

Trifluoroethane (HFC-143a)
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EXECUTIVE SUMMARY

This report has been produced as part of the ECETOC Joint Assessment of Commodity Chemicals (JACC) programme. It presents a critical evaluation of the available data on the ecotoxicity and toxicity of 1,1,1-trifluoroethane (HFC-143a), including results of recent and unpublished studies conducted by the Programme for Alternative Fluorocarbon Toxicity Testing (PAFT)^a.

1,1,1-Trifluoroethane (HFC-143a) is a colourless, flammable gas that is mainly used as a blend component for air conditioning and refrigeration systems.

When released into the environment, HFC-143a is expected to volatilise almost entirely into the atmosphere, where it will be slowly degraded via trifluoroacetaldehyde to HF and CO₂ as final products. HFC-143a does not deplete the stratospheric ozone layer, but its global warming potential (3,800 relative to CO₂) is comparable to 4,000 for trichlorofluoromethane (CFC-11).

HFC-143a has not been tested in aquatic organisms. Its environmental toxicity is assumed to be negligible because it volatilises to air.

Following inhalation, HFC-143a is poorly absorbed and rapidly excreted in both laboratory animals and humans. Trifluoroethanol is the principal metabolite in rats.

HFC-143a has a low acute toxicity in rats following inhalation. Cardiac sensitisation to adrenaline was induced in dogs when the HFC-143a was inhaled at a level of 300,000 ppm. Following a 4-week exposure study, there were effects on the testicles of male rats in one study, but two other repeat-exposure studies, one 4 weeks and the other 13 weeks at the same exposure levels, were without any toxic effect. This effect was attributable to confounding factors related to the method of exposure.

In vitro, the genotoxic potential of HFC-143a is low: the majority of the tests were negative. There was no genotoxicity in a micronucleus test *in vivo*.

Following oral ingestion of HFC-143a for one year, no tumours were observed in rats.

Possible reproductive effects of HFC-143a have not been studied specifically. There was no developmental toxicity seen in studies in rats and rabbits.

Human volunteers showed no adverse effect when exposed for 2 hours to 500 ppm HFC-143a.

In the USA, an occupational exposure limit (8-hour time-weighted average) of 1,000 ppm is recommended by the American Industrial Hygiene Association.

^a A cooperative research effort (1987-2000) sponsored by 16 of the leading CFC producers [www.afeas.org/paft/].

ECETOC SCHEME FOR THE JOINT ASSESSMENT OF COMMODITY CHEMICALS

This report has been produced as part of the ECETOC programme for preparing critical reviews of the toxicology and ecotoxicology of selected existing industrial chemicals. In the programme, commodity chemicals (i.e. those produced in large tonnage by several companies and having widespread and multiple uses) are jointly reviewed by experts from a number of companies with knowledge of the chemical. It should be noted that in a JACC review only the chemical itself is considered; products in which it appears as a component or an impurity are not normally taken into account.

This document presents a critical evaluation of the available toxicology and ecotoxicology of 1,1,1-trifluoroethane (CAS No. 420-46-2).

Where relevant, the Task Force has graded the (eco)toxicological studies by means of a 'code of reliability' (CoR) to reflect the degree of confidence that can be placed on the reported results. The codes and criteria used to assess reliability are included in Appendix A.

1. SUMMARY AND CONCLUSIONS

1,1,1-Trifluoroethane (HFC-143a^a) is a flammable colourless gas produced by hydrofluorination of 1,1-dichloroethylene. It is mainly used as a blend component for air conditioning and refrigeration systems.

When released into the environment, HFC-143a is expected to partition almost exclusively into the atmosphere, with a minimal distribution into water and solids environmental compartments. The atmospheric degradation of HFC-143a occurs via indirect photolysis by hydroxyl radicals, with the formation of trifluoroacetaldehyde as a stable intermediate, which may subsequently be degraded to HF and CO₂ as final products. A global atmospheric lifetime of 52 years is estimated for HFC-143a.

HFC-143a does not contribute to the depletion of stratospheric ozone layer. A global warming potential of 3,800 has been calculated for a time horizon of 100 years.

No experimental data are available for the environmental effects of HFC-143a in aquatic organisms. Due to its physico-chemical properties, HFC-143a is not expected to distribute into water, thus its environmental toxicity may be assumed to be negligible.

Toxicokinetics of HFC-143a were studied in rats exposed by inhalation. The results of the study showed a poor absorption and accumulation of HFC-143a into blood and tissues. Trifluoroethanol was identified as the principal excreted metabolite in rats exposed to 40,000 ppm HFC-143a (137,000 mg/m³). A toxicokinetic study carried out in human volunteers confirmed the low absorption rate and the rapid excretion of HFC-143a in mammals.

A low acute toxicity was observed in rats exposed via inhalation to HFC-143a. The 4-hour LC₅₀ was greater than 500,000 ppm (1,720,000 mg/m³) in two different rat strains. Cardiac sensitisation was observed in dogs exposed to 300,000 ppm (858,000 mg/m³) and concurrently injected with adrenaline. The NOAEL for this effect was 250,000 ppm (858,000 mg/m³).

A dose-related decrease in absolute testicular weight, accompanied by microscopical degenerative changes in testicles was observed in male rats exposed nose-only to HFC-143a for 4 weeks. This effect was attributable to confounding factors related to the method of exposure. The effects in male gonads were not replicated in a second 28-day study or in a subsequent 90-day study, in which rats were exposed whole-body. No treatment-related adverse effect was observed in this last study in rats exposed to HFC-143a up to 40,000 ppm (137,000 mg/m³).

^a The naming and numbering convention is explained in Appendix B.

In vitro genotoxicity tests carried out with HFC-143a indicated a low genotoxic potential. HFC-143a gave negative results in two independent bacterial mutagenicity tests and in a chromosomal aberration test in human lymphocytes. It gave a weak mutagenic response in two strains of *Salmonella typhimurium* during a limited Ames test, but it did not induce a positive response in a concurrent Styles Assay carried out in the mammalian cell line BHK21. *In vivo*, HFC-143a was not active in a mouse micronucleus assay conducted with exposure levels up to 40,000 ppm.

There are no available studies for prolonged exposure to HFC-143a by inhalation.

In a limited oral study, HFC-143a was administered by gavage to male and female rats for 52 consecutive weeks, and the animals were held for an additional 73 weeks. No compound-related neoplastic or non-neoplastic findings were observed in this study.

There are no available studies for the reproductive effects of HFC-143a. The effect observed in the male rat gonads during a 28-day study cannot be considered treatment-related, since it was not replicated in two other repeated exposure studies.

The developmental toxicity of HFC-143a was studied in rats and rabbits. There were no treatment-related findings on maternal toxicity or foetal parameters for concentrations of HFC-143a up to 40,000 ppm (137,000 mg/m³).

A preliminary report on a human volunteer toxicokinetic study did not indicate any adverse effect in individuals exposed to 500 ppm HFC-143a (1,720 mg/m³) for 2 hours.

In the USA, an occupational exposure limit (8-hour time-weighted average) of 1,000 ppm (3,433 mg/m³) is recommended by the American Industrial Hygiene Association.

2. IDENTITY, PHYSICAL AND CHEMICAL PROPERTIES, ANALYTICAL METHODS

2.1 Identity

Name:	Trifluoroethane
IUPAC name:	1,1,1-Trifluoroethane
Synonyms:	Ethane, trifluoro- Methyl fluoroform HFA-143a HFC-143a
Danish:	Trifluorethan
Dutch:	Trifluorethaan
Finnish:	Trifluorietaani
French:	Trifluoréthane, trifluoroéthane
German:	Trifluorethan
Greek:	Τριφλοροαιθάνιο
Italian:	Trifluoroetano
Norwegian:	Trifluoretan
Portuguese:	Trifluoretano, trifluoroetano
Spanish:	Trifluoretano
Swedish:	Trifluoretan
CAS name:	Ethane, trifluoro-
CAS registry number:	420-46-2
EC (EINECS) number:	206-996-5
Formula:	$C_2H_3F_3$
Molecular mass:	84.0
Chemical structure:	$\begin{array}{c} \text{F} \quad \text{H} \\ \quad \\ \text{F}-\text{C}-\text{C}-\text{H} \\ \quad \\ \text{F} \quad \text{H} \end{array}$

2.2 EU classification and labelling

HFC-143a is classified and labelled in accordance with the Dangerous Substances Directive 67/548/EEC and its subsequent amendments as:

Classification: F+, extremely flammable
Labelling: R phrase R12, extremely flammable.

2.3 Physical and chemical properties

Trifluoroethane is a flammable, colourless gas. Physical and chemical properties are reported in Table 1.

Table 1: Physical and chemical properties of HFC-143a

Parameter	Value, unit	Reference
Melting point	-111.3°C	Smart and Fernandez, 2000
Boiling point at 1,013 hPa	-47.4°C	Smart and Fernandez, 2000
Liquid density at -50 °C	1.176 g/ml	Smart and Fernandez, 2000
Relative density D_4^{20} (density of water at 4°C is 1,000 kg/m ³)	Not applicable	
Viscosity of liquid, mPa·s at 20°C	Not applicable	
Refractive index n_D at 20°C	Not applicable	
Vapour pressure at 25°C	1,272 kPa 1,262 kPa	Daubert and Danner, 1989 ^a Fujiwara <i>et al</i> , 1998
Vapour density at 25°C (air = 1)	2.9	Solvay, 2001
Threshold odour concentration, ppm (mg/m ³)	Not applicable	
Surface tension, mN/m at 20 °C	Not applicable	
Solubility in water at 25 °C and atmospheric pressure	761 mg/l	SRC, 2004
Partition coefficient, log K_{ow} (octanol/water) at 20°C	1.74	SRC, 2004
Partition coefficient, log K_{oc} (organic carbon/water) at 20°C	No data	
Henry's Law constant at 25°C	11.2 kPa m ³ /mol	Calculated ^b
Flash point	No data	
Flammability limits at 20 - 25°C	7.1% - 16.1%	Solvay, 2001
Explosion limits in air at 1,013 hPa, at ambient temperature	No data	
Auto-flammability, ignition temperature	750°C	Solvay, 2001

^a Cited by SRC, 2004^b Molecular mass × 1 atm / solubility in water at 1 atm (1,013 hPa).

Typically, commercial HFC-143a has a purity of > 99.9% (Brock *et al*, 1996). Common impurities are various other fluorocarbons, depending on the conditions of the production process (Section 3.1).

2.4 Conversion factors

Conversion factors for HFC-143a concentrations in air at 25°C and 1,013 hPa are:

- 1 ppm = 3.433 mg/m³
- 1 mg/m³ = 0.291 ppm.

In this report, converted values are given in parentheses.

The generic formula, from which the conversion factors for vapour concentrations in air are derived, is given in Appendix C. According to European standard conditions (20°C and 1,013 hPa) these would be: 1 ppm = 3.492 mg/m³ and 1 mg/m³ = 0.286 ppm.

2.5 Analytical methods

2.5.1 Air

HFC-143a in air is detected by headspace gas-chromatography (GC). A capillary column coated by a stationary phase with the following composition: 6 % cyanopropyl + 94 % methyl siloxane is used. HFC-143a is detected by means of a flame ionisation detector (FID). The limit of detection is 1 ppm (3.43 mg/m³) with this method (Solvay, 2002).

2.5.2 Water

HFC-143a in water can be detected by means of headspace GC. A semi-capillary column coated with polymeric styrene-divinylbenzene and an FID detector are used in this method. The detection limit is 1 mg/l (Solvay, 2004).

3. PRODUCTION, STORAGE, TRANSPORT AND USE

3.1 Production

HFC-143a, together with 1,1-dichloro-1-fluoroethane (HCFC-141b) and 1-chloro-1,1-difluoroethane (HCFC-142b), is commonly produced by means of hydrofluorination of 1,1-dichloroethylene or 1,1,1-trichloroethane. The degree of fluorination of the raw material can be controlled by varying the reaction conditions such as HF-reactant ratio, temperature and catalyst. Other producers use 1,1,1-trichloroethane. IPCC (2005a) also reports production from trichloroethylene. A further possibility is addition of hydrogen fluoride to 1,1-difluoroethylene.

Production of HFC-143a began in 1995 and there has been a steady increase in annual quantity to 13 kt in 2003, as reported by companies covered by the Alternative Fluorocarbons Environmental Acceptability Study (AFEAS, 2004).

3.2 Storage

As a flammable liquefied gas, HFC-143a is stored in fireproofed tanks in cool, well-ventilated areas and kept away from sunrays, heat sources and incompatible materials, such as alkaline metals.

3.3 Transport

HFC-143a is transported in special fireproofed containers.

3.4 Use

HFC-143a is mainly used as a blend component for air conditioning systems and commercial refrigeration.

4. ENVIRONMENTAL DISTRIBUTION AND TRANSFORMATION

4.1 Emissions

4.1.1 Natural sources

HFC-143a has no natural sources of emission.

4.1.2 Emissions during production and use

No data are available.

4.2 Environmental distribution

HFC-143a is a gas at room temperature and normal atmospheric pressure. Due to its vapour pressure (1,272 kPa at 25 °C) and water solubility (761 mg/l) values, HFC-143a is expected to partition exclusively into the atmosphere, when it is released in the environment.

The environmental partitioning of HFC-134a has been assessed (Binaglia, 2006) by means of the fugacity-based equilibrium criteria (EQC) Level I and Level III models (Mackay, 1996).

In the Level I model, a fixed quantity of a supposedly non-degradable chemical is introduced into a closed evaluative environment and equilibrium achieved between the various environmental compartments (air, water, soil, sediment). The Level III model simulates a situation in which a chemical is emitted at a constant rate into one or more of the compartments, in each of which it may degrade; the steady-state distribution between compartments is then calculated. Due to the resistance to mass transfer between compartments, the various phases are not in equilibrium and the steady-state partitioning depends on its 'mode of entry', i.e. the compartment(s) into which the chemical is injected.

EQC modelling has been performed for HFC-143a using the physico-chemical properties listed in Table 1 and an atmospheric lifetime of 52 years, corresponding to a half-life of 36 years (Section 4.3.1). Degradation in other media was not taken into account. Two simulations were considered at Level III, assuming emission of HFC-143a to air alone or to the water alone. The results are shown in Table 2.

Table 2: Partitioning (%) into the environment (Binaglia, 2006)

Compartment	EQC level I	EQC level III	
		Emission to air alone	Emission to water alone
Air	99.996	99.993	19.9
Water	0.0036	0.0026	79.8
Soil	0.00017	0.0039	0.0008
Sediment	0.000004	0.000008	0.25

The Level III simulation with emission of HFC-143a to air alone and the Level I simulation predicted a distribution of HFC-143a almost exclusively into the atmosphere. However, when the emissions are to water alone, a significant proportion of HFC-143a is expected to partition to the aqueous compartment at the steady-state. This is due to the resistances in the water-to-air transfer introduced in the Level III model.

In conclusion, HFC-143a released to air is expected to remain almost exclusively in that compartment and any HFC-143a emitted to water will ultimately be found in the air.

4.3 Environmental fate and biotransformation

4.3.1 Atmospheric fate and impact

Atmospheric degradation of HFC-143a is mainly attributable to tropospheric reaction with hydroxyl (OH) radicals. A global atmospheric lifetime of 52 years is listed in WMO (2002), corresponding to a half-life of 36 years. In NASA/JPL (2003), all reported experimental determinations of the rate constant for reaction of HFC-143a with the OH radical were evaluated, leading to a recommended value of $1.1 \times 10^{-12} \times e^{-(2010/T)}$ cm³/molecule/s as a function of temperature (T).

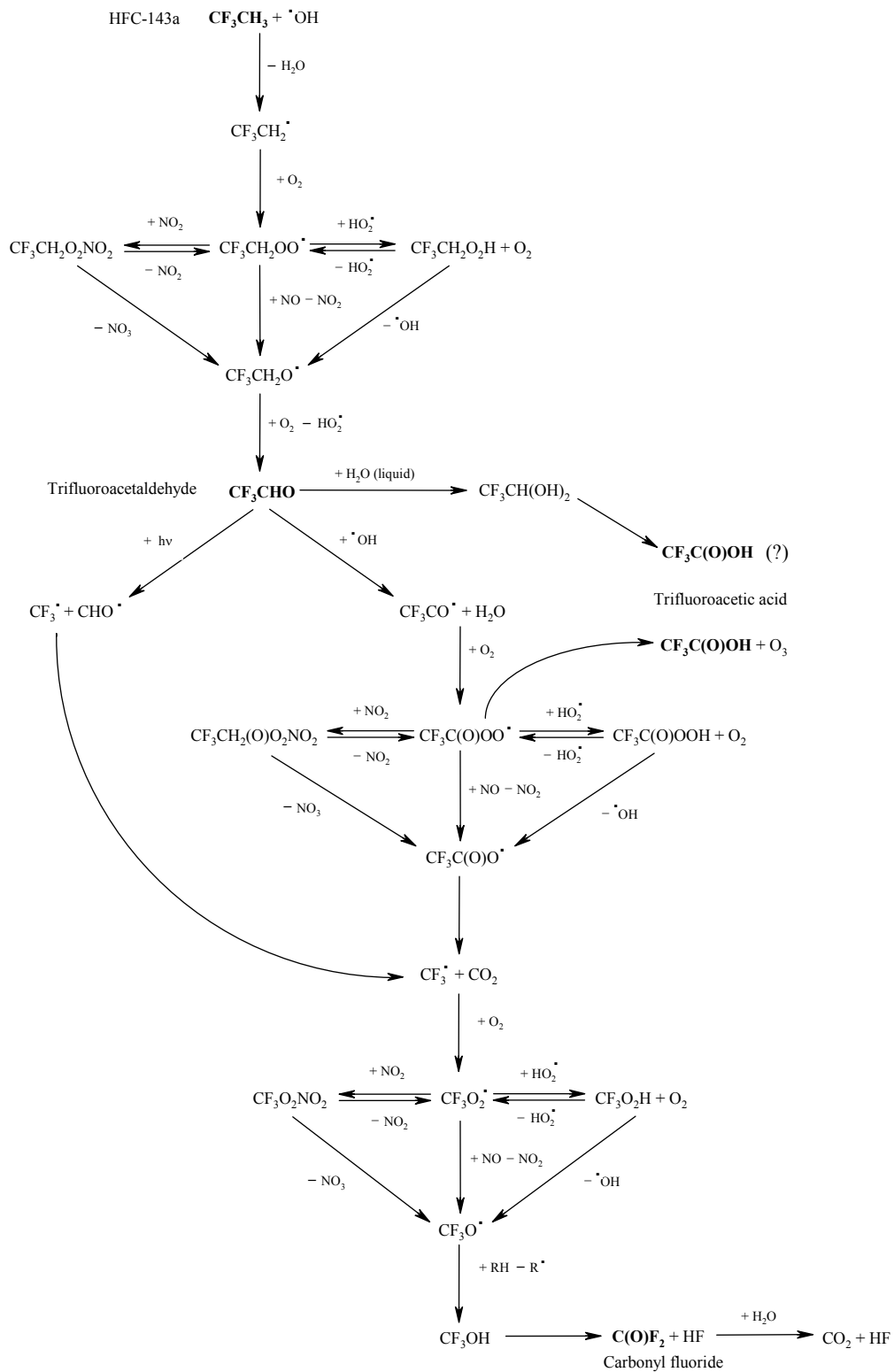
The scheme for the atmospheric degradation pathway for HFC-143a is reported in Figure 1. Following hydrogen abstraction, due to reaction of HFC-143a with OH radicals, trifluoroacetaldehyde (CF₃CHO) is formed as a stable intermediate. This molecule can be subjected to two different processes, photolytic cleavage to form CF₃ and CHO radicals, or further reaction with OH radicals. According to recent studies, the tropospheric lifetimes are: $\tau_{\text{photol}}(\text{CF}_3\text{CHO}) > 27$ days for direct photolysis and $\tau_{\text{OH}}(\text{CF}_3\text{CHO}) \approx 26$ days for OH-mediated photolysis (Sellevåg *et al.*, 2004).

Trifluoroacetaldehyde may also be subject to uptake into cloud droplets or rain to give the hydrate CF₃CH(OH)₂, which may possibly be subsequently oxidised to trifluoroacetic acid

[CF₃C(O)OH] in the aqueous phase. The uptake of water-soluble species such as trifluoroacetaldehyde into cloud droplets and their subsequent deposition in precipitation is estimated to require a minimum of a few days. For example, using a general circulation model, Giorgi and Chameides (1986) derived wet deposition lifetimes of 2 to 3 days for such substances emitted from ground level and 15 to 20 days for such species formed uniformly in the bottom 10 km of the atmosphere. The latter case would apply to products formed in the atmospheric degradation of HFC-143a on account of the long atmospheric lifetime and consequently thorough vertical mixing of this compound in the troposphere.

In principle, trifluoroacetic acid can also be formed by means of the reaction between the peroxyradical CF₃C(O)OO and the radical HO₂. According to Franklin (1993), the probable fate of the CF₃O radical is the conversion to trifluoromethanol (CF₃OH) and the possible decomposition, via carbonyl fluoride [C(O)F₂], leading to CO₂ and HF as final products.

Figure 1: Atmospheric degradation pathway for HFC-143a^a
 (adapted from Sidebottom, 1993; Nielsen and Wallington, 1993; Nielsen *et al*, 1994)



^a O₃, NO, NO₂ and NO₃, free radicals.

Stratospheric ozone depletion

Due to the absence of chlorine and bromine atoms, HFC-143a has no potential for stratospheric ozone depletion.

Global warming potential

Global warming potential (GWP) is a measure of the relative radiative effect of a given substance compared to CO₂, integrated over a chosen time horizon. It indicates the relative global warming contribution of an emission of 1 kg of a given compound in the atmosphere.

Global warming potential values of 5,540, 4,400 and 1,600, based on a lifetime of 52 years for time horizons of 20, 100 and 500 years, respectively, were calculated for HFC-143a (WMO, 2002; IPCC, 2001). The official 100-year GWP mentioned in the Kyoto Protocol is 3,800 (IPCC, 1996).

4.3.2 Aquatic fate

No studies for abiotic degradation in water of HFC-143a are available. HFC-143a is a gas at ambient conditions and its environmental distribution into the water compartment is considered negligible.

4.3.3 Terrestrial fate

HFC-143a is a gas at ambient conditions with a low log K_{ow} value. Its environmental distribution into the soil compartment is considered negligible.

5. ENVIRONMENTAL LEVELS AND HUMAN EXPOSURE

5.1 Environmental levels

Background levels of HFC-143a were analysed by means of high-resolution GC and mass spectrometry in air samples collected at Cape Meares, Oregon (from 1978 to 1997), Point Barrow, Alaska (from 1995 to 1998) and Palmer Station, Antarctica (from 1991 to 1997). The annual average concentrations of HFC-143a measured at Cape Meares increased linearly from about 0.2 ppt to 0.7 ppt during the period 1978 to 1992. This represents a rise of nearly 0.04 ppt/year. Between 1992 and 1997, the increase was faster at approximately 0.24 ppt/year. In 1997, the level reached 1.9 ppt. Similar trends were measured in 1997 in Alaska (1.7 ppt) and in Antarctica (1.3 ppt). Concentrations in Alaska were systematically higher than in Antarctica, indicative of a higher environmental release occurring in the northern hemisphere (Culbertson *et al*, 2004). In 2003, an atmospheric concentration of 3.3 ppt was measured in Cape Grim, Tasmania, indicating a further increase in the annual growth rate, estimated at 0.5 ppt/year between 2001 and 2003 (IPCC, 2005b).

5.2 Human exposure levels and hygiene standards

5.2.1 Non-occupational exposure

Consumer exposure has not been measured directly.

5.2.2 Occupational exposure

No published sources of industrial hygiene monitoring data are available.

5.2.3 Hygiene standards

The American Industrial Hygiene Association's Workplace Environmental Exposure Level (WEEL) Committee has assigned HFC-143a an occupational exposure limit of 1,000 ppm (3,433 mg/m³) as an 8-hour time-weighted-average concentration. This is the highest level given for substances of very low toxicity. It is based on the good house-keeping principle that exposures to all substances except CO₂ should be maintained at or below 1,000 ppm (AIHA, 1996).

6. EFFECTS ON ORGANISMS IN THE ENVIRONMENT

No environmental toxicity studies are available for HFC-143a. Ecotoxicity values were calculated by means of the ECOSAR programme (US-EPA, 2003; CoR 2f) (Table 3).

Table 3: Predicted acute toxicity to aquatic organisms

Organism	Duration (h)	Effect	Concentration (mg/l) at 25°C
Fish	96	LC ₅₀	109
<i>Daphnia</i>	48	LC ₅₀	115
Green <i>algae</i>	96	EC ₅₀	71

Furthermore, a low aquatic toxicity may be expected for HFC-143a in view of the test results obtained with the structural analogue HFC-134a (ECETOC, 2006).

7. KINETICS AND METABOLISM

7.1 Studies in humans

Nine male human volunteers were exposed to 500 ppm HFC-143a (1,720 mg/m³) for 2 hours during light physical exercise in an exposure chamber. Blood, urine and exhaled air were collected before, during and up to 2 days after the exposure period.

The presence of HFC-143a in biological samples was analysed by means of head-space GC. Trifluoroacetic acid and fluoride in urine were analysed using high performance liquid chromatography and a selective ion electrode, respectively.

The study results showed a low metabolic rate and a low solubility in blood for HFC-143a. Rapid but low uptake was observed in the blood of exposed volunteers. A plateau blood concentration of about 1.4 ppm HFC-143a (1.4 µg/g) was measured. Two elimination phases were observed with half times of about 4 and 300 minutes. Increased concentration of fluoride was detected in urine of 2 volunteers (Gunnare *et al*, 2003; CoR 4a).

7.2 Studies in animals

The metabolism of HFC-143a was studied in Crl:CD BR rats (3 males/group) exposed to 100, 390, 1,040, 2,050 and 4,800 ppm HFC-143a (343, 1,340, 3,570, 7,040, 16,500 mg/m³) for 4 to 5 hours. The HFC-143a concentration was measured by GC every 10 minutes. At the same time, partition coefficients of HFC-143a between air and blood, fat, liver and muscle were measured with the method described by Gargas *et al* (1989 cited by Keller, 1994). The rate of absorption and the measured partition coefficient were analysed with a physiologically-based pharmacokinetic (PBPK) model. Detection of metabolites was performed by exposing rats to 40,000 ppm HFC-143a (137,000 mg/m³) for 4 hours and collecting the urine overnight after the exposure period. Urine samples of exposed animals were analysed with ¹⁹F-nuclear magnetic resonance spectroscopy.

The results showed a low absorption of HFC-143a into the blood and a poor solubility in tissues. PBPK model calculations indicated that HFC-143a is rapidly cleared from the blood and that accumulation in tissues is unlikely. The study of metabolism showed that HFC-143a is slowly metabolised in rats. The major metabolite identified in rats exposed to 40,000 ppm HFC-143a was trifluoroethanol (TFE). Glucuronide conjugate to TFE, trifluoroacetic acid, trifluoroacetaldehyde and the urea conjugate of trifluoroacetaldehyde were also identified as minor metabolites. Only low traces of TFE were measured in the urine samples of rats exposed to 4,800 ppm or below (Keller, 1994; CoR 2e).

A correlation study between pharmacokinetic behaviour and physico-chemical properties of a series of trihaloethanes was carried out. Male Wistar albino rats (4 - 6/group) were individually exposed by inhalation to 5,500; 10,000; 16,000; 20,000 and 30,000 ppm HFC-143a (18,900; 34,300; 54,900; 68,700; 103,000 mg/m³) for 4 hours. The concentrations of the tested substances in the exposure chamber were monitored by GC. The amount of chemical retained in the body was calculated from measurements of the final concentration in the chamber during the exposure period. A PBPK model was used to calculate the kinetic parameters of absorption and metabolism of the administered substances. HFC-143a showed the lowest absorption and metabolic rates in comparison with the other tested trihaloethanes (trichloroethane, dichloro-fluoroethane and chloro-difluoroethane). A significant decrease in glutathione concentration was observed in the liver of rats exposed to concentrations $\geq 10,000$ ppm HFC-143a. According to the authors, this effect may be related to the uncoupling effect of halogenated ethanes on cytochrome P450 function (Loizou *et al*, 1996; CoR 2e).

8. EFFECTS ON EXPERIMENTAL ANIMALS AND *IN VITRO* SYSTEMS

8.1 *Single exposure*

8.1.1 Acute inhalation

When male Crl:CD BR rats were exposed nose-only to concentrations of up to 540,000 ppm HFC-143a for 4 hours, there were no deaths during the exposure or during the 14-day recovery period. Exposed animals showed weight loss on the day following the exposure, but a normal weight gain was recorded for all animals during the recovery period (Du Pont, 1990; CoR 1a).

When Sprague-Dawley rats were exposed whole-body to 300,000 or 600,000 ppm HFC-143a for 4 hours, no mortality was observed at either concentration. Changes in respiratory pattern were observed for one male and one female exposed at 300,000 ppm and for one female exposed at 600,000 ppm. Peripheral vasodilatation was observed for one male and 4 females exposed at 600,000 ppm. No treatment-related clinical signs were recorded during the observation period. Macroscopic pathology and organ weight examinations did not reveal any treatment-related effect. The 4-hour LC₅₀ was greater than 600,000 ppm (Cracknell, 1992).

Details of the available acute toxicity studies with HFC-143a are summarised in Table 4.

8.1.2 Other acute toxicity studies

Cardiac sensitisation potential of HFC-143a was studied in Beagle dogs. The experimental design of this study consisted of 2 stages. Initially, 9 animals were tested for the individual responsiveness to adrenaline administration, to assess the adrenaline dose necessary to evoke a minimal but clear cardiac effect recorded by means of an electrocardiogram (up to approximately 10 ectopic beats). Six dogs were selected from the available 9 for the second stage. In order to consider the individual variability, one animal with a maximal response and one with a minimal response to adrenaline were included in the test group.

The tested animals were then exposed to 50,000; 100,000; 150,000; 200,000; 250,000 and 300,000 ppm HFC-143a (172,000; 343,000; 515,000; 687,000; 858,000 mg/m³) for 5 minutes by inhalation, according to the experimental procedure shown in Table 5.

Adrenaline was administered intravenously before and during the exposure. Electro-cardiograms were recorded continuously during the experiment. Ventricular fibrillation and multifocal ventricular ectopic beats were considered clear positive responses.

Table 4: Acute toxicity in rats

Strain/ Number and sex/group	Concentration tested (ppm) (mg/m ³)	Time (h)	LC ₅₀ (ppm) (mg/m ³)	Remark	Reference	CoR
CrI:CD BR						
6 M	0; 97,000; 540,000	4	> 540,000 (> 1,850,000)	No lethality. Loss of body weight on the day following the exposure	Du Pont, 1990; Brock <i>et al</i> , 1996	1a
Sprague-Dawley						
5 M, 5 F	0; 300,000; 600,000	4	> 600,000 (> 2,060,000)	No lethality. Increased respiratory depth observed at 300,000 and 600,000 ppm. Peripheral vasodilatation at 600,000 ppm	Cracknell, 1992	1a

Table 5: Experimental procedure (Hardy, 1993)

Time (minutes)	Event
0	Start electrocardiogram recording
2	First adrenaline challenge administration
7	Start HFC-143a testing
12	Second adrenaline challenge administration
17	Stop

Animals exposed to HFC-143a up to 250,000 ppm gave all negative responses. At 300,000 ppm HFC-143a, 2 dogs out of 5 gave clear positive responses: one dog had several ectopic beats with 2 that were very close together and another had a multifocal ectopic activity followed by a period of ventricular fibrillation. The level of 250,000 ppm HFC-143a was the no-observed adverse effect level (NOAEL) (Hardy, 1993; CoR 1d; Brock *et al*, 1996; Brock *et al*, 2003).

8.1.3 Summary

No mortality was observed in two independent studies for HFC-143a up to 600,000 ppm (2,060,000 mg/m³). HFC-143a has a very low acute toxic potential by inhalation. HFC-143a induced cardiac sensitisation in dogs concurrently injected with adrenaline. The NOEC for this effect was 250,000 ppm (858,000 mg/m³).

8.2 Skin and eye irritation/skin sensitisation

Since HFC-143a is a gas at environmental temperature and atmospheric pressure, specific studies on dermal and ocular irritation or skin sensitisation were not carried out. However, no findings of irritation were observed during clinical observation in rats exposed whole-body to HFC-143a up to 40,000 ppm (137,000 mg/m³) for 90 days and there was no evidence of mucosal irritation in rats exposed nose-only to 540,000 ppm (1,850,000 mg/m³) HFC-143a for 4 hours.

8.3 Repeated exposure

Two 28-day and one 90-day inhalation studies were carried out with HFC-143a in rats. Results are summarised in Table 6.

Crl:CD BR rats were exposed (nose-only) to 0; 2,000; 10,000 and 39,000 ppm HFC-143a for 4 consecutive weeks. One animal from each exposure group died within the exposure period, but these premature deaths were not considered to be related to treatment. During the exposure period, male rats treated at 2,000; 10,000 and 39,000 ppm HFC-143a had statistically significant decreased body weights and body weight gains compared to controls. However, no dose-dependency was observed for this effect. There were no treatment-related effects on food consumption, clinical signs, haematology or biochemistry. Functional observational batteries carried out to assess neurotoxicological endpoints gave negative results. A slight, non-statistically significant, dose-related decrease in absolute testicular weight was recorded in exposed male rats and gross pathology examinations showed small testes in one rat at 10,000 and 2 rats at 39,000 ppm. Microscopically, degenerative changes in the testes of male rats were seen at all the exposure levels. Minimal to mild accumulation of eosinophilic debris within the lumen of seminiferous tubules, associated with decreased sperm density and increased exfoliated germ cell debris in the epididymides, were observed in affected animals. The severity of testicular and epididymal changes were similar for all dose-levels. A NOAEL was not established for this study, but the occurrence of testicular changes was attributable to confounding factors related to the method of exposure. The rats had suffered heat stress due to the design of the nose-only exposure unit (Warheit, 1991).

In order to confirm the results, a second 28-day study was carried out in Crl:CD BR rats exposed (whole-body) to 0; 2,000; 10,000 and 40,000 ppm HFC-143a. Toxicity evaluations were limited to body weight, clinical signs and pathological and histopathological examination of testes and epididymides. Under these exposure conditions all the animals survived to exposure period. There was no effect on body weights and there were no clinical signs. There were neither gross nor microscopic changes in testes or epididymides of exposed animals. Based on the results of the latter study, the NOAEL for subacute exposure is 40,000 ppm (Warheit, 1992).

Crl:CD BR rats were exposed to 0; 2,000; 10,000 and 40,000 ppm HFC-143a for 13 consecutive weeks, followed by one month of recovery after the exposure period. No compound-related effects were observed on body weights, food consumption. Three rats died or were sacrificed during the study (one control male, one male treated at 2,000 ppm and one female treated at 10,000 ppm), but these deaths were not considered to be compound-related. There were no compound-related effects on ophthalmological examination, haematology, biochemistry or urinalysis. Gross and microscopic pathology examinations did not give any treatment-related findings. Hepatic beta-oxidation activity was similar to control for all exposure concentrations. The NOAEL for this study was considered to be 40,000 ppm (Malley, 1993; Brock *et al*, 1996).

Table 6: Repeated dose toxicity in Crl:CD BR rats

Number and sex/group	Exposure regime and duration	Concentration ^a		Result and remarks	Reference	CoR
		(ppm)	(mg/m ³)			
10 M, 10 F	6 h/d, 5 d/wk, 4 wk, nose-only	0; 2,000; 10,000; 39,000	(0; 6,870; 34,300; 134,000)	One animal/group died during exposure period. Decreased body weight for males of all treated groups. No clinical signs, effects on haematology, blood chemistry or urinalysis. Negative results in functional observational batteries. Dose-related decrease in absolute testicular weights in exposed males. Small testes in one and 2 males at 10,000 and 39,000 ppm, respectively. Degenerative changes in the testes of male rats at all dose levels. NOAEL was not established.	Warheit, 1991; Brock <i>et al</i> , 1996	3b
10 M	6 h/d, 5 d/wk, 4 wk, whole-body	0; 2,000; 10,000; 40,000	(0; 6,870; 34,300; 137,000)	No mortality. No effects on body weight, no adverse clinical signs. Gross pathology and histopathology limited to testes and epididymides. No changes related to exposure were observed in any group. NOAEL = 40,000 ppm.	Warheit, 1992; Brock <i>et al</i> , 1996	1a
20 M, 20 F	6 h/d, 5 d/wk, 13 wk, whole-body + 4 wk recovery	0; 2,000; 10,000; 40,000	(0; 6,870; 34,300; 137,000)	3 rats died during the study. Deaths were not related to treatment. No effects on body weights or food consumption, no clinical signs. No effects on ophthalmological examinations, haematology, biochemistry or urinalysis. No changes in gross pathology or histology. No proliferation of hepatic peroxisomes. NOAEL = 40,000 ppm.	Malley, 1993; Brock <i>et al</i> , 1996	1a

8.3.1 Summary

Effects of repeated exposure to HFC-143a were evaluated in three studies. A non-statistically significant decrease of testicular weight, accompanied with microscopical changes in testicles of males of all exposure groups, was observed in the first 28-day inhalation study. This effect was judged by the authors to be caused by external confounding factors and not treatment-related. A second subacute study, limited to pathologic examinations of male gonads, did not show any effect related to HFC-143a exposure.

The low toxicity of HFC-143a following repeated inhalation was further confirmed by the 13-week inhalation study. No adverse effects were observed in this study at concentrations up to 40,000 ppm HFC-143a (137,000 mg/m³).

8.4 Genotoxicity

Results of genotoxicity tests carried out for HFC-143a are summarised in Table 7.

Table 7: Genotoxicity tests

Endpoint / Organism	Strain / Target cells	Exposure time (h)	Nominal concentration		Result	Remark	Reference	CoR
			(ppm)	(mg/m ³)				
Gene mutation <i>in vitro</i>								
<i>Salmonella typhimurium</i>	TA1535,	48	0; 100,000;	(0; 343,000;	Negative	With and without metabolic activation	May, 1993; Brock <i>et al.</i> , 1996	1a
	TA1537,		300,000;	1,030,000;				
	TA1538, TA98		500,000;	1,720,000;				
	and TA100		700,000;	2,400,000;				
		900,000	3,090,000)					
<i>Escherichia coli</i>	WP2 <i>uvrA</i>	48	0; 100,000;	(0; 343,000;	Negative	With and without metabolic activation	May, 1993; Brock <i>et al.</i> , 1996	1a
			300,000;	1,030,000;				
			500,000;	1,720,000;				
			700,000;	2,400,000;				
		900,000	3,090,000)					
<i>S. typhimurium</i>	TA1535, TA97, TA98 and TA100	48	0; 5,000;	(0; 17,200;	Negative	With and without metabolic activation	Bentley, 1994a; Brock <i>et al.</i> , 1996	1a
			15,000; 25,000;	51,500; 85,800;				
			35,000	120,000)				
<i>E. coli</i>	WP2 <i>uvrA</i>	48	0; 5,000;	(0; 17,200;	Negative	With and without metabolic activation	Bentley, 1994a; Brock <i>et al.</i> , 1996	1a
			15,000; 25,000;	51,500; 85,800;				
			35,000	120,000)				

Table 7: Genotoxicity tests (cont'd)

Endpoint / Organism	Strain / Target cells	Exposure time (h)	Nominal concentration (ppm)	Nominal concentration (mg/m ³)	Result	Remark	Reference	CoR
<i>S. typhimurium</i>	TA100 and TA1535	48	0; 500,000	(0; 1,720,000)	Positive	With and without metabolic activation	Longstaff <i>et al</i> , 1984	2e
Cell transformation <i>in vitro</i>								
Baby hamster kidney fibroblast	Cell line BHK21	Not stated	Not stated		Negative	Styles assay, with metabolic activation	Longstaff <i>et al</i> , 1984	2e
Chromosome aberration <i>in vitro</i>								
Human lymphocyte		3	0; 5,000; 150,000; 250,000; 350,000	(0; 17,200; 51,500; 85,800; 120,000)	Negative	With and without metabolic activation	Bentley, 1994b; Brock <i>et al</i> , 1996	1a
Micronucleus frequency <i>in vivo</i>								
Mouse	CrI:CD-BR, bone marrow	6 h/d, 2 d	0; 2,000; 10,000; 40,000	(0; 6,870; 34,300; 137,000)	Negative		Reynolds, 1993; Brock <i>et al</i> , 1996	1a

8.4.1 *In vitro*

Mutagenic potential of HFC-143a was assessed in two independent bacterial back-mutation assays.

Five histidine-dependent strains of *Salmonella typhimurium* (TA1535, TA1537, TA1538, TA98 and TA100) and one tryptophan-dependent strain of *Escherichia coli* (WP2 uvrA) were exposed to HFC-143a concentrations of up to 90% in air, either in the presence or in the absence of a metabolic activator derived from rat liver (S9 mix). No increases in reversion to prototrophy were observed in any bacterial strain following exposure to HFC-143a. Negative results were observed also with 100% HFC-143a, a concentration tested in a first experiment only in the absence of S9 mix. However, due to the difficulties experienced in generating a 100% concentration, further testing was carried out using 90% as maximal concentration (May, 1993; Brock *et al*, 1996).

In a similar study, four strains of *Salmonella typhimurium* (TA1535, TA97, TA98 and TA100) and one of *Escherichia coli* (WP2 uvrA) were exposed to HFC-143a (up to 3.5%) for 48 hours (Bentley, 1994a), in the presence or in the absence of S9 mix. The maximum concentration tested in the test was selected on the ground of explosive potential. No evidence of mutagenic effects was detected in this study.

Longstaff *et al* (1984) studied the predictivity of short-term *in vitro* tests for assessment of carcinogenicity potential of a series of chlorofluoro- and fluoro-alkanes. HFC-143a (50%) gave positive results in Ames test carried out in two strains of *Salmonella typhimurium* (TA1535 and TA100), but HFC-143a was not mutagenic in a cell transformation assay (Styles, 1977), carried out in baby hamster kidney fibroblast (BHK21) cell line.

Despite the controversial results obtained in Longstaff's study, the overall results indicate that HFC-143a can be considered not mutagenic in *in vitro* assays.

Chromosome aberration was studied in *in vitro* human lymphocytes assay by Bentley (1994b; Brock *et al*, 1996). Cells were exposed to HFC-143a up to 3.5% for 3 hours with and without S9 mix. Clastogenic activity was evaluated at 20 and 43 hours after exposure to HFC-143a. No statistically significant increase in the number of chromosomal aberrations was detected at any concentration tested, either in the presence or in the absence of metabolic activation.

HFC-143a did not show clastogenic potential under these test conditions.

8.4.2 *In vivo*

No statistically significant increase in micronucleated polychromatic erythrocytes was observed in male or female mice exposed to 0; 2,000; 10,000 or 40,000 ppm for 2 days. Furthermore, no significant depression of polychromatic erythrocytes among 1,000 red blood cell counts was observed in the treated groups (Reynolds, 1993; Brock *et al*, 1996) (Table 7).

Due to the low flammability limit of HFC-143a, no other *in vivo* tests were carried out.

8.4.3 Summary

HFC-143a did not induce mutations in two Ames tests carried out in several strains of *S. typhimurium* and one strain of *E. coli* with and without metabolic activation. It was mutagenic in the limited Ames test carried out by Longstaff *et al* (1984), but gave negative results in Styles assay (Styles, 1977) carried out in mammalian cell line BHK21. A chromosomal aberration test in human lymphocytes gave negative results. HFC-143a was also negative in a mouse micronucleus assay with mice receiving two consecutive daily 6-hour exposures at 40,000 ppm.

8.5 Long-term exposure

No data are available for inhalation.

Longstaff *et al* (1984; CoR 2e) carried out a limited chronic study for a series of chlorofluoro- and fluoro-alkanes, including HFC-143a. Groups of 36 male and 36 female Alpk/Ap (Wistar derived) rats were exposed for 52 weeks to the test compounds. Each chemical was administered in single daily doses for one year of 300 mg/kg by gavage after solubilisation in corn oil. Parallel undosed and vehicle-dosed control groups were included in the study. Animals were held for an additional 73 weeks. There were no compound-related neoplastic or non-neoplastic lesions following oral administration of HFC-143a. Despite the methodological limitations (oral exposure, small group size, only one dose for each compound), the study indicated a clear carcinogenic response for two other compounds, chlorofluoromethane (HCFC-31) and 1-chloro-2,2,2-trifluoromethane (HCFC-133a).

8.6 Reproductive and developmental toxicity

8.6.1 Reproductive effects

No specific reproductive toxicity study was performed for HFC-143a. However, two similar compounds, HFC-134a and HFC-141b, did not show any effect in 2-generation reproduction toxicity studies (Rusch *et al*, 1995; Alexander *et al*, 1996; both CoR 1a).

Effects observed in reproductive organs of male rats exposed to HFC-143a in a 28-day inhalation study (Warheit, 1991) have to be considered as not treatment-related, since they were not reproducible in a second 28-day study (Warheit, 1992) and in a 90-day study (Malley, 1993), and were likely to have been caused by confounding factors related to the exposure method (Section 8.3).

8.6.2 Embryotoxicity and teratogenicity

A full developmental study was performed in Crl:CD BR rats (25 females/group) exposed (whole body, 6 h/d) to 0; 2,000; 10,000 and 40,000 ppm HFC-143a (6,870; 34,300 and 137,000 mg/m³) on days 7 to 16 of gestation. There were no significant findings on maternal mortality, clinical observations or gross pathology examinations. No treatment-related findings were observed in litter size, embryo-foetal loss or litter and foetal weight. No effects on the incidence of malformation were observed at any exposure level. There was a slight, but significant increase in the incidence of foetal visceral variations in the litters of all the exposed groups in comparison to the control group. However, since there was no evidence of any other developmental toxicity, the increased incidences were not dose-dependent and fell into the average of variation incidence of historical controls, and this effect was not considered biologically significant. The level of 40,000 ppm was considered to be the maternal and foetal NOAEL by the authors (Murray, 1993; Brock *et al*, 1996; CoR 1a).

An inhalation developmental toxicity study was carried out in New Zealand White rabbits (24 females/group) exposed (whole-body, 6 h/d) to 0; 2,000; 10,000 and 40,000 ppm HFC-143a (6,870; 34,300 and 137,000 mg/m³) on days 6 to 18 of gestation. One female in the 2,000 ppm group aborted on gestation day 17. No other findings were observed in adult females within the scheduled period and the abortion was judged spontaneous. No indication of developmental toxicity was present at any exposure level. Foetal malformation and variation incidences were similar among all the groups. Based on these results a NOAEL of 40,000 ppm was concluded for both maternal and foetal toxicity (Holson 1993; Brock *et al*, 1996; CoR 1a).

9. EFFECTS ON HUMANS

Nine male volunteers were exposed to 500 ppm HFC-143a (1,720 mg/m³) for 2 hours for a human toxicokinetic study (Section 7.1). The electrocardiogram of the exposed volunteers was monitored during and until 20 hours after exposure. Irritative and central nervous system symptoms were rated in a questionnaire prior to, during and after the exposure. The authors stated that preliminary analyses suggested no increases in symptoms ratings during or after exposure (Gunnare *et al*, 2003; CoR 4a).

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APPENDIX A: CRITERIA FOR RELIABILITY CATEGORIES

Adapted from Klimisch *et al* (1997)

Code of Reliability (CoR)	Category of reliability
1	Reliable without restriction
1a	GLP guideline study (OECD, EC, EPA, FDA, etc.)
1b	Comparable to guideline study
1c	Test procedure in accordance with national standard methods (AFNOR, DIN, etc.)
1d	Test procedure in accordance with generally accepted scientific standards and described in sufficient detail
2	Reliable with restrictions
2a	Guideline study without detailed documentation
2b	Guideline study with acceptable restrictions
2c	Comparable to guideline study with acceptable restrictions
2d	Test procedure in accordance with national standard methods with acceptable restrictions
2e	Study well documented, meets generally accepted scientific principles, acceptable for assessment
2f	Accepted calculation method
2g	Data from handbook or collection of data
3	Not reliable
3a	Documentation insufficient for assessment
3b	Significant methodological deficiencies
3c	Unsuitable test system
4	Not assignable
4a	Abstract
4b	Secondary literature
4c	Original reference not yet available
4d	Original reference not translated
4e	Documentation insufficient for assessment

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 (Du Pont, 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 C₂F₆
- HFC-23 = 3 Fs, 1 H, 1 C, and 0 Cls \rightarrow CF₃H
- PFC-1216 = 6 Fs, 0 Hs, 3 Cs, 0 Cls with 1 double bond \rightarrow C₃F₆ \rightarrow CF₂ = CF-CF₃

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-C₄F₈.

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 C₂H₂F₄ can have two structural isomers:

- CF₂H-CF₂H, more symmetrical, HFC-134
- CF₃-CFH₂, 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 Letter central carbon

- a = CCl₂
- b = CClF
- c = CF₂
- d = CClH
- e = CHF
- f = CH₂

For example:

HFC-236fa = C₃F₆H₂ → Central carbon designated 'f' → CH₂ → 'a' designation → CF₃CH₂CF₃.

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. Always start 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 = CCl₃
- k = CCl₂F
- l = CClF₂
- m = CF₃
- n = CHCl₂
- o = CH₂Cl
- p = CHF₂
- q = CH₂F
- r = CHClF
- s = CH₃
- t = C
- x = CCl
- y = CF
- z = CH

Example: HFC-43-10mee = 10 Fs, 2 Hs, 5 Cs, no Cls → C₅H₂F₁₀

- m indicates CF₃ . . . CF₃
- e indicates CHF, so CF₃CHF
- e indicates CHF, so CF₃CHFCHF
- HFC-43-10mee → CF₃CHFCHF₂CF₃.

The assignment of a string of letters, to denote structural groups, is stopped when the structure is unambiguous (i.e. one does not need to call the compound HFC-43-10mee**cm**, since once one reaches 'mee', one knows that 5 fluorine atoms still need to be attached to the remaining two carbons, so the rest of the molecule must be -CF₂CF₃).

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.

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

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

where M_w = 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:

$$1 \text{ mg/m}^3 = 24.0556/M_w \text{ ppm} \dots\dots\dots(\text{Eq. C.3})$$

$$1 \text{ ppm} = M_w/24.0556 \text{ mg/m}^3 \dots\dots\dots(\text{Eq. C.4})$$

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

$$1 \text{ mg/m}^3 = 24.4661/M_w \text{ ppm} \dots\dots\dots(\text{Eq. C.5})$$

$$1 \text{ ppm} = M_w/24.4661 \text{ mg/m}^3 \dots\dots\dots(\text{Eq. C.6})$$

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