 Cardiac sensitisation

No data are available.

3.9.3.9 Neurological data

No data are available.

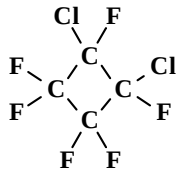
3.9.4 Human data

No data are available.

3.10 Substance profile: CFC-C316cbb

3.10.1 Identity

Name: 1,2-Dichloroperfluorocyclobutane
IUPAC name: Cyclobutane, 1,2-dichloro-1,2,3,3,4,4-hexafluoro-
CAS registry number: 356-18-3
Molecular formula: $C_4Cl_2F_6$
Molecular mass: 232.9
Chemical structure:



3.10.2 Physico-chemical properties

Melting point: –15.1°C
Boiling point: 59°C
Vapour pressure: 213 mm Hg (284 hPa) (Calculated [a])
Solubility in water: No data
Conversion factors: 1 ppm = 9.519 mg/m^3; 1 mg/m^3 = 0.105 ppm

3.10.3 Toxicological data

3.10.3.1 Acute Toxicity

No data are available on oral or dermal toxicity.

Inhalation

The 4-hour LC_{50} in 6 male ChR-CD rats was 53,000 ppm CFC-C316 (504,500 mg/m^3). No pathology evaluation was conducted (Kwon, 1969).

[a] Using Advanced Chemistry Development Software V8.14 from ACD/Labs,Toronto, Ontario, Canada [www.acdlabs.com/products/phys_chem_lab/bp/]

Inhalation toxicity and anaesthetic effects of CFC-C316 were investigated in albino mice (1/group; strain and sex not stated). There was no response following exposure to 60,000 ppm (570,100 mg/m^3) for an undisclosed period of time. Exposure to 136,000 ppm (1,295,000 mg/m^3) produced convulsions and 209,000 ppm (1,989,000 mg/m^3) caused death in 30 seconds. Heart and lung effects were noted, but not defined (Burns *et al*, 1961).

3.10.3.2 Irritation and sensitisation

No data are available.

3.10.3.3 Repeated dose toxicity

Subacute toxicity

Ten male albino rats exposed (6 h/d) to CFC-C316 at a concentration of 10,000 ppm (95,200 mg/m^3) for 40 days survived without detectable cumulative effects or pathological changes (Limperos, 1951).

Subchronic toxicity

No data are available.

3.10.3.4 Genetic toxicity

No data are available.

3.10.3.5 Chronic toxicity and carcinogenicity

No data are available.

3.10.3.6 Reproductive and developmental toxicity

No data are available.

3.10.3.7 Kinetics and metabolism

No data are available.

3.10.3.8 Cardiac sensitisation

Beagle dogs challenged with 8 µg/kgbw epinephrine and briefly exposed by inhalation to CFC-C316 to 10,000 or 15,000 ppm (95,200, 142,800 mg/m^3) for 5 minutes, resulted in 0/6 and 3/6 "marked responses", respectively. Exposure to 25,000 or 50,000 ppm (238,000, 476,000 mg/m^3) produced 2/2 "marked responses" in each group (Reinhardt, 1968).

3.10.3.9 Neurological data

No data are available.

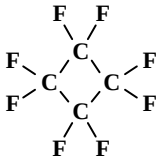
3.10.4 Human data

No data are available.

3.11 Substance profile: FC-C318

3.11.1 Identity

Name:	Perfluorocyclobutane
IUPAC name:	Cyclobutane, octafluoro-
CAS registry number:	115-25-3
Molecular formula:	C_4F_8
Molecular mass:	200.0
Chemical structure:	



3.11.2 Physico-chemical properties

Melting point:	–41°C
Boiling point:	–6°C
Relative density D_4^{20}:	1.48
Vapour pressure:	2,010 mm Hg (2,680 hPa) at 21°C (DuPont, 1998)
Vapour density (air = 1):	7.88
Solubility in water:	0.025 mg/l [a] at 25°C
Solubility in olive oil:	1% w/w at 25°C
Conversion factors:	1 ppm = 8.175 mg/m^3; 1 mg/m^3 = 0.122 ppm

3.11.3 Toxicological data

3.11.3.1 Acute Toxicity

No data are available on oral or dermal toxicity.

Inhalation

Four female Wistar rats and 2 guinea pigs were exposed to 600,000 ppm FC-C318 (4,910,000 mg/m^3) for 2 hours. Oxygen was supplied to maintain the level at 19 to 20%. All of

[a] Reported as 0.0025% w/w; density of water at 25°C is 0.997044 g/ml

the animals showed normal behaviour during inhalation and the subsequent 7 days of observation (Weigand, 1971).

Six rats (not further specified) were exposed to 800,000 ppm FC-C318 (6,540,000 mg/m^3) for 4 hours. The oxygen level was maintained at 20%. No deaths were observed. During exposure, the rats showed red ears, mild lachrymation (2/6) and hyperaemia (2/6). Following exposure, all of the rats showed mild mydriasis with pupil accommodation for approximately 15 minutes. All animals appeared normal 15 minutes after exposure (Toppan, 1965).

Six mice (2/group; strain and sex not specified) were exposed by inhalation to a mixture (80:20 by volume) of FC-C318 and oxygen (800,000 ppm; 6,540,000 mg/m^3) for 10 minutes. There was evidence of laboured breathing during the exposure in 5 out of 6 animals but the symptoms rapidly subsided when the exposure was terminated. There was no indication of anaesthesia or central nervous system (CNS) effects in any animal. One week after exposure no gross pathological changes were noted (Clayton, 1959a).

Two rats (not further specified) were exposed by inhalation to a mixture (80:20 by volume) of FC-C318 and oxygen (800,000 ppm; 6,540,000 mg/m^3) for 10 minutes. The animals appeared normal during and for 11 days after exposure. There was no indication of anaesthesia or CNS effects in any animal. At 11 days after exposure no gross pathological changes were noted (Clayton, 1959a).

3.11.3.2 Irritation and sensitisation

Skin irritation

No data are available.

Eye irritation

FC-C318 (0.1 ml gas) was injected into the vitreous humour of one eye of 8 anaesthetised rabbits, and control air into the other eye. Ophthalmoscopic evaluation of all injected eyes and histological examination of 2 treated eyes in which the FC-C318 remained longest (up to 11 days, as judged by the presence of gas bubbles in the vitreous humour) showed no evidence of a toxic reaction. The FC-C318 remained in the eye an average of 7.47 days (Vygantas *et al*, 1973).

Sensitisation

No data are available.

3.11.3.3 Repeated dose toxicity

Subacute toxicity

No data are available.

Subchronic toxicity

Six male albino rats were exposed (6 h/d, 5 d/wk) to 10,000 ppm FC-C318 (81,800 mg/m^3) for 4 weeks. No signs of toxicity were seen. Haematological examination revealed no significant differences between exposed and control animals, and no gross or microscopic pathological changes were detected in the organs (Limperos, 1956).

Charles River rats (10/sex), Swiss Webster mice (10 females), albino rabbits (2/sex), and male mongrel dogs (4) were exposed (6 h/d, 5 d/wk) to 100,000 ppm FC-C318 (818,000 mg/m^3) for 90 days. The average oxygen concentration was 18%. The exposure revealed no harmful effects as judged by clinical behaviour, growth rate, haematological parameters, organ weights, and gross or microscopic pathological examination (Clayton, 1959b; Clayton *et al*, 1960).

Five Wistar rats, five guinea pigs, three beagle dogs, and two cats (animals not further specified) were exposed (3.5 h/d, 5 d/wk) to 200,000 ppm (1,640,000 mg/m^3) of FC-C318 for 4 weeks. No supplemental oxygen was used. No adverse effects were seen. Pathological examination revealed no treatment-related effects (Weigand, 1971).

3.11.3.4 Genetic toxicity

FC-C318 was evaluated for mutagenic activity in the Ames test using *Salmonella typhimurium* strains TA97a, TA98, TA100, TA1535 and *Escherichia coli* strain WP2 uvrA(pKM101) at concentrations of up to 1,000,000 ppm (8,180,000 mg/m^3) in the presence and absence of a metabolic activation (rat liver S9). There was no evidence of mutagenicity in the strains tested (Gladnick, 2001).

Male and female *Drosophila melanogaster* were exposed to FC-C318 (concentration not stated) for 10 minutes. The gas acted as an "impressively rapid anaesthetic". On being removed from the FC-C318 atmosphere, the flies quickly resumed full activity with no signs of abnormal or disoriented behaviour. Five mutations were scored among 1,300 females tested: 3 eye colour mutants and 2 cut wing mutants. The frequency of 5/1,300 sex chromosomes tested gave an induced visible mutation rate of 0.38% compared with a spontaneous control rate of 0.008%. The recessive mutation rate among males was 1.3%. Another strain of flies had a 0.54% lethal mutation rate. Statistical analysis showed that the visible mutations were significantly increased ($p = 0.05$) while the increase in sex-linked recessive lethal mutation rates was not statistically significant (Foltz and Fuerst, 1974).

3.11.3.5 Chronic toxicity and carcinogenicity

Chronic exposure of laboratory animals to 100,000 ppm (818,000 mg/m^3) revealed no differences between experimental and control animals in general state, body weight, state of gas exchange, catalase activity, functional state of the CNS, morphological composition of the peripheral blood and internal organs (Evdokimov and Kerekesha, 1975). No additional information is available as this was presented in an English abstract prepared from a Russian report.

3.11.3.6 Reproductive and developmental toxicity

No data are available.

3.11.3.7 Kinetics and metabolism

No data are available.

3.11.3.8 Cardiac sensitisation

Anaesthetised male Swiss mice were exposed by inhalation to FC-C318 with and without an adrenaline challenge (6 µg/kgbw *i.v.*). The oxygen level was maintained at 20%. With FC-C318 alone, no arrhythmias were noted at concentrations of up to 400,000 ppm (3,270,000 mg/m^3). When the mice were injected with adrenaline, arrhythmias occurred at 200,000 ppm (1,640,000 mg/m^3) and 400,000 ppm, but not at 100,000 ppm (818,000 mg/m^3) (Aviado and Belej, 1974).

Beagle dogs were exposed to 800,000 ppm FC-C318 (6,540,000 mg/m^3) (20% oxygen concentration maintained) for 1 to 5 minutes while simultaneously being frightened by loud noises to stimulate the release of endogenous epinephrine. One dog exposed to the noise and one control dog not exposed to noise had marked responses. A number of other dogs were exposed to other forms of noise without any cardiac effects (Mullin, 1970).

In the standard test for cardiac sensitisation, male beagle dogs (6 or 12/group) were exposed to up to 500,000 ppm FC-C318 (4,090,000 mg/m^3) for 5 minutes and adrenaline (8 mg/kgbw) was injected *i.v.* The exposure was continued for an additional 5 minutes after the adrenaline challenge. The 500,000 ppm exposure was conducted with and without oxygen supplement (level 20% or 10%). The results are summarised in Table 1, showing the FC-C318 concentrations and number of dogs with "marked responses", i.e. arrhythmias including multiple consecutive ventricular beats.

Table 1: Cardiac sensitisation in dogs (Reinhardt et al, 1971)

Number of dogs	Concentration		Number of marked responses
	(ppm)	(mg/m^3)	
12	100,000	818,000	1
12	250,000	2,040,000	2
6	500,000	4,090,000	5
6	500,000 + O_2	4,090,000	6

In 3 anaesthetised, adrenaline challenged Rhesus monkeys (*Macaca mulatta*), FC-C318 did not influence cardiac rhythm, heart rate, contractility, aortic blood pressure, left atrial pressure or pulmonary arterial pressure, when inhaled at concentrations up to 200,000 ppm (1,640,000 mg/m^3) (Belej *et al*, 1974).

A Rhesus monkey exposed to 50,000 or 100,000 ppm FC-C318 (409,000, 818,000 mg/m^3) developed an increase in pulmonary resistance. There was no effect on minute volume, heart rate, or blood pressure (Aviado and Smith, 1975).

3.11.3.9 Neurological data

No data are available.

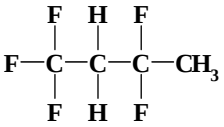
3.11.4 Human data

No data are available.

3.12 Substance profile: HFC-365mfc

3.12.1 Identity

Name:	Pentafluorobutane
IUPAC name:	Butane, 1,1,1,3,3-pentafluoro-
CAS registry number:	406-58-6
Molecular formula:	$C_4H_5F_5$
Molecular mass:	148.1
Chemical structure:	



3.12.2 Physico-chemical properties

Melting point:	No data
Boiling point:	40°C
Vapour pressure:	433 hPa at 20°C
Solubility in water:	1.7 g/l
Conversion factors:	1 ppm = 6.053 mg/m^3; 1 mg/m^3 = 0.165 ppm

3.12.3 Toxicological data

3.12.3.1 Acute Toxicity

No data are available on oral or dermal toxicity.

Inhalation

When male and female Wistar rats were exposed (nose-only) to 105,000 ppm HFC-365mfc (636,000 mg/m^3) for 4 hours no mortality was observed during 14 days. At necropsy no abnormalities were seen (Mommers, 2001; Muijser, 2001).

3.12.3.2 Irritation and sensitisation

No data are available.

3.12.3.3 Repeated dose toxicity

No data are available.

3.12.3.4 Genetic toxicity

No data are available.

3.12.3.5 Chronic toxicity and carcinogenicity

No data are available.

3.12.3.6 Reproductive and developmental toxicity

No data are available.

3.12.3.7 Kinetics and metabolism

No data are available.

3.12.3.8 Cardiac sensitisation

No data are available.

3.12.3.9 Neurological data

No data are available.

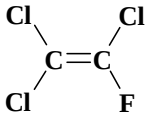
3.12.4 Human data

No data are available.

3.13 Substance profile: CFC-1111

3.13.1 Identity

Name:	Fluorotrichloroethylene
IUPAC name:	Ethene, trichlorofluoro-
CAS registry number:	359-29-5
EC number:	206-627-8
Molecular formula:	$C_2Cl_2F_3$
Molecular mass:	132.9
Chemical structure:	



3.13.2 Physico-chemical properties

Melting point:	No data
Boiling point:	71°C
Vapour pressure:	No data
Solubility in water:	No data
Conversion factors:	1 ppm = 5.432 mg/m^3; 1 mg/m^3 = 0.184 ppm

3.13.3 Toxicological data

3.13.3.1 Acute Toxicity

No data are available.

3.13.3.2 Irritation and sensitisation

No data are available.

3.13.3.3 Repeated dose toxicity

Subacute toxicity

Alpk:ApfSD rats (5/sex/group) were exposed (6 h/d, 5 d/wk) to 0, 25.8, 108 or 1,015 ppm CFC-1111 (0, 140, 587, 5,514 mg/m^3) (measured concentrations) for 2 weeks. No deaths or severe clinical effects were seen in any of the exposed groups. A number of effects were seen in those groups exposed to 1,000 ppm; transient decreases in body weight, changes in blood and urine chemistry, increase in liver and kidney weights and histopathological changes in the proximal convoluted tubules of the kidney. The no observed adverse effect level was 1,000 ppm (Parr-Dobrzanski, 1993b).

Subchronic toxicity

No data are available.

3.13.3.4 Genetic toxicity

CFC-1111 (up to 5,000 µg/plate) was without mutagenic activity in the Ames test using *Salmonella typhimurium* strains TA1535, TA1537, TA1538, TA98 and TA100 with and without metabolic activation (rat liver S9) (Callandar and Priestley, 1990a) and in an *in vitro* cytogenetics study using human lymphocytes up to 350 µg/ml, both in the presence and absence of a metabolic activation system (rat liver S9). A small but statistically significant increase in the percentage of aberrant cells exposed at the highest concentration in the absence of S9 mix was confined to a single culture and was considered not to be biologically relevant (James and Mackay, 1991).

The chemically synthesised cysteine conjugate of CFC-1111, dichlorofluorovinyl cysteine, was tested for mutagenic activity in the Ames test. *Salmonella typhimurium* (strain TA100 only) was used, both with and without a metabolic activation system based on the S9 kidney fraction derived from enzyme-induced rats. Dichlorofluorovinyl cysteine gave a positive response, both in the presence and absence of the metabolic activation system (Elliot *et al*, 1988a).

The mutagenicity of both cysteine and glutathione conjugates of CFC-1111 was studied in *Salmonella typhimurium* strains TA100 and TA98. Dichlorofluorovinyl cysteine gave a positive response in both strains, in the absence of a rat kidney S9 metabolic activation system. The mutagenicity of the glutathione conjugate, dichlorofluorovinyl glutathione, was also studied in strain TA100 only, both in the presence and absence of a rat kidney S9 metabolic activation system. A positive response was observed in both test systems (Dreeßen *et al*, 2003).

3.13.3.5 Chronic toxicity and carcinogenicity

No data are available.

3.13.3.6 Reproductive and developmental toxicity

No data are available.

3.13.3.7 Kinetics and metabolism

No data are available.

3.13.3.8 Cardiac sensitisation

CFC-1111 is reported as being able to induce cardiac arrhythmias in dogs although the effective concentration is not specified (Burgison *et al*, 1955).

3.13.3.9 Neurological data

No data are available.

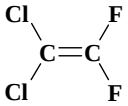
3.13.4 Human data

No data are available.

3.14 Substance profile: CFC-1112a

3.14.1 Identity

Name:	1,1-Dichloro-2,2-difluoroethylene
IUPAC name:	Ethene, 1,1-dichloro-2,2-difluoro-
CAS registry number:	79-35-6
EC number:	201-198-3
Molecular formula:	$C_2Cl_2F_2$
Molecular mass:	132.9
Chemical structure:	



3.14.2 Physico-chemical properties

Melting point:	–115°C
Boiling point:	19°C
Vapour pressure:	1,137 mg Hg (1,516 hPa)
Solubility in water:	No data
Conversion factors:	1 ppm = 5.432 mg/m^3; 1 mg/m^3 = 0.184 ppm

3.14.3 Toxicological data

3.14.3.1 Acute Toxicity

No data are available on oral or dermal toxicity.

Inhalation

The acute inhalation toxicity of CFC-1112a has been studied in the rat, the mouse, and the guinea-pig.

In the rat, the reported 4-hour LC_{50} values range from 107 ppm (581 mg/m^3) (Sakharova and Tolgskaya, 1977) to > 437 ppm CFC-1112a (2,374 mg/m^3) (Mould, 1988a). In the second study, groups of 25 male and female Alpk:ApfSD rats were exposed by inhalation to target concentrations of 25, 100 or 400 ppm CFC-1112a for 4 hours and subsequently observed for 14 days. No deaths and no severe clinical effects were observed in the exposed rats, although those

exposed to the highest concentration of CFC-1112a (actual mean exposure level 437 ppm) showed a body-weight reduction from day 2 to 8 post exposure and a statistically significant reduction in body-weight gain by day 15. These rats also showed slight increases in kidney weight and kidney/body weight ratios, which may have been treatment-related. Although there was some macroscopic evidence of kidney toxicity, no microscopic evidence of kidney damage was reported.

In addition, an approximate ALC of 1,000 ppm CFC-1112a (5,430 mg/m^3) following a 4-hour exposure has been reported (Carpenter *et al*, 1949), along with a lowest lethal concentration (LC_{Lo}) following a 1-hour exposure of 1,000 ppm (5,430 mg/m^3) (Torkelson *et al*, 1971). Histopathological changes in the liver and the kidneys were observed in rats exposed to 1,000 ppm CFC-1112a. Anaesthetic effects were also noted in rats exposed to 5,000 ppm (27,200 mg/m^3) (Torkelson *et al*, 1971). The weight of evidence suggests that the 4-hour LC_{50} reported by Sakharova and Tolgskaya (1977) is not consistent with the three other quantitative estimates of the acute toxicity of CFC-1112a.

In the mouse, a 4-hour LC_{50} value of 112 ppm (608 mg/m^3) has been reported for CFC-1112a (Carpenter *et al*, 1949).

In the guinea pig, a 4-hour LC_{50} of 129 ppm (701 mg/m^3) has been reported for CFC-1112a. A variety of sublethal effects were seen including narcosis and histological changes in the lung, kidney and brain (Sakharova and Tolgskaya, 1977). Given the discrepancy of the quantitative estimates of the acute toxicity of CFC-1112a in the rat by these authors, compared with other estimates, these data should be viewed with caution until confirmed by other studies.

Groups of 4 male Wistar rats were exposed to CFC-1112a by intraperitoneal injection at concentrations of 75, 150, 375, 600 or 750 μmol/kgbw (10, 20, 50, 80, 100 mg/kgbw). Rats receiving the lowest dose of CFC-1112a (75 μmol/kgbw) showed early signs of nephrotoxicity (increase in kidney-to-body weight ratio, increase in urinary glucose levels), whilst those receiving doses of 150 μmol/kgbw and higher showed signs of marked nephrotoxicity in rats as judged by increased urinary glucose and protein levels, and increases in N-acetyl-D-glucosaminidase (NAG), alkaline phosphatase (ALP) and γ-glutamyl transferase (GT). Rats receiving doses of 375 μmol/kgbw and higher showed signs of liver toxicity (increase in urinary enzymes; histopathology) (Commandeur *et al*, 1987).

3.14.3.2 Irritation and sensitisation

No data are available.

3.14.3.3 Repeated dose toxicity

Subacute toxicity

No data are available.

Subchronic toxicity

Twenty-five rats and ten guinea pigs were exposed (regime not stated) by inhalation to 0.037, 0.23 or 2.47 ppm CFC-1112a (reported as 0.2, 1.26 or 13.4 mg/m^3) for 4 months. Following exposure to 2.47 ppm CFC-1112a, there were signs of CNS and respiratory tract effects together with kidney and brain lesions. The effects were not fully reversible. The no observed effect level (NOEL) was 0.23 ppm (Sakharova and Tolgskaya, 1977).

Male and female Alpk:ApfSD rats (5 or 10/group) were exposed (6 h/d) by inhalation (whole body) to CFC-1112a at concentrations of 0, 0.1, 1.0 or 10.0 ppm CFC-1112a (0, 0.54, 5.43, 54.3 g/m^3) for 10 consecutive days and observed for a further 14 days. Bodyweights were recorded throughout the study and urine analysis and haematology was conducted at the end of the observation period. Macro- and histopathology was also conducted on a number of organs, including the lung, liver, kidneys and testes. No toxicologically significant effects were seen on clinical examination, clinical chemistry, haematology, bone marrow cytology, body weights, organ weights or the histological examination of the major organs. The NOAEL for CFC-1112a in this study was concluded to be 10.0 ppm (54.3 mg/m^3) (Mould, 1988b).

3.14.3.4 Genetic toxicity

CFC-1112a (5,000 - 40,000 ppm; 27,200 - 218,000 mg/m^3) was evaluated for mutagenic activity in the Ames test using *Salmonella typhimurium* strains TA98 and TA100. The plates were exposed for 72 hours both with and without rat liver S9 metabolic activation. CFC-1112a was not mutagenic (Waskell, 1979).

CFC-1112a (5,000 - 200,000 ppm; 27,200 - 1,090,000 mg/m^3) was evaluated for mutagenic activity in the Ames test using *Salmonella typhimurium* strains TA1535, TA1537, TA1538, TA98 and TA100. The plates were exposed for 72 hours with and without rat liver S9 metabolic activation. CFC-1112a was not mutagenic (Callander and Priestley, 1992a).

An Ames test was also conducted on the cysteine conjugate of CFC-1112a. The same tester strains as above were exposed to concentrations of the conjugate ranging from 0.3 to

1,000 µg/plate, in the presence of a rat kidney metabolic activation system. The cysteine conjugate was not mutagenic (Callander and Priestley, 1992b).

CFC-1112a was found to be positive in an *in vitro* cytogenetics assay with human lymphocytes from a single male donor. It was tested over a range of atmospheric concentrations up to 100,000 ppm (543,000 mg/m^3). The highest concentration caused toxicity (duration of exposure not specified). Statistically significant increases of chromosome aberrations were observed both in the presence and in the absence of S9, in a dose-dependent manner. The response was most marked in the absence of S9 (Elliot *et al*, 1988b).

Human lymphocytes from a single donor were exposed for 3 hours to 10,000 to 120,000 ppm CFC-1112a (54,300 - 652,000 mg/m^3), with and without rat liver S9 metabolic activation. Statistically significant increases of chromosome aberrations were observed, both in the presence and in the absence of S9. It was concluded that CFC-1112a was clastogenic to human lymphocytes *in vitro* (Randall and Mackay, 1992).

3.14.3.5 Chronic toxicity and carcinogenicity

No data are available.

3.14.3.6 Reproductive and developmental toxicity

No data are available.

3.14.3.7 Kinetics and metabolism

The metabolism of CFC-1112a has been studied in the rat. The target organ was the kidney, and toxicity was to the proximal tubule. The N-acetyl cysteine conjugate of CFC-1112a was identified in the urine of rats, suggesting that the major metabolic pathway was conjugation with glutathione with subsequent hydrolysis. There was evidence that the cysteine conjugate was a substrate for the enzyme cysteine conjugate β-lyase, and this metabolic pathway was responsible for the generation of the nephrotoxic species. Oxidation by cytochrome P450 was a comparatively minor pathway, and was associated with the hepatotoxicity of CFC-1112a at high doses (Commandeur *et al*, 1987).

CFC-1112a was reported to undergo some defluorination in rats acutely exposed to high concentrations as demonstrated by an increase of the urinary excretion of fluoride ions (Sakharova and Tolgskaya, 1977).

3.14.3.8 Cardiac sensitisation

No data are available.

3.14.3.9 Neurological data

No data are available.

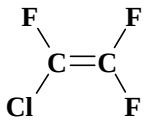
3.14.4 Human data

No data are available.

3.15 Substance profile: CFC-1113

3.15.1 Identity

Name:	Chlorotrifluoroethylene
IUPAC name:	Ethene, 1-chloro-1,2,2-trifluoro-
CAS registry number:	79-38-9
Molecular formula:	C_2ClF_3
Molecular mass:	116.5
Chemical structure:	



3.15.2 Physico-chemical properties

Melting point:	–157.5°C
Boiling point:	–27.9°C
Relative density $D_4^{21.1}$:	1.31 (Honeywell, 2000)
Vapour pressure:	4,800 hPa[a] at 70°C
Vapour density (air = 1):	4
Solubility in water:	380 mg/l at 28°C (Ausimont, 2001)
Flammability limits in air:	14.2 - 43.7% (v/v) according to ASTM E-681 method
Conversion factors:	1 ppm = 4.762 mg/m^3; 1 mg/m^3 = 0.210 ppm

3.15.3 Toxicological data

3.15.3.1 Acute toxicity

Oral

An oral LD_{50} value in mice was 268 mg/kgbw, when CFC-1113 was administered as a 3.5% solution in edible oil (Walther and Fischer, 1968).

Dermal

No data are available.

[a] Reported as 70 psia (pounds/inch^2 absolute pressure; 1 bar = 1,000 hPa = 14.5 psia)

Inhalation

The 2-hour LC_{50} in (unspecified) rats was 5,040 ppm CFC-1113 (24,000 mg/m^3). All animals exposed to 5,544 or 7,560 ppm (26,400, 36,000 mg/m^3) died during the first few days after the exposure. The predominant finding was necrosis of the kidney (Kochanov, 1958 cited by Clayton, 1977).

The 4-hour LC_{50} in male Sprague-Dawley rats (4/group) was 1,000 ppm (4,760 mg/m^3). Renal toxicity was observed by microscopic examination of the tissues (Clayton, 1967 cited by Clayton, 1977).

Male Fischer 344 rats were exposed to CFC-1113 levels of 100, 220, 395 or 540 ppm (476, 1,050, 1,880, 2,570 mg/m^3) for 4 hours. Exposures of 220 ppm and above resulted in degenerative changes in renal tubules. Within two days following the exposure, the rats exhibited dose-related proximal tubular necrosis, diuresis, and increases in blood urea nitrogen and serum creatinine levels, urinary fluoride, and urinary lactic dehydrogenase activity. Exposure to 100 ppm (476 mg/m^3) resulted in diuresis. The effects were reversible (Potter *et al*, 1981; Buckley *et al*, 1982). The LC_{50} in this study was greater than 540 ppm.

The acute toxicity of CFC-1113 was evaluated in male white mice. Exposures were static, but the volume of air was large relative to the number of animals (maximum 20 mice in 60-litre chamber) and the air was changed every half hour. Concentrations were not measured, but the air flow used to make up the standard gas mixtures was kept constant at 120 l/h. The animals were exposed to three different concentrations for up to 36 hours and the mortalities recorded. Under these conditions the 3-hour LC_{50} was 8,000 ppm (38,000 mg/m^3). Additional LC_{50} values for 7 and 24 hours were 3,000 and 1,000 ppm (14,300, 4,760 mg/m^3), respectively (Walther and Fischer, 1968; Walther *et al*, 1970).

Rats and rabbits (unspecified) were exposed to vapours of CFC-1113 for 2 hours. The LC_{50} values for both species were 5,040 ppm (24,000 mg/m^3). The predominant finding was necrosis of the kidney (Kochanov, 1958 cited by Clayton, 1977).

3.15.3.2 Irritation and sensitisation

Skin irritation

No data are available.

Eye irritation

No data are available.

Sensitisation

No data are available.

3.15.3.3 Repeated dose toxicity

Subacute toxicity

Sprague-Dawley rats exposed (6 h/d, 5 d/wk) to 243 ppm CFC-1113 (1,157 mg/m^3) for 2 weeks developed renal tubular necrosis. Exposure up to 119 ppm (567 mg/m^3) did not cause any adverse effects. In another study, male Sprague-Dawley rats exposed (4 h/d) to 395 ppm CFC-1113 (1,881 mg/m^3) for 5 consecutive days, again showed necrosis of the kidney. This effect was found to be reversible (Gad *et al*, 1988).

Subchronic toxicity

A 13-week inhalation study was conducted with Sprague-Dawley rats exposed (6 h/d, 5 d/wk) to levels of 0, 29, 62 or 121 ppm (0, 138, 295, 576 mg/m^3). Exposures at 62 and 121 ppm resulted in dilated tubules. At 62 ppm the effect appeared reversible. The NOEL was 29 ppm (Gad *et al*, 1988).

In a study conducted in the mid-1950s, dogs, guinea pigs, rats and rabbits (strain and sex not stated) were given a series of up to 18 4-hour exposures to 300 ppm of CFC-1113 (1,430 mg/m^3). Deaths occurred among the rabbits and guinea pigs. The rats showed renal damage, while the dogs developed encephalopathy, intermittent leucopenia and granulocytopenia (Clayton, 1977). In a subsequent study, which lasted approximately 14 months, dogs, rabbits, guinea pigs and rats were given 6-hour exposures to progressively higher levels of CFC-1113 at 15, 30, 50, 100 or 150 ppm (71, 143, 238, 476, 714 mg/m^3). No effects were seen in the guinea pigs or rabbits. The rats again developed degenerative changes in the renal tubules and the dogs showed some haematological changes. The exact exposure level causing these changes could not be determined.

Kochanov (1958 cited by Clayton, 1977) conducted two inhalation studies with rabbits (strain and sex not stated). In the first study, mortality was seen at 500 ppm CFC-1113 (2,380 mg/m^3) after 56 exposures. In the second one, exposure at 250 ppm (1,190 mg/m^3) over a period of 70 to 110 days resulted in haematological changes. These findings have not been reported in rabbits in any other study.

When male rats (20/group) (strain not stated) were exposed (5h/d, 5 d/wk) to either 100 or 200 ppm of CFC-1113 (476, 952 mg/m^3) for 17 weeks, renal changes (tubular necrosis) were noted (Zhou *et al*, 1980).

3.15.3.4 Genetic toxicity

In vitro, CFC-1113 was not mutagenic when tested in an Ames Assay using *Salmonella typhimurium* strains TA98, TA100, TA1535 and TA1537, with and without S9 metabolic activation. Both positive and negative controls were included. The vapour concentrations used were 125,000, 250,000 or 500,000 ppm (595,000, 1,190,000, 2,380,000 mg/m^3). The 500,000 ppm level showed marked cytotoxicity (Wudl and Goode, 1982).

In vivo, CFC-1113 was evaluated for its ability to induce sister chromatid exchanges in rats and rabbits. The animals were given 5 exposures (6 h) in the first week and 4 in the second week to levels of 0 (control), 10, 30, and 100 ppm (47.6, 143, 476 mg/m^3) (Stetka *et al*, 1983).

3.15.3.5 Chronic toxicity and carcinogenicity

Other than the studies described in Section 3.15.3 above, where exposures lasted up to 14 months, no data on chronic studies were found.

3.15.3.6 Reproductive and developmental toxicity

A pilot inhalation, developmental study with rats was conducted concurrently with the 13-week study described above with exposures occurring during days 6 to 19 of gestation. At 119 and 241 ppm (567, 1,148 mg/m^3), body-weight gain reductions were seen. No effects were seen at 33 and 61 ppm (157, 290 mg/m^3). There was no evidence of foeto-, embryo- or developmental toxicity (Gad *et al*, 1988).

3.15.3.7 Kinetics and metabolism

The *in vivo* formation of cysteine conjugates has been postulated to account for the nephrotoxicity of CFC-1113. Initially, the glutathione conjugate is formed; it is then cleaved to form the cysteine conjugate (S-(2-chloro-1,1,2-trifluoroethyl)-L-cysteine) (Harris *et al*, 1992; Tanaka and Anders, 1995). This reaction proceeds in both rat and isolated human liver sections at similar rates (Boogaard *et al*, 1989; Dohn *et al*, 1985). Isolated rabbit renal tubule suspensions were also used to demonstrate the bio-transformation of CFC-1113 by glutathione conjugation to form the nephrotoxic metabolite. *In vivo* and *in vitro* evidence supported metabolism of chemically synthesised glutathione conjugates to the nephrotoxic cysteine conjugate (Hassall *et al*, 1984). The mechanism of toxic action is believed to proceed through inhibition of the re-adsorption of glucose in the proximal tubules in the kidney (Dohn *et al*, 1985).

3.15.3.8 Cardiac sensitisation

Exposure of anaesthetised dogs to concentrations of CFC-1113 ranging from 250,000 to 500,000 ppm (1,190,000 - 2,380,000 mg/m^3), with oxygen added to maintain acceptable atmospheric levels, for periods of 5 to 15 minutes, subsequent to intravenous injection of epinephrine (adrenalin), resulted in cardiac sensitisation in four out of four dogs (Burgison *et al*, 1955). As this study was not run at reasonable exposure levels and did not report a no effect level, threshold or even an EC_{50}, it is of minimal value.

3.15.3.9 Neurological data

No data are available.

3.15.4 Human data

CFC-1113 has been produced for over 40 years. Exposure levels have tended to be at or below 20 ppm (95 mg/m^3) as a TWA concentration. No adverse effects have been reported (Kennedy, 1990).

Occupational exposure limit

The OEL value for CFC-1113 is 5 ppm (24 mg/m^3) as an 8-h TWA (AIHA, 2008a). The level was based on kidney effects seen in the subchronic study described above at 62 and 121 ppm and the NOEL of 29 ppm (Gad *et al*, 1988).

Other hygiene standards

A US National Advisory Committee has proposed acute exposure guideline levels (AEGLs) for once-in-a-lifetime, short-term (not repeated chronic) exposures (of the general population) to airborne concentrations of CFC-1113 for up to 8 hours (NAC, 2006a) (Table 2). The AEGL-1 and -2 levels were based on the 4-hour NOAEL of 102 ppm for mild diuresis (without kidney necrosis) and a concentration of 540 ppm for reversible kidney necrosis in the rat, respectively (Potter et al, 1981). The AEGL-3 values were derived from an 8-hour non-lethal concentration of 1,000 ppm in the mouse (Walther and Fischer, 1968).

Table 2: AEGLs (ppm) for CFC-1113

Time:	10 min	30 min	60 min	4 h	8 h
AEGL 1	29	20	16	10	10
AEGL 2	160	110	86	54	54
AEGL 3	360	250	200	130	100

Similarly, the American Industrial Hygiene Association (AIHA, 2008b) has established emergency response planning guideline (ERPG) values for CFC-1113 as the maximum airborne concentration below which it is believed that nearly all individuals could be exposed for up to 1 hour without:

• Experiencing other than mild, transient adverse health effects or without perceiving a clearly defined objectionable odour (ERPG-1: 20 ppm) (**95** mg/m^3);

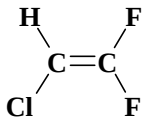
• experiencing or developing irreversible or other serious health effects or symptoms which could impair an individual's ability to take protective action (ERPG-2: 100 ppm) (476 mg/m^3);

• experiencing or developing life-threatening health effects (ERPG-3: 300 ppm) (1,430 mg/m^3).

3.16 Substance profile: HCFC-1122

3.16.1 Identity

Name:	1-Chloro-2,2-difluoroethylene
IUPAC name:	Ethene, 1-chloro-2,2-difluoro-
CAS registry number:	359-10-4
Molecular formula:	C_2HClF_2
Molecular mass:	98.5
Chemical structure:	



3.16.2 Physico-chemical properties

Melting point:	–138.5°C
Boiling point:	–17.5°C - –17.7°C
Vapour pressure:	No data
Solubility in water:	No data
Conversion factors:	1 ppm = 4.026 mg/m^3; 1 mg/m^3 = 0.248 ppm

3.16.3 Toxicological data

3.16.3.1 Acute Toxicity

No data are available on oral or dermal toxicity.

Inhalation

Wistar-derived rats (4 females/group) were exposed to 1,000, 5,000 (nominal) or 8,600 ppm (measured) HCFC-1122 (4,030, 20,100, 34,600 mg/m^3) for 7 hours. The animals were killed 2 to 3 weeks later. No mortality and no clinical signs except a weight loss were observed up to 8,600 ppm. Dose-dependent changes (degenerative, necrotic and congestive effects) were observed in the kidney (Torkelson *et al*, 1971).

Male Alpk:AP strain rats (3/group) were exposed to 500, 1,000 or 2,000 ppm (measured) of HCFC-1122 (2,010, 4,030, 8,050 mg/m^3) for 6 hours. At 18 hours after exposure to 2,000 ppm, marked necrosis of the renal proximal tubules was seen with significant biochemical markers of

renal toxicity. The kidney was unaffected at 500 and 1,000 ppm, as was the liver at all three levels of exposure (Green *et al*, 1991).

3.16.3.2 Irritation and sensitisation

No data are available.

3.16.3.3 Repeated dose toxicity

Subacute toxicity

Alpk:APfSD rats (5/sex/group) were exposed (6 h/d) by inhalation (whole-body) to 0 (control), 25.2, 92.4 or 973 ppm HCFC-1122 (0, 102, 373, 3,925 mg/m^3) for 14 consecutive days. No toxicologically significant changes were seen in clinical observations, body weights, and haematological or histopathological examinations. The major effects seen were confined to those animals exposed to 973 ppm and included increases in male kidney weight and changes in urine parameters (urine volume, protein content and specific gravity) in males and females. The NOEL was 92.4 ppm (Lewis, 1991).

Subchronic toxicity

No data are available.

3.16.3.4 Genetic toxicity

HCFC-1122 was not mutagenic in the Ames test using *Salmonella typhimurium* in the absence or presence of metabolic activation. Up to 1,000,000 ppm (100%) HCFC-1122 (4,030,000 mg/m^3) induced a dose-dependent increase in chromosomal aberrations in human lymphocytes *in vitro* in the absence and in presence of metabolic activation (Table 3).

Table 3: Genotoxicity of HCFC-1122 in vitro

Endpoint / Species, strain	Concentration		S9 [a]	Result [b]	Reference
Gene mutation	(ppm)	(mg/m^3)			
Salmonella typhimurium TA100	5,000 - 100,000	20,100 - 403,000	+/–	–ve [c]	Edmunds *et al*, 1979
Salmonella typhimurium TA98, TA100, TA1535, TA1537, TA1538	50,000 -1,000,000	201,000 - 4,030,000	+/–	–ve	Callander and Priestley, 1990b
Chromosome aberration					
Human lymphocytes	50,000 - 350,000	201,000 - 1,410,000	+/–	+ve	Fox and Mackay, 1992

[a] Presence (+) and absence (–) of S9 metabolic activation system
[b] –ve, negative; +ve, positive
[c] < × 2 compared to control

The cysteine conjugate of HCFC-1122, N-acetyl-S-(1-chloro-2,2-difluoroethyl)cysteine, did not show gene mutation potential in the Ames test using *Salmonella typhimurium* in the absence or presence of metabolic activation, except for a weak positive result with the TA100 strain. The cysteine conjugate did not induce DNA alterations in two different bacterial assays in the absence or in presence of metabolic activation (Table 4).

Table 4: Genotoxicity of HCFC-1122 cysteine conjugate in vitro

Endpoint / Species, strain	Dose	S9 [a]	Result [b]	Reference
Gene mutation	(µg/plate)			
Salmonella typhimurium TA98, TA1535, TA1537, TA1538	0.064 - 200	+	–ve	Callander and Priestley, 1992b
Salmonella typhimurium TA100	0.064 - 200	+/–	Weakly +ve	Callander and Priestley, 1992b
Salmonella typhimurium TA100, TA1535	60 - 3,000	+/–	–ve	Sachdev *et al*, 1980
Primary DNA damage				
Bacillus subtilis H17, M45, recombination-deficient strain	Not stated	+/–	+ve	Sachdev *et al*, 1980
Escherichia coli, DNA polymerase-deficient strain	Not stated	Not stated	–ve	Sachdev *et al*, 1980

[a] Presence (+) and absence (–) of S9 metabolic activation system
[b] –ve, negative; +ve, positive

3.16.3.5 Chronic toxicity and carcinogenicity

No data are available.

3.16.3.6 Reproductive and developmental toxicity

No data are available.

3.16.3.7 Kinetics and metabolism

After inhalation exposure of Alpk:APfSD rats to 2,000 ppm HCFC-1122 (8,050 mg/m^3) for 6 hours, the compound was metabolised to a limited extent by two pathways: (i) an oxidation leading to the excretion of chlorodifluoroacetic acid in urine and (ii) conjugation with glutathione resulting in the excretion of N-acetyl-*S*-(1-chloro-2,2-difluoroethyl)cysteine. The latter was the major metabolite in urine and was present at concentrations of up to 40-fold greater than those of chlorodifluoroacetic acid. As described by Odum and Green (1984), cysteine conjugates can be

metabolised in the kidney either via β-lyase (leading to reactive thiols that are cytotoxic for the proximal tubule) or via N-acetyltransferase. Strong nephrotoxicity of the HCFC-1122 cysteine conjugate was evidenced by microscopic examination of the kidneys from rats given single oral doses of the compound. An *in vitro* assay showed that the HCFC-1122 cysteine conjugate was metabolised by both β-lyase and N-acetyltransferase enzymes, the V_{max} for the transferase enzyme being over 100-fold greater than that of β-lyase. This study confirmed that HCFC-1122 is metabolised and has the toxicological properties expected of this class of chemicals. Because of the low overall rate of metabolism of HCFC-1122 and the high rate of metabolism of the cysteine conjugate by N-acetyltransferases in the kidney, HCFC-1122 is a weak nephrotoxicant with a clear NOEL of 1,000 ppm for a single 6-hour exposure (Lewis, 1991).

Studies in hepatic microsomes from phenobarbital-treated rabbits incubated with HCFC-1122 have shown that the compound is oxidatively metabolised by cytochrome P450 to intermediates which inactivate cytochrome P450 by destroying haem, and to epoxides which may react with cellular macromolecules or decompose to other products (Baker *et al*, 1987). Similar studies have shown that HCFC-1122 is defluorinated by cytochrome P450 and the level of defluorination is enhanced by fluoroethanes like halothane, HCFC-123, HCFC-133a and HCFC-124 (Wang *et al*, 1993). Studies on human hepatic liver microsomes have also shown that HCFC-1122 is defluorinated by cytochrome P450 and this is enhanced by isoflurane probably through CYP 2B6 (Baker *et al*, 1995).

3.16.3.8 Cardiac sensitisation

No data are available.

3.16.3.9 Neurological data

No data are available.

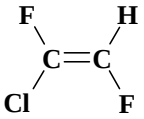
3.16.4 Human data

No data are available.

3.17 Substance profile: HCFC-1122a

3.17.1 Identity

Name:	1-Chloro-1,2-difluoroethylene (mixture of *cis* and *trans* isomers)
IUPAC name:	Ethene, 1-chloro-1,2-difluoro-
CAS registry number:	359-04-6
Molecular formula:	C_2HClF_2
Molecular mass:	98.5
Chemical structure:	



3.17.2 Physico-chemical properties

Melting point:	No data
Boiling point:	–5°C
Vapour pressure:	No data
Solubility in water:	No data
Conversion factors:	1 ppm = 4.026 mg/m^3; 1 mg/m^3 = 0.248 ppm

3.17.3 Toxicological data

3.17.3.1 Acute Toxicity

No data are available on oral or dermal toxicity.

Inhalation

Mice (1/group) were exposed to HCFC-1122a as a mixture of *cis* and *trans* isomers in approximately equal proportion. The duration of exposure was not stated but was in the order of a few minutes. Mice exposed from 129,000 to 167,000 ppm HCFC-1122a (519,900 - 672,000 mg/m^3) became quickly anaesthetised and recovered after the end of exposure (time not stated); one mouse exposed to 147,000 ppm (592,000 mg/m^3) did not recover (death not reported). Mice exposed to 218,000 ppm (878,000 mg/m^3) or higher died without regaining consciousness. The LC_{Lo} was 218,000 ppm (Burns *et al*, 1961).

3.17.3.2 Irritation and sensitisation

No data are available.

3.17.3.3 Repeated dose toxicity

No data are available.

3.17.3.4 Genetic toxicity

No data are available.

3.17.3.5 Chronic toxicity and carcinogenicity

No data are available.

3.17.3.6 Reproductive and developmental toxicity

No data are available.

3.17.3.7 Kinetics and metabolism

No data are available.

3.17.3.8 Cardiac sensitisation

No data are available.

3.17.3.9 Neurological data

No data are available.

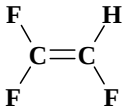
3.17.4 Human data

No data are available.

3.18 Substance profile: HFC-1123

3.18.1 Identity

Name:	Trifluoroethylene
IUPAC name:	Ethene, trifluoro-
CAS registry number:	359-11-5
Molecular formula:	C_2HF_3
Molecular mass:	82.0
Chemical structure:	



3.18.2 Physico-chemical properties

Melting point:	No data
Boiling point:	–51°C (Henne, 1944 cited by Burns, 1961)
	–53°C (Columbia Chemicals, 1954 cited by Burns, 1961)
Vapour pressure:	No data
Solubility in water:	No data
Flammability limits:	17.4 - 25-30% (Burns, 1961)
Log K_{ow}:	1.16 (calculated using SRC method) (HSDB, 2001)
Conversion factors:	1 ppm = 3.352 mg/m^3; 1 mg/m^3 = 0.298 ppm

3.18.3 Toxicological data

3.18.3.1 Acute Toxicity

No data are available on oral or dermal toxicity.

Inhalation

HFC-1123 was not anaesthetic for mice by inhalation at concentrations up to 769,000 ppm (2,578,000 mg/m^3), the highest concentration tested (Burns, 1961).

3.18.3.2 Irritation and sensitisation

No data are available.

3.18.3.3 Repeated dose toxicity

No data are available.

3.18.3.4 Genetic toxicity

No data are available.

3.18.3.5 Chronic toxicity and carcinogenicity

No data are available.

3.18.3.6 Reproductive and developmental toxicity

No data are available.

3.18.3.7 Kinetics and metabolism

Male rats were exposed (whole-body) to a concentration of 3,000 ppm HFC-1123 (10,060 mg/m^3) for 30 minutes. After exposure, animals were kept in metabolism cages for 19 days. Compared to controls, the daily fluoride ion excretion in urine increased only during days 5 and 6 after exposure. Diuresis and creatinine excretion increased during days 2 to 8 after exposure. Potassium excretion increased from day 2 to day 6. No pathological lesions in the kidneys of treated animals were observed. The effect of HFC-1123 on renal function was suspected to be focussed on its action on the proximal renal tubuli (Dilley *et al*, 1974).

HFC-1123 incubated with pre-treated hepatic rat microsomes was metabolised by cytochrome P450 with a moderate degree of conversion to fluoride. However, HFC-1123 metabolism subsequently became inactivated by metabolites of HFC-1123 (Baker *et al*, 1987).

3.18.3.8 Cardiac sensitisation

No data are available.

3.18.3.9 Neurological data

No data are available.

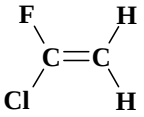
3.18.4 Human data

No data are available.

3.19 Substance profile: HCFC-1131a

3.19.1 Identity

Name:	1-Chloro-1-fluoroethylene
IUPAC name:	Ethene, 1-chloro-1-fluoro-
CAS registry number:	2317-91-1
Molecular formula:	C_2H_2ClF
Molecular mass:	80.5
Chemical structure:	



3.19.2 Physico-chemical properties

Melting point:	No data
Boiling point:	–25°C
Vapour pressure:	No data
Solubility in water:	No data
Conversion factors:	1 ppm = 3.290 mg/m^3; 1 mg/m^3 = 0.304 ppm

3.19.3 Toxicological data

3.19.3.1 Acute Toxicity

No data are available on oral or dermal toxicity.

Inhalation

Two groups of Wistar rats (10/sex/group) were exposed (nose-only) to HCFC-1131a for 4 hours. The first group was exposed to a nominal concentration of 14,136 ppm (46,510 mg/m^3) and the second to a measured concentration of 9,940 ppm (32,700 mg/m^3). There were no mortalities, but during the exposure a decrease in respiratory rate was seen. This was attributed to CNS depression. No other clinical signs were noted. The 4-hour non-lethal concentration (LC_0) was 10,000 ppm (32,900 mg/m^3) (Janssen and Van Doorn, 1993).

3.19.3.2 Irritation and sensitisation

Skin irritation

No data are available.

Eye irritation

No data are available.

Sensitisation

No data are available.

3.19.3.3 Repeated dose toxicity

Subacute toxicity

No data are available.

Subchronic toxicity

No data are available.

3.19.3.4 Genetic toxicity

A gene mutation assay using *Salmonella typhimurium* strains TA1535, TA1537, TA1538, TA98 and TA100, and *Escherichia coli* WP2 uvrA was conducted with HCFC-1131a, both with and without metabolic activation (rat liver S9). Exposure of the bacterial cultures to 450,000 ppm HCFC-1131a (1,480,000 mg/m^3) produced a positive response in all strains tested in the presence of metabolic activation. There was also a positive response in strains TA98 and TA1538 in the absence of metabolic activation (May, 1991).

The clastogenic potential of HCFC-1131a was evaluated in cultured human lymphocytes exposed to concentrations up to 600,000 ppm (1,970,000 mg/m^3), with and without metabolic activation. While an increase in gaps was reported, no other response was seen. It was concluded that HCFC-1131a showed no clear evidence of clastogenic activity (Edwards, 1991).

3.19.3.5 Chronic toxicity and carcinogenicity

No data are available.

3.19.3.6 Reproductive and developmental toxicity

No data are available.

3.19.3.7 Kinetics and metabolism

No data are available.

3.19.3.8 Cardiac sensitisation

No data are available.

3.19.3.9 Neurological data

No data are available.

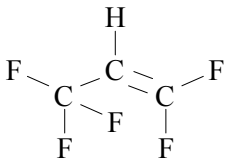
3.19.4 Human data

No data are available.

3.20 Substance profile: HFC-1225zc

3.20.1 Identity

Name:	Pentafluoropropylene
	2-Hydroperfluoropropene
IUPAC name:	Prop-1-ene, 1,1,3,3,3-pentafluoro-
CAS registry number:	690-27-7
Molecular formula:	C_3HF_5
Molecular mass:	132.0
Chemical structure:	



3.20.2 Physico-chemical properties

Melting point:	–153.1°C
Boiling point:	–21°C
Vapour pressure:	No data
Solubility in water:	Insoluble (Henne and Waalkes, 1946)
Conversion factors:	1 ppm = 5.395 mg/m^3; 1 mg/m^3 = 0.185 ppm

3.20.3 Toxicological data

3.20.3.1 Acute Toxicity

No data are available on oral or dermal toxicity.

Inhalation

The 4-hour ALC in male Chr-CD rats was reported to be 851 ppm HFC-1225zc (4,590 mg/m^3). Clinical signs of toxicity during exposure to sublethal concentrations of HFC-1225zc consisted of irregular respiration. Post-exposure, the rats had moderate to severe weight loss (Sarver, 1974).

Male Sprague-Dawley rats undergoing an *in vivo* micronucleus test (Section 3.20.3.4) were exposed (nose-only) to mean atmospheric concentrations of approximately 330, 620 or 1,100 ppm HFC 1225zc (1,780, 3,340, 5,930 mg/m^3) for 6 hours. Animals were killed 24 hours after exposure and additional rats receiving the highest concentration were killed after 48 hours. During the 6-hour exposure, rats exposed to 330 and 620 ppm exhibited a diminished response to an auditory stimulus. As normally seen in nose-only exposures, red discharge from the eyes was evident in all rats immediately after exposure, but persisted only in the high concentration group for 24 hours after exposure. Additional signs of toxicity (some of which persisted in the highest concentration group until the 24 hour kill) included lethargy, shut or half-shut eyes, red discharge from the nose, gasping, involuntary sudden jerking, pallor, yellow stained perineum, irregular respiration, tremors and hypersensitivity. Approximately half of the animals killed after 48 hours showed no signs of toxicity. A statistically significant decrease in body weight occurred at 620 ppm (24 hours post exposure) and 1,100 ppm (24 and 48 hours post exposure) (Ford, 2000).

3.20.3.2 Irritation and sensitisation

Skin irritation

No data are available.

Eye irritation

No data are available.

Sensitisation

No data are available.

3.20.3.3 Repeated dose toxicity

Subacute toxicity

No data are available.

Subchronic toxicity

No data are available.

3.20.3.4 Genetic toxicity

HFC-1225zc was evaluated for mutagenic activity in *Salmonella typhimurium* strains TA97a, TA98, TA100 and TA1535, and in *Escherichia coli* WP2 uvrA (pKM101), both in the presence and absence of metabolic activation. The test concentrations were 0, 760, 1,370, 4,740, 10,900 and 47,600 ppm (0, 4,100, 7,390, 25,570, 58,800, 256,800 mg/m^3). Evidence of mutagenicity was detected with strain TA98 without activation at 4,740, 10,900 and 47,600 ppm, and with strain TA1535 with activation at 47,600 ppm. Both strains exhibited concentration-related increases of the mean number of revertants per plate compared to controls (Lawrence Gladnick, 2000).

HFC-1225zc was evaluated in a micronucleus test using male Sprague-Dawley rats exposed (nose-only) to 0, 330, 620 or 1,100 ppm (0, 1,780, 3,340, 5,930 mg/m^3) for 6 hours. Bone marrow smears were prepared at approximately 24 hours after the end of exposure. For 5 additional control and 5 highest-concentration rats, bone marrow was sampled after 48 hours. A statistically significant increase in the frequency of micronucleated polychromatic erythrocytes (PCEs) was observed in the bone marrow of rats exposed to 1,100 ppm 24 hour after exposure. The test for trends of increasing micronucleated PCE counts was statistically significant (Ford, 2000).

3.20.3.5 Chronic toxicity and carcinogenicity

No data are available.

3.20.3.6 Reproductive and developmental toxicity

No data are available.

3.20.3.7 Kinetics and metabolism

No data are available.

3.20.3.8 Cardiac sensitisation

No data are available.

3.20.3.9 Neurological data

No data are available.

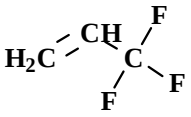
3.20.4 Human data

No data are available.

3.21 Substance profile: HFC-1243zf

3.21.1 Identity

Name:	1,1,1-Trifluoropropylene
IUPAC name:	Prop-1-ene, 3,3,3-trifluoro-
CAS registry number:	677-21-4
Molecular formula:	$C_3H_3F_3$
Molecular mass:	96.1
Chemical structure:	



3.21.2 Physico-chemical properties

Melting point:	No data
Boiling point:	–26°C
Vapour pressure:	No data
Solubility in water:	No data
Conversion factors:	1 ppm = 3.928 mg/m^3; 1 mg/m^3 = 0.255 ppm

3.21.3 Toxicological data

3.21.3.1 Acute Toxicity

No data are available on oral or dermal toxicity.

Inhalation

Male and female Sprague-Dawley rats (number not stated) were exposed by inhalation to 0, 267,000 or 367,000 ppm HFC-1243zf (0, 1,050, 1,440 g/m^3) (reported as 0, 1.05, 1.44 g/l) for 4 hours. No test material-related deaths occurred. Rats exposed to the highest concentration exhibited ataxia and tremors, which subsided within one day after exposure. No dose-related effects were noted during necropsy (Dow Corning, 1993).

Swiss mice (2/sex/group) were exposed by inhalation to HFC-1243zf at concentrations of 158,000, 316,000, 423,000, 530,000 or 634,000 ppm (620, 1,240, 1,660, 2,080, 2,490 g/m^3) (reported as 0.62, 1.24, 1.66, 2.08, 2.49 g/l) for 1 hour. All mice exposed to 530,000 and 634,000 ppm died. No significant clinical signs were noted in mice exposed to 158,000 ppm.

Observations included inactivity, dyspnoea, salivation, anaesthesia, loss of righting reflex, excitation and ataxia. The LC_{50} was 446,000 ppm (1,750,000 mg/m^3) (reported as 1.75 g/l) (Dow Corning, 1993).

Exposure of animals (species and strain not specified) to 10,000 ppm HFC-1243zf (39,300 mg/m^3) for 7 hours was without ill effects (Torkelson, 1956).

3.21.3.2 Irritation and sensitisation

No data are available.

3.21.3.3 Repeated dose toxicity

Subacute toxicity

Ten male and 10 female Sprague-Dawley rats were exposed (6 h/d, 5 d/wk) by inhalation to 987 ppm HFC-1243zf (3,872 mg/m^3) for 2 weeks. No mortality, clinical signs of toxicity, organ weight effects or treatment-related pathology was noted (Dow Corning, 1993).

Subchronic toxicity

No data are available.

3.21.3.4 Genetic toxicity

The mutagenic activity of HFC-1243zf was evaluated in a standard Ames test using *Salmonella typhimurium* strains TA1535, TA1537, TA98 and TA100, in the absence or presence of metabolic activation. The concentrations tested were 0 (control), 90,000, 170,000, 310,000 and 460,000 ppm (0, 354,000, 668,000, 1,220,000, 1,810,000 mg/m^3). HFC-1243zf was without mutagenic activity in TA1537, while it was mutagenic in TA1535, both with and without metabolic activation, at levels of 310,000 ppm and higher. In TA98, HFC-1243zf was mutagenic at 460,000 ppm, both with and without metabolic activation. In TA100, HFC-1243zf was also mutagenic at 460,000 ppm, with a trend below this level, again both with and without metabolic activation (DuPont, 1979).

The mutagenic activity of HFC-1243zf was evaluated in an Ames test using *Salmonella typhimurium* strains TA1535, TA1537, TA98 and TA100 and *Escherichia coli* strains WP2P and WP2PuvrA, in the absence or presence of metabolic activation. HFC-1243zf was without mutagenic activity in all strains, although an equivocal response (< 1.9 × background) was seen in strain TA1535, both with and without metabolic activation. It was concluded that HFC-1243zf was not mutagenic under the conditions of the assay (Elliot *et al*, 1995b).

3.21.3.5 Chronic toxicity and carcinogenicity

No data are available.

3.21.3.6 Reproductive and developmental toxicity

No data are available.

3.21.3.7 Kinetics and metabolism

No data are available.

3.21.3.8 Cardiac sensitisation

No data are available.

3.21.3.9 Neurological data

Dogs exposed via inhalation to 500,000 ppm HFC-1243zf (1,960,000 mg/m^3) were not anaesthetised although there were signs of incoordination and tremors. No additional information was provided in the report (Lu *et al*, 1953).

Anaesthesia was induced in 50% of adult male white mice (13) exposed via inhalation to 600,000 ppm HFC-1243zf (2,360,000 mg/m^3) for 10 minutes. Convulsions occurred during recovery period (Robbins, 1946).

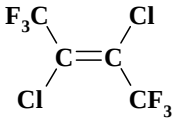
3.21.4 Human data

No data are available.

3.22 Substance profile: CFC-1316

3.22.1 Identity

Name:	2,3-Dichlorohexafluorobutene-2, *cis* and *trans* isomers
IUPAC name:	But-2-ene, 2,3-dichloro-1,1,1,4,4,4-hexafluoro-, *cis* and *trans* isomers
CAS registry number:	303-04-08
Molecular formula:	$C_4Cl_2F_6$
Molecular mass:	232.9
Chemical structure [a]:	



3.22.2 Physico-chemical properties

Melting point:	No data
Boiling point:	66.2, 67.9°C (*cis, trans*)
Vapour pressure:	146, 157 mm Hg (*cis, trans*) (195, 209 hPa)
Solubility in water:	0.0004 µg/100 (Cohen *et al*, 1965)
Conversion factors:	1 ppm = 9.519 mg/m^3; 1 mg/m^3 = 0.105 ppm

3.22.3 Toxicological data

3.22.3.1 Acute Toxicity

Oral

The oral LD_{50} value of CFC-1316 in rats (sex and strain not stated) was 440 mg/kgbw; the LD_{100} was 500 mg/kgbw. Death occurred within 48 hours after administration. On autopsy, there was clear evidence of liver involvement and some evidence of lung involvement (Truhaut *et al*, 1971).

Dermal

The LD_{50} of CFC-1316 in rats after dermal application during 5 days was 2,500 mg/kgbw (Truhaut *et al*, 1971).

[a] Only 1 isomer represented

Inhalation

Male Wistar rats were exposed to concentrations of 26 to 840 ppm CFC-1316 (247 - 8,000 mg/m^3) for 3 hours. Death occurred in rats exposed to 840 ppm within 6 to 24 hours. Delayed mortality (4 to 14 days) occurred in rats exposed to 52 ppm (495 mg/m^3). The latter group lost weight, became lethargic and died. Acute haemorrhagic lung lesions were observed in animals exposed to high concentrations. In rats exposed to 105 to 210 ppm (999 - 2,000 mg/m^3), reversible interstitial pneumonia and central lobular liver necrosis were seen. The LC_{50} was 52 ppm and the LC_{100} 105 ppm (Cohen *et al*, 1965).

CFC-1316 was lethal for rats (not further specified) following exposure at 100 ppm (952 mg/m^3) for 4 hours. Some rats survived 100 ppm exposure of 1 to 2 hours. The response of rats in the lethal exposures was consistent with pulmonary irritation. Pulmonary oedema and congestion were observed *post mortem*. Degenerative changes in kidney and liver were also observed (Chenoweth, 1963 cited by Clayton, 1977).

Rats (strain not specified) were exposed (whole-body) to 0, 25, 100 or 500 ppm CFC-1316 (0, 238, 952, 4,760 mg/m^3) for 15 minutes and observed for 14 days. At all concentrations, animals showed respiratory effects during exposure, severe respiratory effects being observed within the first days after exposure. The LC_{20} was 25 ppm (238 mg/m^3). The 15-minute LC_{50} was 82 ppm (781 mg/m^3). On gross necropsy, discoloration was seen in lungs, kidneys, liver and adrenals (Littlefield, 1968).

The 4-hour LC_{50} (following 15-day of observation) for a *cis-/trans* mixture of CFC-1316 was 16 ppm (152 mg/m^3) in rats, and 26 ppm (247 mg/m^3) in mice (10/group) (animals not further specified). Both rats and mice died between day 3 and 5 post exposure. The 1-hour LC_{50} in the rabbit ranged from 30 to 40 ppm (286 - 381 mg/m^3). The 3-hour LC_{50} in the monkey was 90 ppm (857 mg/m^3). The 4-hour LC_{50} in the dog was 182 ppm (1,732 mg/m^3). All deceased animals showed severe inflammatory lesions in the lungs. Dogs also showed intestinal haemorrhages. Monkeys showed uterine bleeding. No significant liver lesions were observed (Raventos and Lemon, 1965).

When the isomers of CFC-1316 were tested separately in mice, it appeared that the *trans* isomer was approximately 3 times more toxic than the *cis* isomer. The 1-hour LC_{50} values were 61 and 179 ppm (581, 1,704 mg/m^3), respectively (Raventos and Lemon, 1965).

Rabbits (not further specified) were exposed to CFC-1316 by inhalation through tracheotomy and by a 'head-only' system. Tracheotomy exposure to concentrations above 3,600 ppm (34,270 mg/m^3) was lethal 1 to 2 hours after exposure and was characterised by a severe hypotension. Concentrations of 1,950 ppm (18,560 mg/m^3) proved to be anaesthetic but not

lethal. Head-only exposure proved to be lethal after 1-hour exposure to 100 ppm (952 mg/m^3) and above. No explanation was given for the difference in toxicity between the two inhalation modes. In this species, lung lesions (zonal induration and discolouring) were the main pathological observations. The authors hypothesised that the formation of trifluoroacetic acid in the tissues was the main cause of toxic symptoms (Truhaut *et al*, 1971).

Truhaut *et al* (1971) cited a 1-hour LC_{50} value of 100 ppm (952 mg/m^3) in the rat, and 3-hour LC_{50} values of 200 ppm (1,900 mg/m^3) in the dog and 54 ppm (514 mg/m^3) in the Rhesus monkey (*Macaca mulatta)*.

The acute toxicity of CFC-1316 was studied in the dog and the monkey (Cohen et al, 1965). Since these animals were tested under halothane anaesthesia (having a specific acute/subacute toxicity in its own right), the data may not reflect the specific inherent toxic properties of CFC-1316 and are not further discussed here.

An overview of the LC_{50} values discussed above is given in Table 5.

Table 5 : LC50 values for CFC-1316 in different species

Exposure time / Concentration								Reference
15 min		1 h		3 h		4 h		
(ppm)	(mg/m^3)	(ppm)	(mg/m^3)	(ppm)	(mg/m^3)	(ppm)	(mg/m^3)	
Rat								
		100	952					Cited by Truhaut *et al*, 1971
				52	495			Cohen *et al*, 1965
82	781							Littlefield, 1968
						16	152	Raventos and Lemon, 1965
Mouse								
		61, 179 [a]	581, 1,704 [a]					Raventos and Lemon, 1965
						26	247	Raventos and Lemon, 1965
Rabbit								
		30 - 40 [a]	286 - 381 [a]					Raventos and Lemon, 1965
Dog								
				200	1,900			Cited by Truhaut *et al*, 1971
						182	1,732	Raventos and Lemon, 1965
Monkey								
				90	857			Raventos and Lemon, 1965
Rhesus monkey								
				54	514			Cited by Truhaut *et al*, 1971

[a] *trans*-, *cis*-

3.22.3.2 Irritation and sensitisation

No data are available.

3.22.3.3 Repeated dose toxicity

No data are available.

3.22.3.4 Genetic toxicity

No data are available.

3.22.3.5 Chronic toxicity and carcinogenicity

No data are available.

3.22.3.6 Reproductive and developmental toxicity

No data are available.

3.22.3.7 Kinetics and metabolism

No data are available.

3.22.3.8 Cardiac sensitisation

No data are available.

3.22.3.9 Neurological data

No data are available.

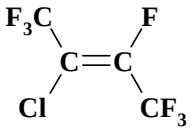
3.22.4 Human data

A case of 11 workers accidentally exposed to CFC-1316 in 1967 is described, following its accidental release during start-up of production in France. The clinical picture was dominated by pulmonary symptoms such as airway irritation, chest tightness, cough, dyspnoea and polypnoea. Other symptoms included headache, muscle weakness, and sweating. The symptoms appeared after a latency of several hours. Three of the 11 cases died from respiratory failure. Exposure concentrations are not given (Bertrand *et al*, 1968; Bertrand and Ciurana, 1969).

3.23 Substance profile: CFC-1317mx

3.23.1 Identity

Name:	2-Chloroheptafluorobutene-2
IUPAC name:	But-2-ene, 2-chloro-1,1,1,3,4,4,4-heptafluoro-
CAS registry number:	434-41-3
Molecular formula:	C_4ClF_7
Molecular mass:	216.5
Chemical structure [a]:	



3.23.2 Physico-chemical properties

Melting point:	No data
Boiling point:	32°C
Vapour pressure:	No data
Solubility in water:	No data
Conversion factors:	1 ppm = 8.849 mg/m^3; 1 mg/m^3 = 0.113 ppm

3.23.3 Toxicological data

3.23.3.1 Acute Toxicity

No data are available.

3.23.3.2 Irritation and sensitisation

No data are available.

3.23.3.3 Repeated dose toxicity

No data are available.

[a] Only 1 isomer represented

3.23.3.4 Genetic toxicity

CFC-1317mx was not mutagenic in the Ames test using *Salmonella typhimurium* strains TA1535, TA1537, TA1538, TA98 and TA100, with and without metabolic activation, up to a concentration of 5 mg/plate (Callander and Priestley, 1990c).

The chromosomal aberration test with CFC-1317mx in human lymphocytes was negative in the presence or absence of metabolic activation (Mackay, 1992).

3.23.3.5 Chronic toxicity and carcinogenicity

No data are available.

3.23.3.6 Reproductive and developmental toxicity

No data are available.

3.23.3.7 Kinetics and metabolism

No data are available.

3.23.3.8 Cardiac sensitisation

No data are available.

3.23.3.9 Neurological data

No data are available.

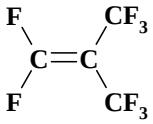
3.23.4 Human data

No data are available.

3.24 Substance profile: FC-1318cy

3.24.1 Identity

Name:	Perfluoroisobutylene
IUPAC name:	Prop-1-ene, 1,1,3,3,3-pentafluoro-2-trifluoromethyl-
CAS registry number:	382-21-8
Molecular formula:	C_4F_8
Molecular mass:	200.0
Chemical structure:	



3.24.2 Physico-chemical properties

Melting point:	No data
Boiling point:	7°C
Vapour pressure:	No data
Solubility in water:	No data
Conversion factors:	1 ppm = 8.175 mg/m^3; 1 mg/m^3 = 0.122 ppm

3.24.3 Toxicological data

3.24.3.1 Acute Toxicity

No data are available on oral or dermal toxicity.

Inhalation

FC-1318cy is very toxic to the respiratory system at low atmospheric concentrations. The 2-hour LC_{50} values are around 1 ppm, which is consistent across the four species tested. In all cases, death was caused by pulmonary oedema and lung haemorrhage. Table 6 summarises the available earlier data. More recent studies are discussed below.

Table 6: Acute inhalation toxicity of FC-1318cy (after AIHA, 1987)

Species / Parameter	Exposure time	Concentration		Reference
Rat		**(ppm)**	**(mg/m^3)**	
LC_{50}	15 s	361	2,960	Smith *et al*, 1982
LC_{50}	30 s	214	1,758	Smith *et al*, 1982
LC_{50}	1 min	122	997	Smith *et al*, 1982
LC_{50}	2 min	86	703	Smith *et al*, 1982
LC_{50}	5 min	28	229	Smith *et al*, 1982
LC_{50}	10 min	17	139	Smith *et al*, 1982
LC_{50}	15 min	6.7	54.8	Karpov, 1975 cited by AIHA, 1987
LC_{50}	2 h	1.05	8.58	Makulova, 1965 cited by AIHA, 1987
LC_{50}	2 h	11.6	94.8	Karpov, 1975 cited by AIHA, 1987
LC_{100}	2 h	1.8	14.7	Danishevskii and Kochanov, 1961 cited by AIHA, 1987
ALC	4 h	0.76	6.21	Clayton, 1977
ALC	6 h	0.5	4.09	DuPont, 1961; Smith *et al*, 1982
Mouse				
LC_{50}	2 h	0.98 [a]	8.01	Paulet and Bernard, 1968 cited by AIHA, 1987
LC_{50}	2 h	1.6	13.1	Karpov, 1975 cited by AIHA, 1987
LC_{50}	15 min	6.1	49.9	Karpov, 1975 cited by AIHA, 1987
ALC	2 h	1.2	9.8	Danishevskii and Kochanov, 1961 cited by AIHA, 1987
LC_{100}	2 h	1.8	14.7	Danishevskii and Kochanov, 1961 cited by AIHA, 1987
Guinea pig				
LC_{50}	2 h	1.05 [a]	8.58	Paulet and Bernard, 1968 cited by AIHA, 1987
Rabbit				
LC_{50}	15 min	12.2	99.7	Karpov, 1975 cited by AIHA, 1987
LC_{50}	2 h	4.3	35.2	Karpov, 1975 cited by AIHA, 1987
LC_{50}	2 h	1.2 [a]	9.8	Paulet and Bernard, 1968 cited by AIHA, 1987
Cat				
LC_{50}	2 h	3.1	25.3	Karpov, 1975 cited by AIHA, 1987

[a] Based on FC-1318cy in waste from Tetrafluoroethylene synthesis

Three studies have evaluated the effects from brief exposure to FC-1318cy.

The effects of FC-1318cy were studied in rabbits following exposure to a concentration of 300 mg/m³ (37 ppm) for 10, 20, 27 or 33 minutes. A control group was also included. All rabbits exposed for 33 minutes died by 9 hours post exposure. Marked pulmonary oedema was seen in both the 20 and 27-minute exposure level groups. This generally occurred 8 hours post exposure. Signs of irritation were seen in the 10-minute exposure level group (Zhang *et al*, 2003).

Male F344 rats were exposed to FC-1318cy at levels of 6.1 to 24.4 ppm (reported as 50 to 200 mg/m³) for 10 minutes. No marked effects were seen at 6.3 or 10.1 ppm (50 or 83 mg/m³). At 11.3 ppm (93 mg/m³) and higher, lung weights were increased. At 12.2 ppm (100 mg/m³) pulmonary oedema was observed 8 hours post exposure. At 13.4 ppm (110 mg/m³) it was seen 4 hours post exposure. At 24.4 ppm effects were seen immediately following the exposure. Severity of findings also showed a dose response relationship (Lehnert *et al*, 1993).

Male F344 rats were exposed to 12.2 ppm FC-1318cy (100 mg/m³) for 10 minutes. The combined effects of the exposure and exercise at different intervals following the exposure were determined. In general, as before, delayed pulmonary oedema was seen 8 hours post exposure. If exercise was done prior to the 8-hour point, potentiation was minimal. When exercise was conducted during the oedema response period, effects were more severe (Lehnert *et al*, 1995).

Overall, these studies show that exposure to a level as low as 12.2 ppm FC-1318cy (100 mg/m³) for 10 minutes can cause lung injury.

3.24.3.2 Irritation and sensitisation

No data are available.

3.24.3.3 Repeated dose toxicity

Subacute toxicity

Male albino rats were exposed (6 h/d) to 0.1 ppm FC-1318cy (0.82 mg/m^3) for 10 days. No deaths or gross or microscopic pathological changes were reported (DuPont, 1961).

Subchronic toxicity

No data are available.

3.24.3.4 Genetic toxicity

No data are available.

3.24.3.5 Chronic toxicity and carcinogenicity

No data are available.

3.24.3.6 Reproductive and developmental toxicity

No data are available.

3.24.3.7 Kinetics and metabolism

No data are available.

3.24.3.8 Cardiac sensitisation

No data are available.

3.24.3.9 Neurological data

No data are available.

3.24.4 Human data

Several deaths have been attributed to acute over-exposure to FC-1318cy. The concentrations responsible for these lethalities have not been specified. Symptoms from accidental exposure to FC-1318cy were respiratory irritation, difficulty in breathing and, in some cases, delayed pulmonary oedema. Pathological examination of fatalities revealed severe pulmonary congestion (AIHA, 1987).

The US-ACGIH and the Danish working environment authority have set an OEL of 0.01 ppm (0.082 mg/m^3) as a 15-minute short-term exposure limit (STEL) (ACGIH, 2008) or ceiling value (Arbejdstilsynet, 2007).

The American Industrial Hygiene Association (AIHA, 1987, 2008b) has established emergency response planning guideline (ERPG) values for FC-1318cy as the maximum airborne concentration below which it is believed that nearly all individuals could be exposed for up to 1 hour without:

• experiencing other than mild, transient adverse health effects or without perceiving a clearly defined objectionable odour (ERPG-1: not applicable);

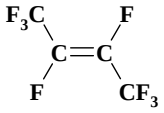
• experiencing or developing irreversible or other serious health effects or symptoms which could impair an individual's ability to take protective action (ERPG-2: 0.1 ppm) (0.82 mg/m^3);

• experiencing or developing life-threatening health effects (ERPG-3: 0.3 ppm) (2.45 mg/m^3).

3.25 Substance profile: FC-1318my

3.25.1 Identity

Name:	Perfluorobutene-2
IUPAC name:	But-2-ene, 1,1,1,2,3,4,4,4-octafluoro-
CAS registry number:	360-89-4
Molecular formula:	C_4F_8
Molecular mass:	200.0
Chemical structure [a]:	



3.25.2 Physico-chemical properties

Melting point:	No data
Boiling point:	No data (gas at normal pressure and temperature)
Vapour pressure:	No data
Solubility in water:	No data
Conversion factors:	1 ppm = 8.175 mg/m^3; 1 mg/m^3 = 0.122 ppm

3.25.3 Toxicological data

3.25.3.1 Acute Toxicity

No data are available on oral or dermal toxicity.

Inhalation

Chr-CD rats (6 males/group) were exposed by inhalation to FC-1318my at concentrations of 4,500, 5,400, 6,100 or 12,000 ppm (36,800, 44,100, 49,900, 98,100 mg/m^3) for 4 hours. There were no deaths at 4,500 and 5,400 ppm, but all animals died at 6,100 ppm and higher (Waritz, 1967).

[a] Only 1 isomer represented

3.25.3.2 Irritation and sensitisation

No data are available.

3.25.3.3 Repeated dose toxicity

No data are available.

3.25.3.4 Genetic toxicity

In vitro

Dose-dependent increases in the number of cells with chromosomal aberrations were observed in cultured human lymphocytes at concentrations of 120,000, 170,000 and 190,000 ppm FC-1318my (981,000, 1,390,000, 1,550,000 mg/m^3) with metabolic activation, and at 100,000 and 120,000 ppm (818,000, 981,000 mg/m^3) without metabolic activation. All increases were concentration-related (Reinhardt, 1992b).

In vivo

In a recessive sex-linked lethal mutation test in *Drosophila melanogaster,* male flies were exposed to 50,000 or 100,000 FC-1318my (409,000, 818,000 mg/m^3) for 6 minutes. After mating with non-exposed females, the lethal mutation rate in the progeny was 1.01 and 1.78% respectively compared to 0.25% for air controls. The authors concluded that FC-1318 is mutagenic to *D. melanogaster* (Garret and Fuerst, 1974).

3.25.3.5 Chronic toxicity and carcinogenicity

No data are available.

3.25.3.6 Reproductive and developmental toxicity

No data are available.

3.25.3.7 Kinetics and metabolism

No data are available.

3.25.3.8 Cardiac sensitisation

No data are available.

3.25.3.9 Neurological data

No data are available.

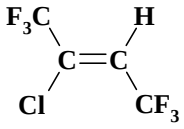
3.25.4 Human data

No data are available.

3.26 Substance profile: HCFC-1326mxz

3.26.1 Identity

Name:	2-Chlorohexafluorobut-2-ene (mixture of *cis* and *trans* isomers)
IUPAC name:	But-2-ene, 2-chloro-1,1,1,4,4,4-hexafluoro-
CAS registry number:	400-44-2
Molecular formula:	C_4HClF_6
Molecular mass:	198.5
Chemical structure [a]:	



3.26.2 Physico-chemical properties

Melting point:	No data
Boiling point:	34.5-35.5°C
Vapour pressure:	No data (volatile)
Solubility in water:	No data
Conversion factors:	1 ppm = 8.113 mg/m^3; 1 mg/m^3 = 0.123 ppm

3.26.3 Toxicological data

3.26.3.1 Acute Toxicity

No data are available on oral or dermal toxicity.

Inhalation

In mice (10/group), a 1-hour exposure to a concentration of 16,000 ppm HCFC-1326mxz (130,000 mg/m^3) did not induce lethality, but convulsions were observed at concentrations above 5,000 ppm (40,600 mg/m^3). Congested lungs and small necrotic foci were noted in the liver after 14 days of observation (Raventos and Lemon, 1965).

The LC_{50} in rats (not further specified) was calculated to be 77 ppm (625 mg/m^3) after 0.5 hour exposure (Reichelt, 1984).

[a] Only 1 isomer represented

HCFC-1326mxz caused 50% mortality in rats (10 males/group, strain not specified) exposed to 78 ppm (633 mg/m^3) for 15 minutes, and 100% mortality after 15 minutes exposure to 250 ppm (2,030 mg/m^3). Autopsy revealed pulmonary haemorrhages and tracheal blockage in all animals (Beasly and Leong, 1966; Ferstandig, 1966).

3.26.3.2 Irritation and sensitisation

No data are available.

3.26.3.3 Repeated dose toxicity

No data are available.

3.26.3.4 Genetic toxicity

HCFC-1326mxz (isomer not specified) was without mutagenic activity in the Ames test using *Salmonella typhimurium* strains TA1535, TA1537, TA1538, TA98 and TA100 in the presence and absence of metabolic activation (Callander and Priestly, 1990d).

3.26.3.5 Chronic toxicity and carcinogenicity

No data are available.

3.26.3.6 Reproductive and developmental toxicity

No data are available.

3.26.3.7 Kinetics and metabolism

No data are available.

3.26.3.8 Cardiac sensitisation

No data are available.

3.26.3.9 Neurological data

No data are available.

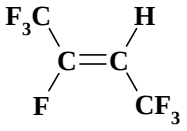
3.26.4 Human data

No data are available.

3.27 Substance profile: HFC-1327mzy

3.27.1 Identity

Name:	Heptafluorobut-2-ene (isomers not specified)
IUPAC name:	But-2-ene, 1,1,1,2,4,4,4-heptafluoro-
CAS registry number:	760-42-9
Molecular formula:	C_4HF_7
Molecular mass:	182.0
Chemical structure [a]:	



3.27.2 Physico-chemical properties

Melting point:	No data
Boiling point:	No data (liquid at normal pressure and temperature)
Vapour pressure:	No data (volatile)
Solubility in water:	No data
Conversion factors:	1 ppm = 7.439 mg/m^3; 1 mg/m^3 = 0.134 ppm

3.27.3 Toxicological data

3.27.3.1 Acute Toxicity

No data are available on oral or dermal toxicity.

Inhalation

The LC_{50} in rats (not further specified) exposed for 4 hours was 200 ppm HFC-1327mzy (1,490 mg/m^3). Rats became sedated during exposure. After exposure, animals showed weight loss, polypnoea and quivering. Death occurred in 2 to 3 days. Necropsy was not conducted (Clayton, 1977).

[a] Only 1 isomer represented

3.27.3.2 Irritation and sensitisation

No data are available.

3.27.3.3 Repeated dose toxicity

No data are available.

3.27.3.4 Genetic toxicity

No data are available.

3.27.3.5 Chronic toxicity and carcinogenicity

No data are available.

3.27.3.6 Reproductive and developmental toxicity

No data are available.

3.27.3.7 Kinetics and metabolism

No data are available.

3.27.3.8 Cardiac sensitisation

No data are available.

3.27.3.9 Neurological data

No data are available.

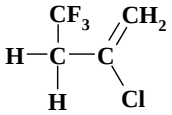
3.27.4 Human data

No data are available.

3.28 Substance profile: HCFC-1353b

3.28.1 Identity

Name:	3-Chloro-1,1,1-trifluorobut-3-ene
IUPAC name:	But-3-ene, 3-chloro-1,1,1-trifluoro-
CAS registry number:	None allocated
Molecular formula:	$C_4H_4ClF_3$
Molecular mass:	144.5
Chemical structure:	



3.28.2 Physico-chemical properties

Melting point:	No data
Boiling point:	60°C
Vapour pressure:	No data (volatile)
Solubility in water:	No data
Conversion factors:	1 ppm = 5.906 mg/m^3; 1 mg/m^3 = 0.169 ppm

3.28.3 Toxicological data

3.28.3.1 Acute Toxicity

No data are available on oral or dermal toxicity.

Inhalation

When male and female Wistar rats were exposed (nose-only) to 61 ppm HCFC-1353b (360 mg/m^3) for 4 hours no mortality was observed for 14 days. At necropsy no abnormalities were seen (Schmit, 2007a).

3.28.3.2 Irritation and sensitisation

No data are available.

3.28.3.3 Repeated dose toxicity

No data are available.

3.28.3.4 Genetic toxicity

No data are available.

3.28.3.5 Chronic toxicity and carcinogenicity

No data are available.

3.28.3.6 Reproductive and developmental toxicity

No data are available.

3.28.3.7 Kinetics and metabolism

No data are available.

3.28.3.8 Cardiac sensitisation

No data are available.

3.28.3.9 Neurological data

No data are available.

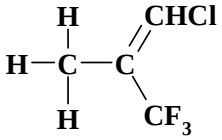
3.28.4 Human data

No data are available.

3.29 Substance profile: HCFC-1353 D-2

3.29.1 Identity

Name:	1-Chloro-2-trifluoromethylpropene
IUPAC name:	Propene, 1-chloro-2-trifluoromethyl-
CAS registry number	666-28-4
Molecular formula:	$C_4H_4ClF_3$
Molecular mass:	144.5
Chemical structure:	



3.29.2 Physico-chemical properties

Melting point:	No data
Boiling point:	No data (liquid at normal pressure and temperature)
Vapour pressure:	No data (volatile)
Solubility in water:	No data
Conversion factors:	1 ppm = 5.906 mg/m^3; 1 mg/m^3 = 0.169 ppm

3.29.3 Toxicological data

3.29.3.1 Acute Toxicity

No data are available on oral or dermal toxicity.

Inhalation

When male and female Wistar rats were exposed (nose-only) to 200 ppm HCFC-1353 D-2 (1,180 mg/m^3) for 4 hours no mortality was observed for 14 days. At necropsy no abnormalities were seen (Schmit, 2007b).

3.29.3.2 Irritation and sensitisation

No data are available.

3.29.3.3 Repeated dose toxicity

No data are available.

3.29.3.4 Genetic toxicity

No data are available.

3.29.3.5 Chronic toxicity and carcinogenicity

No data are available.

3.29.3.6 Reproductive and developmental toxicity

No data are available.

3.29.3.7 Kinetics and metabolism

No data are available.

3.29.3.8 Cardiac sensitisation

No data are available.

3.29.3.9 Neurological data

No data are available.

3.29.4 Human data

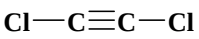
No data are available.

3.30 Substance profile: Dichloroacetylene

Even though it is unlikely to occur as an impurity in commercial fluoroalkanes, the toxicity of dichloroacetylene is profiled here because it is regarded as a degradation product of trichloroethylene, a known starting material for the manufacture of commercial fluoroalkanes, during its use as an anaesthetic agent (Greim *et al*, 1984).

3.30.1 Identity

Name:	Dichloroacetylene (DCA)
IUPAC name:	Ethyne, dichloro-
CAS registry number:	7572-29-4
Molecular formula:	C_2Cl_2
Molecular mass:	94.9
Chemical structure:	



3.30.2 Physico-chemical properties

Melting point:	–66°C
Boiling point:	33°C, decomposes 30-36°C (Kende, 1982)
Vapour pressure:	122 mm Hg (Calculated [a]) (163 hPa)
Solubility in water:	No data
Conversion factors:	1 ppm = 3.879 mg/m^3; 1 mg/m^3 = 0.258 ppm

3.30.3 Toxicological data

3.30.3.1 Acute Toxicity

No data are available on oral or dermal toxicity.

Inhalation

The LC_{50} values in female NMRI mice exposed to DCA (stabilised with trichloroethylene) for either 1 or 6 hours were 124 and 19 ppm (481, 73.7 mg/m^3), respectively. (Reichert *et al*, 1975).

[a] Using Advanced Chemistry Development software V8.14 from ACD/Labs, Toronto, Ontario, Canada [www.acdlabs.com/products/phys_chem_lab/bp/]

The LC_{50} values in male Sprague-Dawley derived rats exposed to DCA for 4 hours, either as a 1:7 parts per volume mixture with trichloroethylene as a stabiliser or as a 1:9 parts per volume with diethyl ether as a stabiliser, were 55 ppm (213 mg/m^3) and 219 ppm (850 mg/m^3), respectively (Siegel *et al*, 1971).

The LC_{50} values in guinea pigs (NMRI:ASH or FTD:Hartley) exposed to DCA for 4 hours, either as a 1:7 parts per volume mixture with trichloroethylene as a stabiliser or as a 1:9 parts per volume with diethyl ether as a stabiliser, were 15 ppm (58 mg/m^3) and 52 ppm (200 mg/m^3), respectively (Siegel *et al*, 1971).

Single exposure of male New Zealand albino rabbits to 126, 202 or 307 ppm DCA (489, 784, 1,191 mg/m^3) for 1 hour or 17 ppm (65.9 mg/m^3) for 6 hours resulted in severe effects on the sensory trigeminal nucleus, including chromatolysis, disintegration of the Nissl bodies and cell shrinkage.

One-hour exposures to 202 and 307 ppm DCA were lethal in the rabbit (Reichert *et al*, 1976). In subsequent studies in rabbits exposed to DCA, focal necrosis of the collecting tubules of the kidneys, increased mitotic activity in the renal epithelium and loss of glycogen in the liver were noted (Reichert *et al*, 1978).

3.30.3.2 Irritation and sensitisation

No data are available.

3.30.3.3 Repeated dose toxicity

Subacute toxicity

No data are available.

Subacute toxicity

Groups of 8 male Sprague-Dawley derived rats were exposed (6 h/d, 5 d/wk) by inhalation to a mixture of DCA and trichloroethylene [a] (TCE) at 2.8, 9.8 or 15.5 ppm DCA (10.9, 38.0, 60.1 mg/m^3) and 3.2, 50 or 150 ppm TCE (12.4, 194, 582 mg/m^3), respectively, for 6 weeks. A continuous (24 h/d) 90-day exposure to 2.8 ppm DCA (10.9 mg/m^3) was also conducted. Rats

[a] C_2HCl_3, molecular weight 131.4 (Appendix C)

exposed to 15.5 ppm DCA in the DCA-TCE mixture group and to 2.8 ppm DCA only in the 90-day continuous exposure study lost weight or gained body weight at a much slower rate than controls. Rats exposed to 2.8 ppm DCA in the 90-day continuous exposure study showed neurological effects with blindness and hind leg weakness. Pronounced morphological changes were observed in the kidneys of rats exposed repeatedly to 15.5 ppm DCA-TCE or continuously to 2.8 ppm DCA alone (Siegel *et al*, 1971).

3.30.3.4 Genetic toxicity

DCA (5,000 ppm; 19,000 mg/m^3) was tested in the Ames test for mutagenic activity with *Salmonella typhimurium* strains TA98 and TA100. A mutagenic response was observed in the TA100 strain if it was suspended in Oxoid medium. No mutagenicity was detected in the TA98 strain. In a second experiment, DCA was tested in both strains at concentrations ranging from 4,000 to 16,000 ppm (16,000 to 62,000 mg/m^3). A clear mutagenic response was seen in TA100 at 10,000 ppm (39,000 mg/m^3) after exposure for 1 hour. No response was seen in strain TA98. DCA stabilised with acetylene (as used in the animal carcinogenicity experiments) was not mutagenic to either strain (Reichert *et al*, 1983).

3.30.3.5 Chronic toxicity and carcinogenicity

Wistar rats (30/sex/group) were exposed (6 h/d, 2 d/wk) by inhalation to a mixture of 14 ppm DCA (54.3 mg/m^3) and 20 ppm acetylene [a] (3.4 mg/m^3) (as stabiliser) for 18 months. A similar group of rats, exposed to air and acetylene, served as controls. Reductions in body-weight gain and mean survival time were observed in treated animals. An increased incidence of kidney cystadenomas was found (male: 7/30, female: 3/30), while no such tumours were found in the controls (animals treated with air plus acetylene). One treated animal had a kidney adenocarcinoma. Furthermore, treatment resulted in increases in the incidence of liver cholangiomas (male: 6/30 versus 0/30 in controls; female: 11/30 versus 4/30) and of malignant lymphomas (female: 11/30 versus 4/30) (Reichert *et al*, 1984).

NMRI mice (30/sex/group) were exposed by inhalation to mixtures of DCA and 20 ppm acetylene (3.4 mg/m^3) as stabiliser. A similar group of mice were exposed to a mixture of air and acetylene and served as controls. The exposure regimens were as follows:

- Group I - 9 ppm DCA (35 mg/m^3), 6 h/d, 1 d/wk for 12 months;
- Group II - 2 ppm DCA (8.0 mg/m^3), 6 h/d, 1 d/wk for 18 months;

[a] C_2H_2, molecular weight 26.0 (Appendix C)

- Group III - 2 ppm DCA (8.0 mg/m^3), 6 h/d, 2 d/wk for 18 months.

The mice were observed for their lifetimes. Exposure-dependent reductions in body-weight gain and mean survival time were observed in all treated male mice and in females of groups I and III. Treatment induced an increase in the incidence of kidney adenomas in male mice (I: 4/30; II: 12/30; III: 3/30; all controls: 0/30). Incidences of kidney cystadenomas and adenocarcinomas combined in male mice (I: 27/30 versus 8/30; II: 27/30 versus 4/30; III: 19/30 versus 4/30) and of kidney cystadenomas in female mice (I: 15/30 versus 0/30; II: 7/30 versus 0/30; III: 6/30 versus 4/30) were increased as well (Reichert *et al*, 1984).

3.30.3.6 Reproductive and developmental toxicity

No data are available.

3.30.3.7 Kinetics and metabolism

The biochemical basis for the DCA-induced renal tumours has been studied in rats and mice. Catalysed by hepatic glutathione S-transferases, DCA was conjugated with glutathione to form S-(1,2-dichlorovinyl) glutathione. The glutathione conjugates were eliminated from the liver in bile and translocated to the kidney intact or after further metabolism to S-(1,2-dichlorovinyl)-L-cysteine. These compounds were further metabolised in the kidney by renal tubular cysteine conjugate β-lyase into reactive intermediates, most likely thioketenes. Interaction of these electrophiles with DNA caused mutagenicity and genotoxicity as observed for S-(1,2-dichloro-vinyl)-L-cysteine. Alternatively to β-lyase cleavage, the cysteine conjugates were acetylated to mercapturic acids, which have been identified in urine after exposure to both DCA and trichloroethylene. The ability of the kidney to concentrate glutathione and cysteine S-conjugates, along with the intensive metabolism of glutathione S-conjugates in this organ, are most probably responsible for the induction of renal tumours following exposure to DCA (Dekant *et al*, 1990).

3.30.3.8 Cardiac sensitisation

No data are available.

3.30.3.9 Neurological data

Male New Zealand albino rabbits were used to determine neurotoxic effects of DCA by histological and neurofunctional methods. Groups of 9 or 10 rabbits were exposed by inhalation to lethal and sublethal concentrations of 126, 202 or 307 ppm DCA (489, 784, 1,191 mg/m^3) for 1 hour. Four rabbits were exposed to 17 ppm (65.9 mg/m^3) for 6 hours. (The level of 126 ppm was a sublethal concentration of DCA, following exposure for 1 hour. Both 202 and 307 ppm caused death of some of the exposed rabbits). Histological examination revealed a dose-related increase in chromatolysis, disintegration of the Nissl bodies and cell shrinkage. The intensity of the lesions was most severe in the sensory trigeminal nerve, followed, in descending order or severity, by the facial, oculomotor, motor trigeminal and acoustic nerves. The most severe changes were always found in the sensory trigeminal nucleus, whereas screening of the other cranial nerve nuclei revealed only discrete or mild alterations (Reichert *et al*, 1976).

Groups of 7 Sprague-Dawley rats were given (5 d/wk) doses of either 17 mg DCA/kgbw or 2,500 mg trichloroethylene/kgbw in corn oil, by gastric intubation for 10 weeks. A third group served as controls. The mean body-weight gain at the end of the exposure period was significantly reduced in the DCA-treated rats but not in the trichloroethylene-treated group. Large nerve fibres had myelin thickness significantly decreased following exposure to DCA. However, the smallest fibres in the treated groups had a significant increase in myelin thickness (Barret *et al*, 1991). Physical manifestations of neuropathy included sensory loss, motor weakness (muscles of mastication), optic nerve conditions including blindness, and herpes type sores on the face and mouth (Spencer and Schaumburg, 1985).

3.30.4 Human data

Exposure to DCA in a variety of scenarios has been associated with CNS effects such as headache, appetite loss, extreme nausea, vomiting, facial twitch and other signs (Humphrey and McClelland, 1944; Defalque, 1961; Saunders, 1967; Henschler *et al*, 1970; Greim *et al*, 1984). Occupational exposure at 0.5 to 1.0 ppm (1.9 - 3.9 mg/m^3) caused disabling nausea in 85% of those exposed (Marhold, 1983).

IARC (1999a) considered that “No epidemiological data relevant to the carcinogenicity of dichloroacetylene were available. There is limited evidence in experimental animals for the carcinogenicity of dichloroacetylene. Overall evaluation: Dichloroacetylene is not classifiable as to its carcinogenicity to humans (Group 3).”

3.30.4.1 Occupational exposure limit values

Denmark: 0.1 ppm (0.4 mg/m^3) ceiling value, carcinogenic (Arbejdstilsynet, 2007).
Finland: 0.1 ppm (0.39 mg/m^3); 15-min STEL: 0.3 ppm (1.2 mg/m^3) (STM, 2005).
Netherlands: 0.1 ppm (0.4 mg/m^3) ceiling value (SER, 2008).
Norway: 0.1 ppm (0.4 mg/m^3) ceiling value (Arbeidstilsynet, 2007).
Switzerland: 0.1 ppm (0.4 mg/m^3), carcinogenic (Suva, 2007).
UK: 0.1 ppm (0.39 mg/m^3) 15-min STEL (HSE, 2007).
USA: 0.1 ppm (0.39 mg/m^3) STEL ceiling; A3 - Animal carcinogen (ACGIH, 2008).
Germany: No limit set (Category 2 carcinogen) (DFG, 2008).

4. COMPOUNDS SUBJECT TO OTHER REVIEWS

Some impurities and by-products are not profiled in this report since the available data on these saturated and unsaturated compounds have been reviewed by ECETOC and other international organisations (Table 7 and 8).

Readers are advised the contact the organisations regarding possible updates. Some of the latest information can also be found via the internet, for example on reviews:

- INCHEM international reviews (www.inchem.org/).
- IARC monographs (http://monographs.iarc.fr/ENG/Monographs/allmonos90.php).
- OECD screening information dataset (SIDS), high production volume chemicals (HPVC) reviews (www.chem.unep.ch/irptc/sids/OECDSIDS/sidspub.html), including those prepared by ICCA (www.cefic.org/activities/hse/mgt/hpv/hpvinit.htm).
- EC risk assessments, IUCLIDs, and classification and labelling (http://ecb.jrc.it/esis/).
- EC classification and labelling (http://ecb.jrc.it/classification-labelling/).
- Acute exposure guideline levels (AEGLs): published reviews (www.epa.gov/opptintr/aegl/%20pubs/final.htm) and all reviewed chemicals (www.epa.gov/oppt/aegl/pubs/chemlist.htm).

Tables 7 and 8 also presents a selection of official national OEL values. The values may be advisory or legally binding. The justification for the OELs is usually based on separate (prior) expert advice and documentation (e.g. DECOS [a], German MAK [b] commission [c], GSSAT [d] and TLV [e] committee of ACGIH [f]), or on another source such as indicative OELs set by the EC following advice from its Scientific Committee for Occupational Exposure Limits (SCOEL).

The various OEL systems in the EU and some other countries are explained on the internet site http://osha.europa.eu/good_practice/topics/dangerous_substances/oel/.

[a] Health Council of the Netherlands, Dutch Expert Commitee on Occupational Standards
[b] Maximale Arbeitsplatzkonzentration
[c] Deutsche Forschungsgemeinschaft (DFG), Senatskommission zur Prüfung gesundheitsschädlicher Arbeitsstoffe (German research community, Senate commission on the investigation of health hazards of chemical compounds in the work area)
[d] Groupe Scientifique pour la Surveillance des Atmosphères de Travail, France
[e] Threshold limit value
[f] American Conference of Governmental Industrial Hygienists, USA

Table 7: Saturated compounds subject to international review, with national OEL values

CAS number	Acronym	Name	Molecular formula (structure)	Review [a]	OEL, 8-hour TWA				Reference
					Country	(ppm) [b]	(mg/m^3) [c]	Remark or notation [d]	
75-69-4	CFC-11	Trichloro-fluoro-methane	CCl_3F ($F–CCl_3$)	EHC 113 Patty's 68					IPCS, 1990a Rusch, 2001
					Denmark	500 [2]	2,810	-	Arbejdstilsynet, 2007
					Finland	1,000 [1.3]	5,600	-	STM, 2005
					France	1,000 [e]	5,600	-	INRS, 2007
					Germany	1,000 [2]	5,700	Not F	BAuA, 2007
					Netherlands	1,000 [f]	5,600	-	SER, 2008
					Norway	500 [1.25]	2,800	-	Arbeidstilsynet, 2007
					Spain	1,000 [e]	5,720		INSHT, 2008
					Sweden	500 [1.5]	3,000	-	AFS, 2005
					Switzerland	1,000	5,600	Not F	Suva, 2007
					USA	1,000 [g]	5,620	Not C	ACGIH, 2008
					USA	1,000 [g]	5,600	-	NIOSH, 2005
					USA	1,000	5,600	-	OSHA, 1993 [h]

Table 7: Saturated compounds subject to international review, with national OEL values (cont'd)

CAS number	Acronym	Name	Molecular formula (structure)	Review [a]	OEL, 8-hour TWA				Reference
					Country	(ppm) [b]	(mg/m^3) [c]	Remark or notation [d]	
75-71-8	CFC-12	Dichlorodifluoro-methane	CCl_2F_2 ($F–CCl_2–F$)	EHC 113 Patty's 68					IPCS, 1990a Rusch, 2001
					Denmark	500 [2]	2,475	-	Arbejdstilsynet, 2007
					Finland	1,000 [1.3]	5,000	-	STM, 2005
					France	1,000	4,950	-	INRS, 2007
					Germany	1,000 [2]	5,000	Not F	BAuA, 2007
					Japan	500	2,500	-	JSOH, 2007
					Netherlands	1,000	5,040	-	SER, 2008
					Norway	500 [1.25]	2,475	-	Arbeidstilsynet, 2007
					Spain	1,000 [1.25]	4,115	-	INSHT, 2008
					Sweden	500 [1.5]	2,500	-	AFS, 2005
					Switzerland	1,000	5,000	Not F	Suva, 2007
					USA	1,000	4,950	Not C	ACGIH, 2008
					USA	1,000	4,950	-	NIOSH, 2005
					USA	1,000	4,950	-	OSHA, 1993 [h]
75-72-9	CFC-13	Chlorotrifluoro-methane	$CClF_3$ ($F_3–CCl$)	EHC 113 Patty's 68					IPCS, 1990a Rusch, 2001
					Denmark	1,000 [2]	4,270	-	Arbejdstilsynet, 2007
					Germany	1,000 [8]	4,300	-	BAuA, 2007
					Netherlands	2,000	8,700	-	SER, 2008
					Spain	1,000	4,300	-	INSHT, 2008
					Switzerland	1,000	4,330	-	Suva, 2007

Table 7: Saturated compounds subject to international review, with national OEL values (cont'd)

CAS number	Acronym	Name	Molecular formula (structure)	Review [a]	OEL, 8-hour TWA				Reference
					Country	(ppm) [b]	(mg/m^3) [c]	Remark or notation [d]	
75-63-8	FC-13B1	Bromotrifluoro-methane	$CBrF_3$ ($CBrF_3$)	None					
					Denmark	1,000 [2]	6,100	-	Arbejdstilsynet, 2007
					Finland	1,000 [1,3]	6,200	-	STM, 2005
					France	1,000	6,100	-	INRS, 2007
					Germany	1,000 [8]	6,200	Not F	BAuA, 2007
					Netherlands	1,000	6,100	-	SER, 2008
					Norway	500 [1.25]	3,050	-	Arbeidstilsynet, 2007
					Spain	1,000	6,195	-	INSHT, 2008
					Switzerland	1,000	6,100	Not F	Suva, 2007
					USA	1,000	6,090	-	ACGIH, 2008
					USA	1,000	6,100	-	NIOSH, 2005
					USA	1,000	6,100	-	OSHA, 1993 [h]

Table 7: Saturated compounds subject to international review, with national OEL values (cont'd)

CAS number	Acronym	Name	Molecular formula (structure)	Review [a]	OEL, 8-hour TWA				Reference
					Country	(ppm) [b]	(mg/m^3) [c]	Remark or notation [d]	
67-66-3	HCC-20	Chloroform (Trichloromethane)	$CHCl_3$ ($H–CCl_3$)	ATP 19 EHC 163 CICAD 58 Mono 73					EC, 1993 IPCS, 1994 IPCS, 2004 IARC, 1999b
					Denmark	2 [2]	10	S, C	Arbejdstilsynet, 2007
					EU	2	10	S	EC, 2000
					France	2 [25]	10	S, C	INRS, 2007
					Finland	2 [2]	10	S	STM, 2005
					Germany	0.5	2.5	S, not F	BAuA, 2007
					Japan	3	14.7	S, C	JSOH, 2007
					Netherlands	1 [5]	5	-	SER, 2008
					Norway	2 [2]	10	S, C, R	Arbeidstilsynet, 2007
					Spain	10	50	-	INSHT, 2008
					Sweden	2 [2.5]	10	C	AFS, 2005
					Switzerland	0.5 [2]	2.5	S, M, R, not F	Suva, 2007
					UK	2	9.9	S	HSE, 2007
					USA	10	49	C	ACGIH, 2008
					USA	2	9.78	-	NIOSH, 2005
					USA	50	240	-	OSHA, 1993 [h]

Table 7: Saturated compounds subject to international review, with national OEL values (cont'd)

CAS number	Acronym	Name	Molecular formula (structure)	Review [a]	OEL, 8-hour TWA				Reference
					Country	(ppm) [b]	(mg/m^3) [c]	Remark or notation [d]	
75-43-4	HCFC-21	Dichlorofluoro-methane	$CHCl_2F$ ($F–CCl_2H$)	JACC 16 EHC 126 Patty's 68					ECETOC, 1990c IPCS, 1991 Rusch, 2001
					Denmark	10 [2]	40	-	Arbejdstilsynet, 2007
					Finland	10 [2]	40	-	STM, 2005
					France	10	40	-	INRS, 2007
					Germany	10 [2]	43	-	BAuA, 2007
					Netherlands	10	43	-	SER, 2008
					Norway	10 [2]	42	-	Arbeidstilsynet, 2007
					Spain	10	43	-	INSHT, 2008
					Switzerland	10 [2]	40	-	Suva, 2007
					UK	10	43	-	HSE, 2007
					USA	10	42	-	ACGIH, 2008
					USA	10	40	-	NIOSH, 2005
					USA	1,000	4,200	-	OSHA, 1993 [h]

Table 7: Saturated compounds subject to international review, with national OEL values (cont'd)

CAS number	Acronym	Name	Molecular formula (structure)	Review [a]	OEL, 8-hour TWA				Reference
					Country	(ppm) [b]	(mg/m^3) [c]	Remark or notation [d]	
75-45-6	HCFC-22	Chlorodifluoro-methane	$CHClF_2$ ($Cl–CF_2H$)	JACC 9 EHC 126 Mono 71 Patty's 68 EU RAR					ECETOC, 1989 IPCS, 1991 IARC, 1999a Rusch, 2001 ECB 2008
					Denmark	500 [2]	1,770	-	Arbejdstilsynet, 2007
					EU	1,000	3,600	-	EC, 2000
					Finland	1,000	3,600	-	STM, 2005
					France	1,000	3,600	-	INRS, 2007
					Germany	1,000 [j]	3,600	-	BAuA, 2007
					Japan	1,000	3,500	-	JSOH, 2007
					Netherlands	1,000	3,600	-	SER, 2008
					Norway	500 [1.25]	1,750	-	Arbeidstilsynet, 2007
					Spain	1,000	3,600	-	INSHT, 2008
					Sweden	500 [1.5]	1,800	-	AFS, 2005
					Switzerland	1,000 [j]	1,800	-	Suva, 2007
					UK	1,000	3,590	-	HSE, 2007
					USA	1,000	3,540	Not C	ACGIH, 2008
					USA	1,000 [1.25]	3,500	-	NIOSH, 2005

Table 7: Saturated compounds subject to international review, with national OEL values (cont'd)

CAS number	Acronym	Name	Molecular formula (structure)	Review [a]	OEL, 8-hour TWA				Reference
					Country	(ppm) [b]	(mg/m^3) [c]	Remark or notation [d]	
75-09-2	HCC-30	Methylene chloride (Dichlorom-ethane)	CH_2Cl_2 ($Cl–CH_2–Cl$)	JACC 4 ATP 19 EHC 164 Mono 71					ECETOC, 1984 EC, 1993 IPCS, 1996 IARC, 1999a
					Denmark	35 [2]	122	S, C	Arbejdstilsynet, 2007
					Finland	100 [2.5]	350	-	STM, 2005
					France	50 [2]	180	C	INRS, 2007
					Germany	75 [4,k]	260	-	BAuA, 2007
					Japan	50 [2,g,l]	170	S, C	JSOH, 2007
					Netherlands	100 [5,f]	350	-	SER, 2008
					Norway	15 [1.5]	50	S, C	Arbeidstilsynet, 2007
					Spain	50 [o]	177	-	INSHT, 2008
					Sweden	35 [2]	120	S, C	AFS, 2005
					Switzerland	50 [m]	180	C, maybe F	Suva, 2007
					UK	100 [3,n]	350	S	HSE, 2007
					USA	50 [o]	174	C	ACGIH, 2008
					USA	-	-	C	NIOSH, 2005
					USA	25 [5]	87	-	OSHA, 1993 [h]
75-10-5	HFC-32	Difluoromethane	CH_2F_2 (CH_2F_2)	Patty's 68 JACC 54					Rusch, 2001 ECETOC, 2008
					USA	1,000	2,130	-	AIHA, 2008a

Table 7: Saturated compounds subject to international review, with national OEL values (cont'd)

CAS number	Acronym	Name	Molecular formula (structure)	Review [a]	OEL, 8-hour TWA				Reference
					Country	(ppm) [b]	(mg/m^3) [c]	Remark or notation [d]	
74-87-3	HCC-40	Methyl chloride (Chloromethane)	CH_3Cl (CH_3–Cl)	ATP 19 CICAD 28 Mono 41 SIAR (ICCA) AEGL draft					EC, 1993 IPCS, 2001 IARC, 1986a OECD, 2002b NAC, 2005
					Denmark	25 [2]	52	C	Arbejdstilsynet, 2007
					Finland	50 [1.5]	100	-	STM, 2005
					France	50 [2]	105	C	INRS, 2007
					Germany	50 [2]	100	S, R	BAuA, 2007
					Japan	50	100	-	JSOH, 2007
					Netherlands	25	52	-	SER, 2008
					Norway	25 [1.5]	50	C	Arbeidstilsynet, 2007
					Spain	50 [2]	105	S, C	INSHT, 2008
					Sweden	10 [2]	20	-	AFS, 2005
					Switzerland	50 [2]	105	F	Suva, 2007
					UK	50 [2]	105	-	HSE, 2007
					USA	50 [2]	103	S, C	ACGIH, 2008
					USA	-	-	C	NIOSH, 2005
					USA	100 [2,p]	207	-	OSHA, 1993 [h]

Table 7: Saturated compounds subject to international review, with national OEL values (cont'd)

CAS number	Acronym	Name	Molecular formula (structure)	Review [a]	OEL, 8-hour TWA				Reference
					Country	(ppm) [b]	(mg/m^3) [c]	Remark or notation [d]	
67-72-1	HCC-110	Hexachloroethane	C_2Cl_6 (CCl_3–CCl_3)	EHC 139 Mono 73					IPCS, 1992 IARC, 1999b
					Denmark	1 [2]	10	S, C	Arbejdstilsynet, 2007
					France	1 [10]	(9.7)	-	INRS, 2007
					Finland	1 [3]	9.8	-	STM, 2005
					Germany	1 [2]	9.8	-	BAuA, 2007
					Netherlands	1	10	S	SER, 2008
					Norway	1 [3]	10	S	Arbeidstilsynet, 2007
					Spain	1	9.8	S	INSHT, 2008
					Switzerland	1 [2]	10	S	Suva, 2007
					USA	1	9.7	S, C	ACGIH, 2008
					USA	1	10	-	NIOSH, 2005
					USA	1	10	S	OSHA, 1993 [h]

Table 7: Saturated compounds subject to international review, with national OEL values (cont'd)

CAS number	Acronym	Name	Molecular formula (structure)	Review [a]	OEL, 8-hour TWA				Reference
					Country	(ppm) [b]	(mg/m^3) [c]	Remark or notation [d]	
76-12-0	CFC-112	Tetrachloro-1,2-difluoroethane	$C_2Cl_4F_2$ ($CCl_2F–CCl_2F$)	EHC 113 Patty's 68					IPCS, 1990a Rusch, 2001
					Denmark	200 [2]	1,665	-	Arbejdstilsynet, 2007
					Finland	500 [1.25]	4,200	-	STM, 2005
					France	500	4,170	-	INRS, 2007
					Germany	200 [2]	1,700	-	BAuA, 2007
					Netherlands	100	850	-	SER, 2008
					Norway	250 [1.25]	2,085	-	Arbeidstilsynet, 2007
					Spain	500	(4,170)	-	INSHT, 2008
					Switzerland	200 [2]	1,690	-	Suva, 2007
					USA	50	417	-	ACGIH, 2008
					USA	500	4,170	-	NIOSH, 2005
					USA	500	4,170	-	OSHA, 1993 [h]

Table 7: Saturated compounds subject to international review, with national OEL values (cont'd)

CAS number	Acronym	Name	Molecular formula (structure)	Review [a]	OEL, 8-hour TWA				Reference
					Country	(ppm) [b]	(mg/m^3) [c]	Remark or notation [d]	
76-11-9	CFC-112	Tetrachloro-2,2-difluoroethane	$C_2Cl_4F_2$ ($CCl_2F–CCl_2F$)	EHC 113 Patty's 68					IPCS, 1990a Rusch, 2001
					Denmark	500 [2]	1,665	-	Arbejdstilsynet, 2007
					Finland	500 [1.25]	4,200	-	STM, 2005
					France	500	4,170	-	INRS, 2007
					Germany	200 [2]	1,700	-	BAuA, 2007
					Netherlands	500	850	-	SER, 2008
					Norway	250 [1.25]	2,085	-	Arbeidstilsynet, 2007
					Spain	500	(4,170)	-	INSHT, 2008
					Switzerland	500	1,690	-	Suva, 2007
					USA	100	417	-	ACGIH, 2008
					USA	500	4,170	-	NIOSH, 2005
					USA	500	4,170	-	OSHA, 1993 [h]

***Table 7: Saturated compounds subject to international review, with national OEL values** (cont'd)*

CAS number	Acronym	Name	Molecular formula (structure)	Review [a]	OEL, 8-hour TWA				Reference
					Country	(ppm) [b]	(mg/m^3) [c]	Remark or notation [d]	
76-13-1	CFC-113	Trichloro-1,2,2-trifluoroethane	$C_2Cl_3F_3$ ($CCl_2F–CClF_2$)	EHC 113 Patty's 68					IPCS, 1990a Rusch, 2001
					Denmark	500 [2]	3,800	-	Arbejdstilsynet, 2007
					Finland	1,000 [1.3]	7,800	-	STM, 2005
					France	1,000 [1.25]	7,600	-	INRS, 2007
					Germany	500	3,900	-	BAuA, 2007
					Japan	500	3,800	-	JSOH, 2007
					Netherlands	150	1,170	-	SER, 2008
					Norway	500 [1.25]	3,800	-	Arbeidstilsynet, 2007
					Spain	1,000 [1.25]	7,795	-	INSHT, 2008
					Sweden	500 [1.5]	4,000	-	AFS, 2005
					Switzerland	500	3,800	-	Suva, 2007
					USA	1,000 [1.25]	7,670	Not C	ACGIH, 2008
					USA	1,000 [1.25]	7,600	-	NIOSH, 2005
					USA	1,000	7,600	-	OSHA, 1993 [h]

***Table 7: Saturated compounds subject to international review, with national OEL values** (cont'd)*

CAS number	Acronym	Name	Molecular formula (structure)	Review [a]	OEL, 8-hour TWA				Reference
					Country	(ppm) [b]	(mg/m^3) [c]	Remark or notation [d]	
76-14-2	CFC-114	Dichloro-1,1,2,2-tetrafluoroethane	$C_2Cl_2F_4$ ($CClF_2$–$CClF_2$)	EHC 113 Patty's 68					IPCS, 1990a Rusch, 2001
					Denmark	500 [2]	3,500	-	Arbejdstilsynet, 2007
					Finland	1,000 [1.3]	7,100	-	STM, 2005
					France	1,000	7,000	-	INRS, 2007
					Germany	1,000 [8]	7,100	-	BAuA, 2007
					Netherlands	1,000	7,130	-	SER, 2008
					Norway	500 [1.25]	3,500	-	Arbeidstilsynet, 2007
					Spain	1,000	7,110	-	INSHT, 2008
					Switzerland	1,000	7,000	-	Suva, 2007
					UK	1,000 [1.25]	7,110	-	HSE, 2007
					USA	1,000	6,990	Not C	ACGIH, 2008
					USA	1,000	7,000	-	NIOSH, 2005
					USA	1,000	7,000	-	OSHA, 1993 [h]
76-15-3	CFC-115	Chloro-pentafluoroethane	C_2ClF_5 ($CClF_2$–CF_3)	EHC 113 Patty's 68					IPCS, 1990a Rusch, 2001
					Denmark	1,000 [2]	6,300	-	Arbejdstilsynet, 2007
					France	1,000	6,320	-	INRS, 2007
					Netherlands	1,000	6,460	-	SER, 2008
					Spain	1,000	6,420	-	INSHT, 2008
					Switzerland	1,000	6,400	-	Suva, 2007
					USA	1,000	6,320	-	ACGIH, 2008
					USA	1,000	6,320	-	NIOSH, 2005

Table 7: Saturated compounds subject to international review, with national OEL values *(cont'd)*

CAS number	Acronym	Name	Molecular formula (structure)	Review [a]	OEL, 8-hour TWA				Reference
					Country	(ppm) [b]	(mg/m^3) [c]	Remark or notation [d]	
76-01-7	HCC-120	Pentachloroethane	C_2HCl_5 ($CHCl_2$–CCl_3)	ATP 29 Mono 71					EC, 2004 IARC, 1999a
					Denmark	5 [2]	40	S, C	Arbejdstilsynet, 2007
					Finland	5 [2]	42	-	STM, 2005
					Germany	5	42	-	DFG, 2008
					Netherlands	5	40	-	SER, 2008
					Switzerland	5 [2]	40	C	Suva, 2007
					USA	-	-	C	NIOSH, 2005
306-83-2	HCFC-123	Dichloro-2,2,2-trifluoroethane	$C_2HCl_2F_3$ ($CHCl_2$–CF_3)	EHC 139 CICAD 23 Patty's 68 JACC 47					IPCS, 1992 IPCS, 2000 Rusch, 2001 ECETOC, 2005b
					Finland	10	63	-	STM, 2004
					Japan	10	62	-	JSOH, 2007
					USA	50	310	-	AIHA, 2008a

Table 7: Saturated compounds subject to international review, with national OEL values *(cont'd)*

CAS number	Acronym	Name	Molecular formula (structure)	Review [a]	OEL, 8-hour TWA				Reference
					Country	(ppm) [b]	(mg/m^3) [c]	Remark or notation [d]	
151-67-7	CFC-123B1	Halothane (2-Bromo-2-chloro-1,1,1-trifluoroethane)	$C_2HBrClF_3$ ($CHBrCl–CF_3$)	None					
					Denmark	5 [2]	40	-	Arbejdstilsynet, 2007
					Finland	1 [3]	8.2	-	STM, 2005
					Germany	5 [8,r]	41	F	BAuA, 2007
					Netherlands	0.05	0.41	-	SER, 2008
					Norway	0.02 [3]	0.2	R	Arbeidstilsynet, 2007
					Spain	50	410	-	INSHT, 2008
					Sweden	5 [2]	40	-	AFS, 2005
					Switzerland	5 [8,]	40	R, F	Suva, 2007
					UK	10	82	-	HSE, 2007
					USA	50	404	Not C	ACGIH, 2008
					USA	2 [z]	16.2	-	NIOSH, 2005
2837-89-0	HCFC-124	1-Chloro-1,2,2,2-tetrafluoroethane	C_2HClF_4 ($CHClF–CF_3$)	EHC 139 Patty's 68 JACC 46					IPCS, 1992 Rusch, 2001 ECETOC, 2004b
					USA	1,000	5,580		AIHA, 2008a

Table 7: Saturated compounds subject to international review, with national OEL values *(cont'd)*

CAS number	Acronym	Name	Molecular formula (structure)	Review [a]	OEL, 8-hour TWA				Reference
					Country	(ppm) [b]	(mg/m^3) [c]	Remark or notation [d]	
354-33-6	HFC-125	Pentafluoroethane	C_2HF_5 (CHF_2–CF_3)	JACC 24 Patty's 68 SIAR (ICCA)					ECETOC, 1994a Rusch, 2001 OECD, 2005
					Sweden	500 [1.5]	2,500	-	AFS, 2005
					USA	1,000	4,910	-	AIHA, 2008a
79-34-5	HCC-130	1,1,2,2-Tetra-chloroethane	$C_2H_2Cl_4$ ($CHCl_2$–$CHCl_2$)	CICAD 3 Mono 71 SIAR (ICCA) ATP 29					IPCS, 1998 IARC, 1999a OECD, 2002b EC, 2004
					Denmark	1 [2]	7	S	Arbejdstilsynet, 2007
					France	1 [5]	7	-	INRS, 2007
					Germany	1 [2]	7	S	BAuA, 2007
					Japan	1	6.9	S	JSOH, 2007
					Netherlands	1	7	S	SER, 2008
					Norway	1 [3]	7	S	Arbeidstilsynet, 2007
					Spain	1	7	S	INSHT, 2008
					Switzerland	1 [2]	7	S, C, R, maybe F	Suva, 2007
					USA	1	6.9	S, C	ACGIH, 2008
					USA	1	7	S, C	NIOSH, 2005
					USA	5	35	S	OSHA, 1993 [h]

Table 7: Saturated compounds subject to international review, with national OEL values *(cont'd)*

CAS number	Acronym	Name	Molecular formula (structure)	Review [a]	OEL, 8-hour TWA				Reference
					Country	(ppm) [b]	(mg/m^3) [c]	Remark or notation [d]	
630-20-6	HCC-130a	1,1,1,2,-Tetrachloroethane	$C_2H_2Cl_4$ ($CHCl_2$–$CHCl_2$)	Mono 71					IARC, 1999a
1649-08-7	HCFC-132b	1,2-Dichloro-1,1-difluoroethane	$C_2H_2F_2Cl_2$ ($CClF_2$–CH_2Cl)	JACC 11 EHC 139 Patty's 68					ECETOC, 1990a IPCS, 1992 Rusch, 2001
75-88-7	HCFC-133a	1-Chloro-2,2,2-trifluoroethane	$C_2H_2F_3Cl$ (CH_2Cl–CF_3)	JACC 14 EHC 139 Mono 71 Patty's 68					ECETOC, 1990b IPCS, 1992 IARC, 1999a Rusch, 2001
811-97-2	HFC-134a	1,1,1,2-Tetrafluoroethane	$C_2H_2F_4$ (CF_3–CFH_2)	CICAD 11 Patty's 68 AEGL JACC 50					IPCS, 1998 Rusch, 2001 NRC, 2002 ECETOC, 2006a
					Germany	1,000 [8]	4,200	Not F	BAuA, 2007
					Netherlands	1,000	4,200	-	SER, 2008
					Sweden	500 [1.5]	2,000	-	AFS, 2005
					Switzerland	1,000	4,200	Not F	Suva, 2007
					UK	1,000	4,240	-	HSE, 2007
					USA	1,000	4,250	-	AIHA, 2001, 2008a

Table 7: Saturated compounds subject to international review, with national OEL values *(cont'd)*

CAS number	Acronym	Name	Molecular formula (structure)	Review[a]	OEL, 8-hour TWA				Reference
					Country	(ppm) [b]	(mg/m^3) [c]	Remark or notation [d]	
79-00-5	HCC-140	1,1,2-Trichloroethane	$C_2H_3Cl_3$ ($CHCl_2$–CH_2Cl)	Mono 71 SIAR (ICCA) ATP 29					IARC, 1999a OECD, 2000, 2003 EC, 2004
					Denmark	10 [2]	54	S, C	Arbejdstilsynet, 2007
					Finland	10 [2]	55	-	STM, 2005
					Germany	10 [2]	55	S	BAuA, 2007
					Japan	10	55	S	SER, 2008
					Netherlands	10 [2]	45	S	JSOH, 2007
					Norway	10 [2]	54	-	Arbeidstilsynet, 2007
					Spain	10	56	S	INSHT, 2008
					Switzerland	10 [2]	55	S	Suva, 2007
					USA	10	54.6	S, C	ACGIH, 2008
					USA	10	45	S, C	NIOSH, 2005
					USA	10	45	S	OSHA, 1993 [h]

***Table 7: Saturated compounds subject to international review, with national OEL values** (cont'd)*

CAS number	Acronym	Name	Molecular formula (structure)	Review [a]	OEL, 8-hour TWA				Reference
					Country	(ppm) [b]	(mg/m^3) [c]	Remark or notation [d]	
71-55-6	HCC-140a	Methyl chloroform (1,1,1-trichloroethane)	CH_3Cl_3 (CCl_3–CH_3)	Mono 71 EHC 136 ATP 19 AEGL draft					IARC, 1999a IPCS, 1992 EC, 1993 NAS/COT, 2000
					Denmark	50 [2]	275	-	Arbejdstilsynet, 2007
					EU	100	555	-	EC, 2000
					Finland	100 [2]	550	-	STM, 2005
					France	100	555	-	INRS, 2007
					Germany	200 [1]	1,100	S, not F	BAuA, 2007
					Japan	200	1,100	-	JSOH, 2007
					Netherlands	100 [2]	555	-	SER, 2008
					Norway	50 [1.5]	270	-	Arbeidstilsynet, 2007
					Spain	100 [2,t]	555	-	INSHT, 2008
					Switzerland	200 [1,s]	1,080	S, not F	Suva, 2007
					Sweden	50 [1.8]	300	-	AFS, 2005
					UK	100 [2]	555	-	HSE, 2007
					USA	350 [1.3]	1,910	-	NIOSH, 2005
					USA	350	1,900	-	OSHA, 1993 [h]

Table 7: Saturated compounds subject to international review, with national OEL values *(cont'd)*

CAS number	Acronym	Name	Molecular formula (structure)	Review [a]	OEL, 8-hour TWA				Reference
					Country	(ppm) [b]	(mg/m^3) [c]	Remark or notation [d]	
1717-00-6	HCFC-141b	1,1-Dichloro-1-fluoroethane	CH_3Cl_2F ($CCl_2F–CH_3$)	EHC 139 JACC 29 ATP 28 Patty's 68 SIAR (ICCA) AEGL					IPCS, 1992 ECETOC, 1994b EC, 2001 Rusch, 2001 OECD, 2001a NRC, 2002
					USA	500 [6]	2,150	-	AIHA, 2008a
75-68-3	HCFC-142b	1-Chloro-1,1-difluoroethane	$C_2H_3ClF_2$ ($CClF_2–CH_3$)	JACC 17 EHC 139 SIAR (ICCA) Patty's 68					ECETOC, 1990d IPCS, 1992 OECD, 2001a Rusch, 2001
					Denmark	1,000 [2]	4,110	-	Arbejdstilsynet, 2007
					Germany	1,000 [8]	4,200	-	BAuA, 2007
					Netherlands	2,000	8,380	-	SER, 2008
					Spain	1,000	4,200	-	INSHT, 2008
					Switzerland	1,000	4,170	-	Suva, 2007
					USA	1,000	4,110	-	AIHA, 2008a

Table 7: Saturated compounds subject to international review, with national OEL values *(cont'd)*

CAS number	Acronym	Name	Molecular formula (structure)	Review [a]	OEL, 8-hour TWA				Reference
					Country	(ppm) [b]	(mg/m^3) [c]	Remark or notation [d]	
420-46-2	HFC-143a	Trifluoroethane	$C_2H_3F_3$ (CF_3–CH_3)	JACC 52					ECETOC, 2006b
					USA	1,000	3,440	-	AIHA, 2008a
107-06-2	HCC-150	Ethylene dichloride (1,2-dichloroethane)	$C_2H_4Cl_2$ (CH_2Cl–CH_2Cl)	ATP 19					EC, 2004
				EHC 176					IPCS, 1995
				CICAD 1					IPCS, 1998
				Mono 71					IARC, 1999a
				SIAR (ICCA)					OECD, 2002a
					Denmark	1 [2]	4	S, C	Arbejdstilsynet, 2007
					Finland	10 [2]	41	-	STM, 2005
					France	10	40	C	INRS, 2007
					Japan	10	40	C	JSOH, 2007
					Netherlands	1.5 [2]	7	-	SER, 2008
					Norway	1	4	S, C	Arbeidstilsynet, 2007
					Spain	5	20	C	INSHT, 2008
					Sweden	1 [3]	4	S, C	AFS, 2005
					Switzerland	1 [5]	20	S, C	Suva, 2007
					UK	5	21	S, C	HSE, 2007
					USA	10	40.5	Not C	ACGIH, 2008
					USA	1	4	-	NIOSH, 2005
					USA	50 [2,p]	200	-	OSHA, 1993 [h]

Table 7: Saturated compounds subject to international review, with national OEL values (cont'd)

CAS number	Acronym	Name	Molecular formula (structure)	Review [a]	OEL, 8-hour TWA				Reference
					Country	(ppm) [b]	(mg/m^3) [c]	Remark or notation [d]	
75-34-3	HCC-150a	Ethylidene chloride (1,1-Dichoroethane)	$C_2H_4Cl_2$ ($CHCl_2$–CH_3)	ATP 29					EC, 2004
					Denmark	100 [2]	412	S	Arbejdstilsynet, 2007
					Finland	100 [2.5]	410	S	STM, 2005
					France	100	412	S	INRS, 2007
					Germany	100 [2]	410	-	BAuA, 2007
					Japan	100	400	-	JSOH, 2007
					EU	100	412	S	EC, 2000
					Netherlands	100 [2]	400	-	SER, 2008
					Norway	50 [1.5]	200	S	Arbeidstilsynet, 2007
					Spain	100	412	-	INSHT, 2008
					Sweden	100	412	-	AFS, 2005
					Switzerland	100 [2]	400	Not F	Suva, 2007
					UK	100	400	S	HSE, 2007
					USA	100	405	Not C	ACGIH, 2008
					USA	100	405	C	NIOSH, 2005
					USA	100	405	-	OSHA, 1993 [h]
75-37-6	HFC-152a	1,1-Difluoroethane	$C_2H_4F_2$ (CHF_2–CH_3)	Patty's 68 JACC 45					Rusch, 2001 ECETOC, 2004b
					USA	1,000	2,700	-	AIHA, 2008a

Table 7: Saturated compounds subject to international review, with national OEL values (cont'd)

CAS number	Acronym	Name	Molecular formula (structure)	Review [a]	OEL, 8-hour TWA				Reference
					Country	(ppm) [b]	(mg/m^3) [c]	Remark or notation [d]	
75-00-3	HCC-160	Ethyl chloride (Chloroethane)	C_2H_5Cl ($CH_2Cl–CH_3$)	ATP 22 Mono 71					EC, 1996 IARC, 1999a
					Denmark	100 [2]	264	S, C	Arbejdstilsynet, 2007
					EU	100	268	-	EC, 2006
					France	100	268	C	INRS, 2007
					Finland	100	268	S	STM, 2005
					Germany	40 [2]	110	-	BAuA, 2007
					Japan	100	260	-	JSOH, 2007
					Netherlands	100	268	-	SER, 2008
					Norway	100 [1.5]	270	C	Arbeidstilsynet, 2007
					Spain	100	268	-	INSHT, 2008
					Sweden	500 [1.4]	1,300	S, C	AFS, 2005
					Switzerland	9	25	-	Suva, 2007
					UK	50	134	S, C	HSE, 2007
					USA	100	260	C	ACGIH, 2008
					USA	-	-	-	NIOSH, 2005
					USA	1,000	2,600	-	OSHA, 1993 [h]

Table 7: Saturated compounds subject to international review, with national OEL values (cont'd)

CAS number	Acronym	Name	Molecular formula (structure)	Review [a]	OEL, 8-hour TWA				Reference
					Country	(ppm) [b]	(mg/m^3) [c]	Remark or notation [d]	
74-84-0	HCC-170	Ethane	C_2H_6 (CH_3–CH_3)	ATP 19					EC, 1993
					Netherlands	-	-	Oxygen repressant	SER, 2008
					Spain	1,000	(1,230)	Aliphatic hydrocarbon	INSHT, 2008
					Switzerland	10,000	12,500	-	Suva, 2007
					USA	1,000	1,230	Aliphatic hydrocarbon	ACGIH, 2008

Table 7: Saturated compounds subject to international review, with national OEL values (cont'd)

CAS number	Acronym	Name	Molecular formula (structure)	Review [a]	OEL, 8-hour TWA				Reference
					Country	(ppm) [b]	(mg/m^3) [c]	Remark or notation [d]	
431-89-0	HFC-227ea	1,1,1,2,3,3,3-Heptafluoropropane	C_3HF_7 (CF_3–CHF–CF_3)	Patty's 68					Rusch, 2001
690-39-1	HFC-236fa	1,1,1,3,3,3-Hexafluoropropane	$C_3H_2F_6$ (CF_3–CH_2–CF_3)	Patty's 68					Rusch, 2001
					USA	1,000	6,220	-	AIHA, 2008a
460-73-1	HFC-245fa	1,1,1,3,3-Pentafluoropropane	$C_3H_3F_5$ (CF_3–CH_2–CHF_2)	JACC 44 Patty's 68					ECETOC, 2006c Rusch, 2001
					USA	300	1,640	-	AIHA, 2008a

Table 7: Saturated compounds subject to international review, with national OEL values (cont'd)

CAS number	Acronym	Name	Molecular formula (structure)	Review [a]	OEL, 8-hour TWA				References
					Country	(ppm) [b]	(mg/m^3) [c]	Remark or notation [d]	
96-18-4	HCC-260da	1,2,3-Trichloro-propane	$C_3H_5Cl_3$ (CH_2Cl–$CHCl$–CH_2Cl)	Mono 63 CICAD 56 ATP 29 SIAR (ICCA)					IARC, 1995 IPCS, 2003 EC, 2004 OECD, 2004
					Denmark	0.1 [2]	0.6	S, C	Arbejdstilsynet, 2007
					Finland	3	18	S	STM, 2005
					Netherlands	0.02	0.108	C	SER, 2008
					Norway	10 [2]	60	S	Arbeidstilsynet, 2007
					Spain	10	(60.3)	S,C	INSHT, 2008
					Switzerland	-	-	C	Suva, 2007
					USA	10	60.3	S, C	ACGIH, 2008
					USA	10	60	S, C	NIOSH, 2005
					USA	50	300	-	OSHA, 1993 [h]

***Table 7: Saturated compounds subject to international review, with national OEL values** (cont'd)*

[a] AEGL, Acute Exposure Guideline Levels; ATP, Adaptation to Technical Progress; CICAD, Concise International Chemical Assessment Document; EHC, Environmental Health Criteria; EU RAR, European Union Risk Assessment Report; ICCA, International Council of Chemical Associations; JACC, Joint Assessment of Commodity Chemicals; Mono, Monographs on the Evaluation of Carcinogenic Risks to Humans; Patty's 68, Patty's Toxicology chapter 68 (Rusch, 2001); SIAR, SIDS Initial Assessment Report; TR, Technical Report

[b] Indicated in superscript are excursion factors for short-time (15 min) exposure limits (STELs)

[c] Official values. Some agencies use (slightly) different conversion factors based on variations in temperature, pressure and/or normal gas volume (Appendix C)

[d] S, possible uptake via the skin; C, carcinogenic; M, mutagenic; A, allergenic (sensitising); F, foetotoxic; R, harmful to reproduction

[e] 15-min STEL

[g] Ceiling value

[f] A protocol for biological monitoring exists

[h] Cited by NIOSH, 2005

[j] Evaluation based on pure substance. Contamination by HCFC-31 (Section 3.1) changes the evaluation (carcinogenic)

[k] Biological monitoring value: 1 mg/l blood (CO-Hb 5 %) (BAuA, 2006)

[l] Biological monitoring value: 0.2 mg/l urine

[m] Biological monitoring value: 0.5 mg/l blood (CO-Hb 5%)

[n] 30 ppm CO in end-tidal breath for biological monitoring

[o] Biological monitoring value: 0.3 mg/l urine

[p] STEL ceiling; maximum 300 ppm (5 min/3 h)

[r] Biological monitoring value: Trifluoroacetic acid 2.5 mg/l blood (BAuA, 2006)

[s] Biological monitoring value: 550 µg/l blood

[t] Biological monitoring value under revision

Table 8: Unsaturated compounds subject to international review, with national OEL values

CAS number	Acronym	Name	Molecular formula (structure)	Review [a]	OEL, 8-hour TWA				Reference
					Country	(ppm) [b]	(mg/m^3) [c]	Remark or notation [d]	
127-18-4	CC-1110	Perchloroethylene (Tetrachloroethene)	C_2Cl_4 (CCl_2=CCl_2)	EHC 31 ATP 22 JACC 39 CICAD 68					IPCS, 1984 EC, 1996 ECETOC, 1999 IPCS, 2006
					Denmark	10 [2]	70	S, C	Arbejdstilsynet, 2007
					France	50	335	C	INRS, 2007
					Germany	- [e]	-	-	
					Japan	- [f]	-	S, C	JSOH, 2007
					Netherlands	20 [1.8,g]	138	S	SER, 2008
					Norway	6 [2]	40	S, C, R	Arbeidstilsynet, 2007
					Spain	25 [j]	172	-	INSHT, 2008
					Sweden	10 [2.5]	70	C	AFS, 2005
					Switzerland	50 [2,h]	345	S, maybe F	Suva, 2007
					UK	50 [2]	345	-	HSE, 2007
					USA	25 [4,j]	170	C	ACGIH, 2008
116-14-3	CFC-1114	Tetrafluoroethylene (Tetrafluoroethene)	C_2F_4 (CF_2=CF_2)	JACC 42 CICAD 68 AEGL draft					ECETOC, 2003 IPCS, 2006 NAC, 2006b
					Spain	2	8.3	-	INSHT, 2008
					USA	2	8.2	C	ACGIH, 2008

Table 8: Unsaturated compounds subject to international review, with national OEL values (cont'd)

CAS number	Acronym	Name	Molecular formula (structure)	Review [a]	OEL, 8-hour TWA				Reference
					Country	(ppm) [b]	(mg/m^3) [c]	Remark or notation [d]	
79-01-6	HCC-1120	Trichloroethylene (Trichloroethene)	C_2HCl_3 ($CHCl=CCl_2$)	ATP 28 FAS 18 EHC 50 TR 60 Mon 63 RAR 31					EC, 2001 JECFA, 1983 IPCS, 1985 ECETOC, 1994c IARC, 1995 ECB, 2004
					Denmark	10 [2]	55	C	Arbejdstilsynet, 2007
					Finland	30 [1.5]	160	-	STM, 2005
					France	75 [2.67]	405	C, M	INRS, 2007
					Germany	- [k]	-		
					Japan	25	135	C	JSOH, 2007
					Netherlands	35 [2.8]	190	-	SER, 2008
					Norway	10 [2]	50	C	Arbeidstilsynet, 2007
					Spain	50 [1]	273	C	INSHT, 2008
					Sweden	10 [2.5]	50	C	AFS, 2005
					Switzerland	50 [2,m]	260	S, C, maybe F	Suva, 2007
					UK	100	550	S, C	HSE, 2007
					USA	0 [2.5,n]	54	C	ACGIH, 2008
					USA	-	-	C	NIOSH, 2005
					USA	100 [2,o]	537	-	OSHA, 1993 [p]

Table 8: Unsaturated compounds subject to international review, with national OEL values (cont'd)

CAS number	Acronym	Name	Molecular formula (structure)	Review [a]	OEL, 8-hour TWA				Reference
					Country	(ppm) [b]	(mg/m^3) [c]	Remark or notation [d]	
75-35-4	HCC-1130a	Vinylidene chloride (1,1-Dichloroethene)	$C_2H_2Cl_2$ ($CH_2=CCl_2$)	Mono 71 EHC 100 CICAD 51 ATP 29					IARC, 1999a IPCS, 1990b IPCS, 2003 EC, 2004
					Denmark	2 [2]	8	C	Arbejdstilsynet, 2007
					Finland	10	40	-	STM, 2005
					France	5	20	C	INRS, 2007
					Germany	2 [2]	8	Not F	BAuA, 2007
					Netherlands	5	20	-	SER, 2008
					Norway	1 [3]	4	-	Arbeidstilsynet, 2007
					Spain	5	20	-	INSHT, 2008
					Sweden	5 [2]	20	-	AFS, 2005
					Switzerland	2 [2]	8	C, not F	Suva, 2007
					UK	10	40	-	HSE, 2007
					USA	5	19.8	Not C	ACGIH, 2008
					USA	-	-	C	NIOSH, 2005

Table 8: Unsaturated compounds subject to international review, with national OEL values (cont'd)

CAS number	Acronym	Name	Molecular formula (structure)	Review [a]	OEL, 8-hour TWA				Reference
					Country	(ppm) [b]	(mg/m^3) [c]	Remark or notation [d]	
540-59-0	HCC-1130	1,2-Dichloro-ethylene, mixed *cis* and *trans* isomers	$C_2H_2Cl_2$ (CHCl=CHCl)	ATP 29 AEGL draft					EC, 2004 NAC, 2007
					Denmark	200 [2]	790	-	Arbejdstilsynet, 2007
					Finland	200 [1.25]	800	-	STM, 2005
					Germany	200 [2]	800	-	BAuA, 2007
					Japan	150	590	-	JSOH, 2007
					Norway	100 [1.5]	395	-	Arbeidstilsynet, 2007
					Spain	200 [1.25]	807	-	INSHT, 2008
					Switzerland	200 [2]	790	-	Suva, 2007
					UK	200 [1.25]	806	-	HSE, 2007
					USA	200	790	-	ACGIH, 2008
156-59-2	HCC-1130 *cis*	*cis*-Dichloroethylene	$C_2H_2Cl_2$ (CHCl=CClH)	ATP 29 AEGL draft					EC, 2004 NAC, 2007
					Denmark	200 [2]	790	-	Arbejdstilsynet, 2007
					Finland	200 [1.25]	800	-	STM, 2005
					Germany	200 [2]	800	-	BAuA, 2007
					Switzerland	200 [2]	790	-	Suva, 2007
					USA	200	790	-	ACGIH, 2008

Table 8: Unsaturated compounds subject to international review, with national OEL values (cont'd)

CAS number	Acronym	Name	Molecular formula (structure)	Review [a]	OEL, 8-hour TWA				Reference
					Country	(ppm) [b]	(mg/m^3) [c]	Remark or notation [d]	
156-60-5	HCC-1130 *trans*	*trans*-Dichloro-ethylene	$C_2H_2Cl_2$ (CHCl=CClH)	ATP 29 AEGL draft					EC, 2004 NAC, 2007
					Denmark	200 [2]	790	-	Arbejdstilsynet, 2007
					Finland	200 [1.25]	800	-	STM, 2005
					Germany	200 [2]	800	-	BAuA, 2007
					Switzerland	200 [2]	790	-	Suva, 2007
					USA	200	790	-	ACGIH, 2008
75-38-7	HFC-1132a	Vinylidene fluoride (1,1-Difluoroethylene)	$C_2H_2F_2$ ($CH_2=CF_2$)	Mon 71 SIAR (ICCA) ATP 29					IARC, 1999a OECD, 2001b EC, 2004
					Spain	500	(1,310)	-	INSHT, 2008
					USA	500	1,310	Not C	ACGIH, 2008
					USA	1 [5,s]	26	-	NIOSH, 2005

Table 8: Unsaturated compounds subject to international review, with national OEL values (cont'd)

CAS number	Acronym	Name	Molecular formula (structure)	Review [a]	OEL, 8-hour TWA				Reference
					Country	(ppm) [b]	(mg/m^3) [c]	Remark or notation [d]	
75-01-4	HCC-1140	Vinyl chloride (Chloroethene)	CH_3Cl (CH_2=CHCl)	ATP 19 SIAR (ICCA)					EC, 1993 OECD, 2001b
					Denmark	1 [2]	3	S, C	Arbejdstilsynet, 2007
					Finland	3	7.7	-	STM, 2005
					France	1	2.59	C	INRS, 2007
					Japan	2.5 [r]	6.5	C	JSOH, 2007
					Netherlands	1	7.77	-	SER, 2008
					Norway	1 [3]	3	C	Arbeidstilsynet, 2007
					Spain	3	7.8	C	INSHT, 2008
					Sweden	1 [5]	2.5	S, C	AFS, 2005
					Switzerland	2	5.2	C	Suva, 2007
					UK	3	7.8	C	HSE, 2007
					USA	1	2.07	C	ACGIH, 2008
					USA	-	-	C	NIOSH, 2005
					USA	1 [5,s]	2.56	-	OSHA, 1993 [p]
75-02-5	HFC-1141	Vinyl fluoride (Fluoroethene)	C_2H_3F (CH_2=CHF)	Mono 39					IARC, 1986b
					USA	1	1.88	C	ACGIH, 2008
					USA	1 [5,s]	1.89	-	NIOSH, 2005

Table 8: Unsaturated compounds subject to international review, with national OEL values (cont'd)

CAS number	Acronym	Name	Molecular formula (structure)	Review [a]	OEL, 8-hour TWA				Reference
					Country	(ppm) [b]	(mg/m^3) [c]	Remark or notation [d]	
74-85-1	HC-1150	Ethylene (Ethene)	C_2H_4 (CH_2=CH_2)	SIAR ATP 29					OECD, 1998 EC, 2004
					Netherlands	250	3330	-	SER, 2008
					Spain	200	818	-	INSHT, 2008
					Sweden	250 [4]	330	-	AFS, 2005
					Switzerland	10,000	11,500	M	Suva, 2007
					USA	200	818	Not C	ACGIH, 2008
116-15-4	CFC-1216	Hexafluoropropylene (Hexafluoropropene)	C_3F_3 (CF_3–CF=CF_2)	ATP 19 JACC 48 AEGL draft					EC, 1993 ECETOC, 2005c NAC, 2006c

Table 8: Unsaturated compounds subject to international review, with national OEL values (cont'd)

[a] AEGL, Acute Exposure Guideline Levels; ATP, Adaptation to Technical Progress; CICAD, Concise International Chemical Assessment Document; EHC, Environmental Health Criteria; EU RAR, European Union Risk Assessment Report; ICCA, International Council of Chemical Associations; JACC, Joint Assessment of Commodity Chemicals; Mono, Monographs on the Evaluation of Carcinogenic Risks to Humans; Patty's 68, Patty's Toxicology chapter 68 (Rusch, 2001); SIAR, SIDS Initial Assessment Report; TR, Technical Report

[b] Indicated in superscript are excursion factors for short-time (15 min) exposure limits (STELs)

[c] Official values. Some agencies use (slightly) different conversion factors based on variations in temperature, pressure and/or normal gas volume (Appendix C)

[d] S, possible uptake via the skin; C, carcinogenic; M, mutagenic; A, allergenic (sensitising); F, foetotoxic; R, harmful to reproduction

[e] Biological monitoring value: 1 mg/l blood (BAuA, 2006)

[f] Pending

[g] A protocol for biological monitoring exists

[h] Biological monitoring value: 1 mg/l blood (trichloroacetic acid 7 mg/l urine)

[j] Biological monitoring value: 5 ppm (34 mg/m^3) in exhaled air, 0.5 mg/l blood (trichloroacetic acid 3.5 mg/l urine)

[k] Biological monitoring value: Trichloroethanol 5 mg/l blood (BAuA, 2006)

[l] Biological monitoring value: Trichoroethanol 4 mg/l blood, trichloroacetic acid 100 mg/g creatinine (300 mg/g including trichoroethanol) in urine

[m] Biological monitoring value: Trichoroethanol 5 mg/l blood, trichloroacetic acid 100 mg/g creatinine in urine

[n] Biological monitoring value: None in exhaled air and blood (trichloroethanol 0.5 mg/l blood, trichloroacetic acid 15 mg/l urine)

[o] STEL ceiling; maximum 300 ppm (5 min/2 h)

[p] Cited by NIOSH, 2005

[r] Provisional OEL based on non-carcinogenic health effects; exposure concentration should be kept below a detectable limit

[s] 15-min STEL

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5.2 Databases consulted

The literature was searched from 1995 to 2005 via STN International host, including BIOSIS, EMBASE, MEDLINE, SCISEARCH and TOXLINE. Chemical Abstracts Service, Columbus, Ohio, USA [www.cas.org].

APPENDIX A: SPECIAL ABBREVIATIONS

ALC	Acute lethal concentration
bw	Body weight
CAS	Chemicals Abstracts Service
CNS	Central nervous system
CYP2B6	Cytochrome P450 2B6
CYP2E1	Cytochrome P450 2E1
d	Day
DMSO	Dimethyl sulphoxide
DNA	Deoxyribonucleic acid
Eq.	Equation
F344	Fischer 344
FC	Fluorocarbon
h	Hour
HCFC	Hydrochlorofluorocarbon
HFC	Hydrofluorocarbon
Hg	Mercury
hPa	Hectopascal
kgbw	Kilogramme body weight
LC_0	Non-lethal concentration
LC_{50}	Median lethal concentration
LC_{Lo}	Lowest lethal concentration
LD_{50}	Median lethal dose
mg	Milligramme
min	Minute
mmol	Millimole
ml	Millilitre
µmol	Micromole
µg	Microgramme
NOAEL	No-observed adverse effect level
OEL	Occupational exposure limit (value)
P450	Cytochrome P450
PCE	Polychromatic erythrocyte
ppm	Parts per million (10^{-6})
s	Second
S9	Supernatant of centrifuged 9,000 × g liver homogenate
STEL	Short-term exposure limit (value)
TWA	Time-weighted average (concentration)
v/v	By volume
wk	Week
y	Year

APPENDIX B: NAMING AND NUMBERING SYSTEM FOR FLUOROCARBON COMPOUNDS

The naming and numbering system currently used by industry was officially adopted as Standard 34 of the American Society of Heating, Refrigeration, and Air-conditioning Engineers (ASHRAE) on June 3, 1957 (DuPont, 1999).

B.1 Prefixes

These prefixes are generally applicable:

- FC = Fluorocarbon
- CFC = Chlorofluorocarbon
- HFC = Hydrofluorocarbon
- PFC = Perfluorocarbon (also Perfluorocompound, Persistent Fluorinated Compound)
- HFOC = Hydrofluoroether
- HCFC = Hydrochlorofluorocarbon
- FOC = Fluoroether

B.2 Numbering code

The first digit from the right is the number of fluorine atoms in the molecule. The second digit from the right is one more than the number of hydrogen atoms in the molecule. The third digit from the right is one less than the number of carbon atoms in the molecule (omit if zero).

The number of chlorine atoms in the compound is calculated by subtracting the sum of fluorine and hydrogen atoms from the total atoms which can be connected to the carbon atoms. If some of the chlorine has been replaced by bromine, then the number is followed by a 'B' and the number of chlorine atoms so replaced.

The fourth digit from the right indicates the number of double bonds in the molecule, for example:

- PFC-116 = 6 Fs, 0 Hs, 2 Cs and 0 Cls $\rightarrow C_2F_6$
- HFC-23 = 3 Fs, 1 H, 1 C, and 0 Cls $\rightarrow CF_3H$
- PFC-1216 = 6 Fs, 0 Hs, 3 Cs, 0 Cls with 1 double bond $\rightarrow C_3F_6 \rightarrow CF_2 = CF\text{-}CF_3$.

For cyclic molecules, the letter C is used before the identifying number, for example:

- PFC-C318 = 8 Fs, 0 Hs, 4 Cs and 0 Cls with cyclic structure → c-C_4F_8.

For isomeric compounds, each has the same number designation, but the various isomers are indicated by a lowercase letter following the number; the letters are assigned based on the symmetry of the molecule. The most symmetrical structure has no letter, followed by the next most symmetrical isomer designated 'a', and so on. The symmetry is determined by summing the atomic weights of all atoms attached to each carbon, and comparing the two numbers. The smaller their difference, the more symmetrical the molecule. For example $C_2H_2F_4$ can have two structural isomers:

- CF_2H-CF_2H, more symmetrical, HFC-134
- CF_3-CFH_2, less symmetrical, HFC-134a.

B.3 Extension to 3-carbon molecules

For C3s, the isomer designation is slightly different, and uses a two-letter code. The codes below are used to determine the substituents on the central carbon, which determines the first letter of the code. The second letter in the code designates the various isomers based on symmetry, with the most symmetrical structure designated 'a', and so forth.

B.4 Central carbon letter

- a = CCl_2
- b = CClF
- c = CF_2
- d = CClH
- e = CFH
- f = CH_2

For example:
HFC-236fa = $C_3F_6H_2$ → Central carbon designated 'f' → CH_2 → 'a' symmetry designation → $CF_3CH_2CF_3$.

B.5 C4 and larger molecules

For 4-carbon atom and larger molecules, string together the letter designations from the above and following lists to indicate the current isomer. Designation always starts either at the

molecule's more fluorinated end or at the end needing the least number of suffix letters to assign the structure. If a digit is larger than 9, it is offset by a dash.

- j = CCl_3
- k = CCl_2F
- l = $CClF_2$
- m = CF_3
- n = $CHCl_2$
- o = CH_2Cl
- p = CHF_2
- q = CH_2F
- r = CHClF
- s = CH_3
- t = C
- x = CCl
- y = CF
- z = CH

Example: HFC-43-10mee = 10 Fs, 2 Hs, 5 Cs, no Cls → $C_5H_2F_{10}$

- m indicates CF_3 . . . CF_3
- e indicates CHF, so CF_3CHF
- e indicates CHF, so $CF_3CHFCHF$
- HFC-43-10mee → $CF_3CHFCHFCF_2CF_3$.

The assignment of a string of letters, to denote structural groups, is stopped when the structure is unambiguous (i.e. it is not necessary to call the compound HFC-43-10mee**cm**, since once the letter string reaches 'mee', it is clear that 5 fluorine atoms still need to be attached to the remaining two carbons, so the rest of the molecule must be $–CF_2CF_3$).

APPENDIX C: CONVERSION FACTORS FOR VAPOUR CONCENTRATIONS IN AIR

Conversion factors for vapour concentrations in air can be calculated from the molar volume of an ideal gas at 0°C: 22.4136 litre.

$1\ mg/m^3 = 22.4136/Mw \times 1{,}013.25/P \times (273+T)/273\ ppm$ .....(Eq. C.1)
$1\ ppm = Mw/22.4136 \times P/1{,}013.25 \times 273/(273+T)\ mg/m^3$ .....(Eq. C.2)

where Mw = molecular weight, T = temperature (°C) and P = pressure (hPa).

For European standard conditions, 20°C and 1,013.25 hPa (=1 atm = 760 mm Hg), the formulae become:

$1\ mg/m^3 = 24.0556/Mw\ ppm$ .....(Eq. C.3)
$1\ ppm = Mw/24.0556\ mg/m^3$ .....(Eq. C.4)

In the USA and other countries 25°C is used, and the formulae are:

$1\ mg/m^3 = 24.4661/Mw\ ppm$ .....(Eq. C.5)
1 ppm = Mw/24.4661 mg/m3.....(Eq. C.6)

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