

Review

An overview of environmental hazards and exposure risk of hydrofluorocarbons (HFCs)

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Abstract

Hydrofluorocarbons (HFCs) are being used as replacements for chlorofluorocarbons (CFCs) and hydrochlorofluorocarbons (HCFCs) that cause significantly stratospheric ozone depletion and global warming. HFCs under commercial uses as cleaning solvents in the electronic components, blowing agent in the foamed plastics, refrigerant in the air conditioning units and refrigerators, fire suppression agent in the fire protection, propellant in the metered dose inhalers (MDIs), and dry etching agent in the semiconductor manufacturing. Among these HFCs, 1,1,1,2-tetrafluoroethane (HFC-134a) is the most widely used one. From the environmental, ecological, and health points of view, it is urgent to mitigate and control the emissions of these HFCs from a diversity of commercial applications and industrial processes. This article aims to introduce these HFCs in commercial uses and environmental hazards (i.e., global warming, photochemical potential, flammability safety, environmental partition and ecotoxicity). Further, the updated data on the human toxicity, occupational exposure and health risk of these HFCs (esp., HFC-134a) are addressed in this review paper. © 2005 Elsevier Ltd. All rights reserved.

Keywords: Hydrofluorocarbons (HFCs); Environmental hazard; Human toxicity; Occupational exposure

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1. Introduction

Scientists recognized as early as 1974 that the rampant use of chlorofluorocarbons (CFCs) will cause the adverse impact on the dynamic equilibrium of stratospheric ozone (Molina and Rowland, 1974). The depletion of the ozone layer, shields the earth from the harmful effects of the sun's ultraviolet radiation, is caused by chlorine molecules in so-called ozone depleting substances (ODS) that are migrated to the stratosphere and then react catalytically with ozone, thus destroying it. Under a treaty known as the Montreal Protocol on Substances that Deplete the Ozone Layer which was first established in 1987 and thereafter revised several times, the CFCs, which are mainly used as refrigerants, cleaning solvents, foam-blowing agents, and aerosol propellants, are requested to phase out prior to the mid-1990s (Miller et al., 1994). Besides participating in the destruction of stratospheric ozone, the release of CFCs may also contribute to global warming, which means that CFCs influence the reflection of infrared radiation from the surface of the earth and thus causes to global climate change (Dekant, 1996; Hayman and Derwent, 1997).

Hydrochlorofluorocarbons (HCFCs) and hydrofluorocarbons (HFCs), because of their similarity to CFCs in physiochemical properties, have been used as interim replacements for CFCs. However, it should be noted that HCFCs still contain chlorine, although the release of this chlorine to the stratosphere is expected to be small due to the attenuation processes in the troposphere (Hayman and Derwent, 1997). According to the updated Montreal Protocol, a virtual phase-out of HCFCs is scheduled by 2020 (Berends et al., 1999). Currently, HFCs have been used as acceptable alternatives to CFCs and HCFCs because they possess several characteristics including near-zero ozone depletion potentials (ODP) (Ravishankara et al., 1994), similarity to CFCs and HCFCs in physical properties, short atmospheric lifetimes, less- or non-flammable, low global warming potentials (GWPs), and not expensive (Good and Francisco, 2003). However, there are some environmental hazards and health risks to be still pointed out while using HFCs. Table 1 lists chemical identifications and principal uses of common HFCs.

HFCs have high volatility and very low solubility in water. Following their releases into the environment, these compounds almost reside in the atmosphere. Tri-

Table 1
Chemical identifications and principal uses of HFCs

Compound	HFCs nomenclature	Chemical formula	CAS Registry number	Principal uses
Trifluoromethane	HFC-23	CHF ₃	75-46-7	Fire extinguisher, dry etching agent
Difluoromethane	HFC-32	CH ₂ F ₂	75-10-5	Refrigerant, dry etching agent
Pentafluoropentane	HFC-125	CHF ₂ CF ₃	354-33-6	Fire extinguisher, dry etching agent
1,1,2,2-Tetrafluoroethane	HFC-134	CHF ₂ CHF ₂	359-35-3	Refrigerant
1,1,1,2-Tetrafluoroethane	HFC-134a	CH ₂ FCF ₃	811-97-2	Refrigerant, blowing agent, aerosol inhaler, dry etching agent
1,1,1-Trifluoroethane	HFC-143a	CF ₃ CH ₃	420-46-2	Refrigerant
1,1-Difluoroethane	HFC-152a	CH ₃ CHF ₂	75-37-6	Refrigerant
1,1,1,2,3,3,3-Heptafluoropropane	HFC-227ea	CF ₃ CHFCF ₃	431-89-0	Fire extinguisher, refrigerant, aerosol inhaler
1,1,1,2,3,3-Hexafluoropropane	HFC-236ea	CHF ₂ CHFCF ₃	431-63-0	Refrigerant, blowing agent, fire extinguisher
1,1,1,3,3,3-Hexafluoropropane	HFC-236fa	CF ₃ CH ₂ CF ₃	690-39-1	Blowing agent, refrigerant
1,1,2,2,3-Pentafluoropropane	HFC-245ca	CH ₂ FCF ₂ CHF ₂	679-86-7	Blowing agent, refrigerant
1,1,1,3,3-Pentafluoropropane	HFC-245fa	CHF ₂ CH ₂ CF ₃	460-73-1	Refrigerant, blowing agent
1,1,1,3,3-Pentafluoro- <i>n</i> -butane	HFC-365mfc	CF ₃ CH ₂ CF ₂ CH ₃	406-58-6	Blowing agent
1,1,1,2,2,3,4,5,5,5-Decafluoropentane	HFC-43-10mee	CF ₃ CHFCHFCF ₂ CF ₃	138495-42-8	Solvent

fluoroacetic acid (TFA, CF_3COOH) is thus produced in the tropospheric atmosphere by the photolytic degradation of some HFCs such as HFC-134a and HFC-227ea (Tang et al., 1998). TFA, which is a strong carboxylic acid, can be irritating to tissue and skin. With respect to the safety and health factors, most of HFCs have been used as fire suppression agents or refrigerants due to their no-flammability potential at atmospheric pressure and room temperature. However, few HFCs such as HFC-32, HFC-143a and HFC-152a can form flammable mixtures with air. On the other hand, HFCs generally are less toxic than HCFCs. The Program for Alternative Fluorocarbon Toxicity Testing (PAFTT) has conducted comprehensive toxicological evaluations on common HFCs such as HFC-134a and HFC-125. Due to the low acute inhalation toxicity, the 1000 ppm exposure levels/standards of some HFCs have been established by the American Industrial Hygiene Association's Workplace Environmental Exposure Level (WEEL) and German Commission's maximum concentration at the workplace (MAK) as an 8 h Time-Weighted Average (TWA) (Rush, 2001). This paper aims to present the commercial/industrial uses, and environmental hazards (e.g., global warming, photochemical potential, flammability safety and environmental partition) of common HFCs. Further, recent studies on the toxicity, exposure and health risk of common HFCs in humans are also summarized in this review paper.

2. Commercial and industrial uses of HFCs

It has been recognized that HFCs can be acceptably used as replacements for CFCs and HCFCs because these chemicals possess many of similar physical and thermochemical properties as CFCs and HCFCs, including high volatility, low thermal conductivity, low surface tension and low-flammability. Table 1 lists the principal uses of HFCs in industries such as cleaning solvent, foaming agent, fire suppression agent and pharmaceutical propellant, which are further described as follows (Miller et al., 1994; Rydberg, 1994; Leach, 1995; Thom and Higgins, 1995; Midgley and McCulloch, 1999; Rush, 2001; Powell, 2002; Ural, 2003).

2.1. Refrigerant

Prior to 1990, the majority of domestic refrigerators, freezers and air conditioners use CFC-12 and CFC-11 as the working fluids due to their thermodynamic properties, chemical stability, non-flammability and non-toxicity. With the recognition that the productions of CFCs and HCFCs (as interim replacements for CFCs) will be totally banned and the existing appliances and equipments will ultimately need to be replaced, it is expected that HFCs will be more widely used as promising

alternative refrigerants. It is again emphasized that a significant consideration in using HFCs is that they have been targeted as important greenhouse gases (GHGs) in the Kyoto Protocol. In Taiwan, the sources of HFCs are totally from the import. In 2003, annual import of HFC-134a was close to 1500 metric tons, which is equivalent to about 95% of the total HFCs consumption. Its principal application is to be used as refrigerants for air conditioners in cars and refrigerators in electronic appliances in Taiwan (Lee, 2003). It is thus expected that its consumption will gradually increase with its more extensive applications because of its lower cost than other HFCs. As shown in Table 1, other HFCs are also used as refrigerants such as HFC-32, HFC-134, HFC-143, HFC-152a, HFC-227ea, HFC-236ea, HFC-236fa, HFC-245ca and HFC-245fa.

2.2. Cleaning solvent

In the past decade, the most common organic cleaning solvents applied in the electronic components, precision cleaning and metal finishing were chlorinated solvents (i.e., CFC-113 and 1,1,1-trichloroethane) and HCFCs (i.e., HCFC-141b and HCFC-225ca/cb). However, they were also phased out according to the Montreal Protocol (Tsai, 2002). Although there are many available methods or alternatives (incl. non-cleaning process, semi-aqueous cleaner, aqueous cleaner, supercritical fluid cleaner, plasma cleaning, mechanical cleaning etc.) for reducing or eliminating fluorocarbons in industries (Miller et al., 1994; Stone and Springer, 1995; Thom and Higgins, 1995), it is necessary to use HFCs as cleaning solvent in the some precision processes or equipments. Precision cleaning must be performed on equipment that requires a high level of cleanliness to keep the working components operating effectively. Several electronic parts, aerospace military, medical, and analytical equipments/instruments use these solvents to ensure the extreme level of cleanliness and product integrity required. Currently, the only promising HFCs in precision cleaning must be HFC-43-10mee (1,1,1,2,3,4,4,5,5,5-decafluoropentane), which has been used for replacing HCFCs (i.e., HCFC-141b and HCFC-225ca/cb).

2.3. Blowing agent

Prior to 1996, CFCs (esp. CFC-11) were widely used as blowing agents in the production of flexible and rigid foam plastics that were applied to thermal insulation and packages (Kjeldsen and Scheutz, 2003). With the implementation of the Montreal Protocol, alternatives to CFCs in the production of foam plastics are extremely urgent. Presently, HCFCs are considered as interim replacements because they possess many properties similar to those of CFCs. HCFC-22 and

HCFC-141b have, so far, been the primary substitutes for CFCs in Taiwan. Although HCFCs have been used as blowing agents instead of CFCs to produce appliances (e.g., refrigerators and freezers) insulation, they are still phased out due to the significant contribution to the greenhouse effect or global warming. It is expected that HFCs such as HFC-245fa (1,1,1,3,3-pentafluoropropane) and HFC-365mfc (1,1,1,3,3-pentafluoro-*n*-butane) will be rapidly used as available alternatives to HCFCs in the near future due to the import restriction of HCFCs from the beginning of 2004. It is also noted that some cellular foams retain most of the foaming agents during manufacturing and release them gradually over the life of the product and when the product is disposed of, or mechanically destroyed (Miller et al., 1994; Kjeldsen and Scheutz, 2003).

2.4. Fire extinguisher or fire suppression agent

In the past decades, halons have been used extensively as effective fire extinguishers in fixed, total flooding systems for protecting sensitive electrical equipments. Due to the same reasons as CFCs, the phase-out of production of halons (i.e., halon 1301 and halon 1211) under the Montreal Protocol and its amendments was effective in the developed countries on December 31, 1993. The regulation stimulated tremendous efforts to search for acceptable replacements and alternatives. There are two broad categories to be currently developed as clean fire suppression agents. One is the halocarbon compound. Among them, HFCs have been used as fire extinguishers in industries as listed in Table 1 (Di-Nenno, 2002) because they possess desirable properties in the electrical non-conductivity, ready vaporization, low toxicity, and non-flammability. Current HFCs fire suppression agents include HFC-23, HFC-125, and HFC-227ea.

2.5. Medical propellant

For many years, CFCs (i.e., CFC-11, CFC-12 and CFC-114) have been used as medical aerosols in pharmaceutical formulations in metered dose inhalers (MDIs) for the treatment of asthma and other pulmonary diseases, because they can provide very good density and vapor pressure in the aerosolization system, and also exhibit an excellent long-term safety profile and the advantage of non-flammability (Leach, 1995). With the phase-out of CFCs, the pharmaceutical industry was actively progressive to seek alternative agents. To date, some MDIs propellants have been marketed for many years. HFC-134a (1,1,1,2-tetrafluoroethane) and HFC-227ea (1,1,1,2,3,3,3-heptafluoropropane) are now used as medical aerosols in MDIs mainly based on their low acute, subchronic, and chronic toxicity (Emmen et al., 2000).

2.6. Other applications

For example, HFCs such as HFC-23, HFC-32, HFC-125 and HFC-134a has been introduced or developed to find applications in the dry etching of dielectric films and the fabrication of thin-film devices (Allgood, 1998; Misra et al., 2004).

3. Environmental hazards of HFCs

The fact that any organic chemical has the potential to impact the environments has been known for many years. HFCs, also considered as volatile organic compounds (VOCs), have extremely attractive properties, particularly high volatility and hydrophobicity compared to similar chemicals such as saturated chlorocarbons. It means that the atmosphere is the most likely fate for their accumulations of emissions. Therefore, there are to exist inherently the different environmental hazards, such as global warming, photochemical potential, flammability, partition coefficient and ecotoxicity, between them, as summarized in Table 2, which are further discussed below.

3.1. Global warming

Several anthropogenic compounds including HFCs are once emitted into the atmosphere that may cause the earth's average temperature to enhance, which is called global warming, or greenhouse effect. Therefore, HFCs are thus considered as one of six target GHGs under the Kyoto Protocol of the United Nations' Framework Convention on Climate Change (UNFCCC) in 1997 (Johnson, 1998). According to the Kyoto Protocol, governments around the world are voluntarily committed to reduce target GHGs emissions to atmosphere.

Global warming potential (GWP) expresses the relative increase in earthward IR radiation flux due to the emission of GHGs. HFCs have relative values of atmospheric lifetime and GWP (Table 2) compared to CFCs and HCFCs because these replacements contain one or more C–H bonds, which are susceptible to attack by hydroxyl radicals and hence shorter atmospheric lifetimes in the troposphere (Midgley and McCulloch, 1999; Naik et al., 2000; Wallington and Nielsen, 2002). Notably, some HFCs (i.e., HFC-23, HFC-143a and HFC-236fa) have high GWP values relative to the reference compound, carbon dioxide. Hence, it is possible at this point to selectively eliminate or reduce these HFCs emissions.

3.2. Photochemical potential

From the viewpoint of chemical structures and physical properties, HFCs belong to volatile organic compounds (VOCs), which have a high vapor pressure that

Table 2
Environmental hazards of commercial HFCs

HFCs	Atmospheric lifetime (year)	GWP ^a	Flammability (%)		log K_{ow} ^d
			LFL ^b	UFL ^c	
HFC-23	260	12000	None		0.58 (0.64)
HFC-32	5	550	12.7–33.5		0.71 (0.21)
HFC-125	29	3400	None		0.84 (1.48)
HFC-134	9.6	1100	None		0.94
HFC-134a	13.8	1300	None		0.98 (1.06)
HFC-143a	52	4300	7.0–19.0		1.03
HFC-152a	1.4	120	4.2–20.2		1.13 (0.75)
HFC-227ea	33	3500	None		1.10
HFC-236ea	10	1200	None		1.20
HFC-236fa	220	9400	None		1.24
HFC-245ca	5.9	640	7.0–14.4		1.33
HFC-245fa	7.2	950	None		1.33 (1.35)
HFC-365mfc	9.9	890	3.8–13.3		1.79 (1.61)
HFC-43-10mee	15	1500	None		1.72

^a Global warming potential with 100 year time horizon (relative to GWP of CO₂ = 1).

^b Lower flammability level in air.

^c Upper flammability level in air.

^d Octanol/water partition coefficient, estimated by Meylan & Howard method (Allen, 2002), reported data in parenthesis.

allows them to evaporate quickly. Hence, HFCs are volatile and insoluble in water. Following release into the environment, these compounds possibly reside in the lower atmosphere (i.e., troposphere) where they are photochemically oxidized into a variety of degradation products. As mentioned above, HFCs do not contain chlorine and are hence not ODS. Also, the presence of C–H bond in HFCs means that they can contribute to photochemical oxidants formation in the troposphere, in a similar manner to those of typical VOCs. It has been recognized that hydrocarbon compounds are readily liable to react with OH radical to convert them into carbonyl species, which are then removed by wet deposition via rainfall and dry deposition to the surface (Wallington et al., 1994).

With respect to the gas-phase photochemistry of HFCs, it has been well established by many researchers (Wallington et al., 1994; Hayman and Derwent, 1997; Tang et al., 1998; McCulloch, 1999; Wallington and Nielsen, 2002). As described above, HFC-134a (CF₃CFH₂) is the most widely used HFCs, its atmospheric oxidation mechanism is mainly initiated by reaction with OH radicals. The alkoxy radical derived from HFC-134a, CF₃CFHO, is further decomposed via two pathways: one is to react with O₂. It has been shown that this reaction produces CF₃COF, which is preferably dominated by incorporation into cloud water followed by rapid hydrolysis to trifluoroacetic acid (TFA). The other is to be thermally decomposed via C–C bond scission, giving CF₃ radicals and HCOF. The CF₃ radicals further react with O₂/NO and/or hydrolysis in droplets to finally form degradation products COF₂, HF, CO₂ and CF₃OH. The HCOF can incorporate into droplets

to give formic acid (HCOOH) and HF. Among these degradation products, although TFA is produced in aqueous-phase droplets, the evaporation of cloud droplets can transfer it to the gas phase. Noticeably, TFA is a strong organic acid with a pK_a of 0.23 and relatively high vapor pressure (Tang et al., 1998). TFA is miscible with water with solubility over 10000 g/dm³, and was also shown to be acutely toxic to biosystem (Tang et al., 1998; Hanson et al., 2002). Its partition coefficient *n*-octanol/water (log) is –0.2, indicating that the bioaccumulation in animals (e.g., fish) is unlikely. In addition, that carbonyl fluoride (COF₂) is a powerful irritating gas. The carbonyl fluoride is easily hydrolyzed to form hydrogen fluoride, which is moderately toxic to human by inhalation due to the release of fluoride ions in contact with moist body tissues. Unfortunately, there are no available data on the atmospheric concentrations of the degradation product.

It has been shown that photochemical smog, which is a complex atmospheric pollutant mixture consisting of ozone, aldehydes, peroxyacyl nitrates, nitrogen dioxide and fine particulates, can cause burning eyes, throat irritation, and difficulty in breathing in many people, especially children and the elderly. Although HFCs are chemically classified as VOCs, they are not legally regulated as VOCs. According to the U.S. EPA's definition in the federal register (FR), "VOC means any compound of carbon, excluding carbon monoxide, carbon dioxide, carbonic acid, metallic carbides or carbonates, and ammonium carbonate, which participates in atmospheric photochemical reactions" (Zysman and Skelly, 2000). The regulation was then established based on the atmospheric lifetimes of organic compounds

compared to reference compound (i.e., ethane), it would be regarded as a VOC-exempt compound. These compounds could be further announced to have negligible photochemical reactivity in FR and formally listed in the code of federal register (CFR) (i.e., 40 CFR 51.100). Fortunately, HFCs listed in Table 1 are on the VOC-exempt lists (Zysman and Skelly, 2000).

3.3. Flammability

Flammability limits in air at room temperature and atmospheric pressure are the terms used to describe the well-specified range of compositions in which organic vapor-air mixtures will burn or combust with a flame or ignition (Crowl and Louvar, 2002). From the view of occupational and environmental safety, this safety feature must be considered to be non-flammable or low flammable nature while using these HFCs in industries. Table 2 also shows that most of HFCs have non-flammable properties except HFC-32, HFC-143a, HFC-152a and HFC-365mfc (Richard and Shankland, 1992; Dekleva et al., 1993; Wilson and Richard, 2002; Ural, 2003). However, it is noted that HFC-152a having the flammability limits of 4.2–20.2% can be considered as one of the most flammable CFC replacements. Also, although most of HFCs possess low- and no-flammability potential at atmospheric pressure and room temperature, these substances can form high- or low-flammability potential with air at increased temperature and pressure (Ural, 2003).

3.4. Partition coefficient

Partition coefficient is empirically derived dimensionless property that describes how a chemical substance distributes itself between two phases. Hence, it is useful for describing and modeling the environmental fate of an organic compound. Because the octanol–water partition coefficient (K_{ow}) characterizes partitioning between aqueous and organic, lipid-like phases, it provides a significant indication of how much of an organic compound will be taken up by aquatic organisms. Due to values of K_{ow} ranging from 10^{-3} to 10^7 , values for K_{ow} are often reported as $\log K_{ow}$ (Lyman et al., 1985). Generally, organic compounds with high values of K_{ow} tend to be hydrophobic and partition to organic matter, lipids (fat) and soil. Thus they are less mobile in the environment. Further, the coefficient can be applied in estimating other partition coefficients such as bioconcentration factor (BCF), organic carbon partition coefficient (K_{oc}) and water solubility (Lyman et al., 1985; Allen, 2002).

Table 2 lists the estimated values of $\log K_{ow}$ for common HFCs (Rush, 2001). The reported values of $\log K_{ow}$ for some HFCs, which are compiled from the manufacturers' material safety data sheets and available refer-

ences (Howard, 1993; Rush, 2001), are also shown in Table 2. It is well known that several methods are available for the estimation of K_{ow} for organic chemicals (Lyman et al., 1985). However, these approaches are somewhat complicated and not easy to use them. In the present paper, a simple group contribution method, or Meylan & Howard method was used for estimating the partition coefficient of HFCs as follows (Meylan and Howard, 1995).

$$\log K_{ow} = 0.229 + \sum n_i f_i$$

where $\log K_{ow}$ is the base 10 logarithm of the ratio the chemical's concentration in octanol to the chemical's concentration in water, n_i is the number of groups of type i in the molecule, f_i is the contribution of each group to the partition coefficient, and the summation is taken over all groups. For example, HFC-134a has the molecular structure $\text{CH}_2\text{F}-\text{CF}_3$. Referring to the contribution groups in the method, this compound can be represented by one $-\text{CH}_2-$ group, one $>\text{C}<$ group and four $-\text{F}$ (aliphatic attachment) groups. The estimated value of $\log K_{ow}$ is thus given by:

$$\log K_{ow} = 0.229 + 0.4911 + 0.2676 + 4(-0.0031) = 0.98$$

The reported value for $\log K_{ow}$ is 1.06 (Rush, 2001), so the predicted value of K_{ow} is in error by 17.0%. From the predicted data in Table 2, it can be summarized that the values of $\log K_{ow}$ for HFCs are below 3.5, showing that these fluorocarbons have very low potential bioaccumulation in the environment (Allen, 2002).

3.5. Biotoxicity

On first insight, most of HFCs are gases and have very low solubility in water at room temperature; therefore, they are unlikely to remain in water. Generally, HFCs are chemically safe compound in the environment. Based on the data of octanol/water partition coefficient described above, and the results of closed-battle tests (Berends et al., 1999), these HFCs (i.e., HFC-32, HFC-125 and HFC-134a) are considered not tardily biodegradable. With respect to the ecotoxicity of these HFCs, it was also revealed to be not very toxic to aquatic organisms (i.e., algae, water fleas, and fish) and terrestrial plants. For example, HFC-134a, which is the most used HFCs, shows a very low toxicity towards aquatic species such as bacterium (*P. putida*), water flea (*D. magna*) and rainbow trout (*O. mykiss*) (Berends et al., 1999). In addition, from the view of the effect on air quality, HFCs discussed in this article have been listed as having "negligible photochemical reactivity", and do not contribute to smog formation and ground-level ozone (Zysman and Skelly, 2000). Therefore, they are exempt from VOC regulation according to U.S. Clean Air Act Amendments of 1990. However, some

HFCs (e.g., HFC-134a) have shown to form trifluoroacetic acid (TFA) in the tropospheric atmosphere by various degradation pathways. Although no significant effects on aqueous species, terrestrial plants and mammals have been identified from TFA, it has anticipated that no significant environmental risk is derived from the product of atmospheric degradation from HFCs (Tang et al., 1998).

4. Human toxicity and exposure hazards

Due to their physiochemical properties of HFCs, there is only a low potential for human toxicity from the results of mammalian (i.e., rat) tests and no significant health risk is expected (Dekant, 1996). There are no observable evidences to support the assumption of carcinogenic, genetic, reproductive and developmental effects of HFCs in humans (Rush, 2001; Mitchell et al., 2004). Briefly, the biotransformation of HFCs has been shown to undergo cytochrome P450-catalyzed oxidation or reduction reactions. The formed acyl halides are further hydrolyzed to give excretable trifluoroacetic acid (i.e., TFA) in urine (Monte et al., 1994; Dekant, 1996). Evidently, it can be seen that many of HFCs are not highly toxic to human at air exposure levels up to few percent or even over 10% (Rush, 2001). The most significant response under the overexposure circumstances is central nervous system (CNS) depression and/or cardiac sensitization related to the anesthetic properties of HFCs.

Based on the uses of some HFCs in metered-dose inhalers (MDI) and fire suppression applications, the human toxicity of HFCs has been evaluated by many industrial, pharmaceutical, and governmental organizations (Alexander and Libretto, 1995; Leach, 1995), such as the Program for Alternative Fluorocarbon Toxicology Testing (PAFTT), the International Pharmaceutical Aerosol Consortium for Toxicity Testing (IPACTI) and the Significant New Alternatives Policy (SNAP) program of Environmental Protection Agency (USEPA). Because the risk to HFCs from exposure is generally discharges in high concentrations over short periods of time that occur infrequently, chronic effects are not the usual concern. Accordingly, the acute inhalation toxicity data associated with exposure to HFCs, such as cardiotoxicity, are (1) no observed adverse effect level (NOAEL), (2) lowest observed adverse effect level (LOAEL), and (3) lethal concentration (LC₅₀) or approximate lethal concentration (ALC). Table 3 summarizes NOAEL, LOAEL, and LC₅₀ or ALC values, which are also compiled from the manufactures' material safety data sheets and available references (Brock et al., 1996; Brock et al., 2000; Vinegar et al., 2000; DiNenno, 2002). Thus, the exposure limits or approximate lethal concentrations of these HFCs are expected to be set at high-level values, shown in Table 3. It is obvious from Table 3 that the 1000 ppm as an 8 h time-weighted average (TWA) for most of HFCs has recommended as exposure level or exposure guidance level by the American Industrial Hygiene Association's Workplace Environmental Exposure Level (WEEL)

Table 3
Exposure level/limit and toxicity data for some HFCs

HFCs	Exposure level/limit (ppm)	NOAEL (v/v%) ^a	LOAEL (v/v%) ^b	LC ₅₀ or ALC (v/v%) ^c
HFC-23	NA ^d	50	50	66.3
HFC-32	1000 ^c	NA ^d	NA ^d	52
HFC-125	1000 ^c	7.5	10.0	80
HFC-134a	1000 ^{e,f}	NA ^d	NA ^d	50
HFC-143a	1000 ^c	NA ^d	NA ^d	54
HFC-152a	1000 ^c	NA ^d	NA ^d	38.3
HFC-227ea	1000 ^g	9.0	10.5	78.9
HFC-236ea	NA ^d	NA ^d	NA ^d	8.5
HFC-236fa	1000 ^c	NA ^d	15.0	45.7
HFC-245fa	300 ^c	NA ^d	NA ^d	20.0
HFC-365mfc	NA ^d	NA ^d	NA ^d	10
HFC-43-10mee	200 ^g	NA ^d	NA ^d	1.1

^a No observed adverse effect level.

^b Lowest observed adverse effect level.

^c The concentration lethal to 50 percent of a population (rat) by 4 h inhalation; ALC: approximate lethal concentration.

^d No available data.

^e American Industrial Hygiene Association (AIHA) Workplace Environmental Exposure Limits (WEEL) based on 8 h time-weighted average.

^f Maximum workplace concentration (MAK) (DFG, Germany).

^g Acceptable exposure limit (AEL) (DuPont Co., USA).

(American Industrial Hygiene Association, 2000). However, there is a noticeable feature in the case of HFC-134a, that the German MAK Commission has adopted 1000 ppm as an 8 h TWA exposure limit.

Human exposure to HFCs may occur via inhalation from accidental leaks and/or spills from the refrigeration system, recycling system for electronic appliances, degreasing process for precision cleaning, gas delivery pipeline of the semiconductor manufacturing or medical delivery system for treatment of asthma. With respect to human risk hazards to overexposure of HFCs, there are to exist scarce cases in literatures. In the study by Gjolstad et al. (2003), it was found that the highest measured concentrations of HFC-134a, HFC-125 and HFC-143a during refrigeration repair work were 1448 mg/m³ (348 ppm), 5891 mg/m³ (1203 ppm) and 4950 mg/m³ (1444 ppm), respectively, showing that the occupational exposure to HFCs is moderate and can be considerable during the short exposure periods (i.e., up to approximately 20 min). It should be noted that the repair works could involve welding operations and possibly cause the occupational exposure to decomposition toxic products including hydrogen fluoride (HF), carbon monoxide (CO) and carbonyl fluoride (COF₂). In the study by Kjeldsen and Scheutz (2003), the blowing agent (e.g., HFC-245fa) for insulating foam used in home appliances could suddenly release during the shredding operations for recycling. In order to prevent the fluorocarbons from emitting to the workplace atmosphere and reduce the exposure risk, the blowing agent in the foaming insulation materials shall be recycled with the refrigerant freezing system or adsorption equipment during the shredding of scrap refrigerator.

5. Conclusions

Though HFCs discussed in this review paper have been exempted from U.S. EPA's definition of volatile organic compounds (VOCs) due to their negligible effects on photochemical smog contribution, these chemicals still possess some environmental hazards, including global warming, flammability hazard, adverse effect of exposure, and ecotoxicity. The Kyoto Protocol has further agreed to call for a voluntary reduction on the production and emission of these HCFCs and halon replacements by 2010. For the protection of the environmental hazard and of human health, the emission of organic vapors containing HFCs in the workplace environment still needs to be mitigated and even prevented to reduce the overexposure risk. One of the most available control/prevention technologies employed for these purposes is to adopt new, environmentally friendly alternatives such as hydrofluoroethers (HFEs) and hydrofluoropolyethers (HFPEs).

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