EXTERNAL REVIEW DRAFT

HYDROFLUOROCARBONS AND HYDROCHLOROFLUOROCARBONS

INTERIM REPORT

U.S. Environmental Protection Agency
Office of Toxic Substances
Washington, DC 20460

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UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

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OFFICE OF
PESTICIDES AND TOXIC
SUBSTANCES

Dear Reader:

The Montreal Protocol, as recently amended last June in London, calls for a worldwide effort to phase out the use of all fully halogenated chlorofluorocarbons (CFCs), carbon tetrachloride, halons, and methylchloroform. In addition, the new Clean Air Act Amendments contain similar provisions for phasing out these substances domestically. An important key to phasing out these substances successfully is the development of functionally similar substitutes. An important key to the latter process is the development of information that can be used by chemical manufacturers, processors, equipment manufacturers, users, and others to make near-term decisions on which substitutes and technologies to pursue. To this end, EPA made a commitment during the Second International Conference on CFC and Halon Alternatives held in Washington, DC (October 1989) to prepare interim assessments on the most promising substitute chemicals.

The attached document represents EPA's first effort at interim assessments of the hydrochlorofluorocarbons (HCFCs) and hydrofluorocarbons (HFCs). As new information on these substitutes becomes available, the assessments will be revised. EPA is also releasing an interim assessment on aqueous and terpene cleaners. Additional substitutes, such as non-HCFC refrigerants and semi-aqueous cleaners, will be considered as data become available.

The interim assessments contain available information on the toxicity of the substitutes and on potential exposure levels incurred by workers, consumers, and the general population from the manufacture, formulation, and use of these chemicals. Because many of these chemicals are not yet in commerce and are still undergoing toxicity testing, the assessment rests on incomplete data and, therefore, should not be interpreted as a final judgment. Nonetheless, the results of these preliminary analyses indicate that HCFCs and HFCs can be used in a manner safe to workers, consumers, and the general population given appropriate technological changes and exposure control practices.

In reaching this conclusion, we must emphasize the interim nature of these assessments in two respects. First, as more and better information becomes available on the toxicity of the alternatives and their likely exposures, a more definitive assessment can be conducted. Second, the data used in these analyses are, in many cases, limited and assumptions are often based more on analogy than direct measurement. As new equipment is developed that utilizes these chemicals and as work practices are modified to facilitate use of the substitute chemicals and to meet the needs of the new Clean Air Act Amendments, exposures are likely to be reduced. We urge all companies and workers involved with the production and use of CFC substitutes to take reasonable efforts to ensure that exposures to these chemicals are controlled while additional data are being developed.

We look forward to an increased level of communication with all parties that are affected by the phaseout of CFCs and other substances subject to the Protocol. We hope that these documents will serve as a good starting point for this dialogue at the Third International Conference in Baltimore, Maryland (November 27 through 29), as well as in the months ahead.

Sincerely,

Linda J. Fisher

Linda J. Fisher
Assistant Administrator

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1. EXECUTIVE SUMMARY

BACKGROUND

Over the past decade, there has been heightened concern worldwide over the slow but progressive depletion of the Earth's stratospheric ozone layer, the shield which protects the Earth from ultraviolet (UV-B) radiation. In the 1970s, scientists hypothesized that chlorine from chlorofluorocarbons (CFCs) could destroy stratospheric ozone, thus increasing the amount of UV-B radiation reaching the Earth's surface. Increased UV-B radiation can lead to increased cases of skin cancers and cataracts and has been linked to crop, fish, and materials damage. Bromochlorofluorocarbons (halons) also destroy stratospheric ozone, and are believed to do so at a faster rate than CFCs.

In 1978, the United States banned the use of CFCs in non-essential aerosols (40 CFR 762) in an effort to halt ozone depletion. By 1982, however, the global production of CFCs had risen, thereby negating the decrease in use that had resulted from the 1978 aerosol ban in the U. S. and other nations. Uses of CFCs include refrigeration, metal and electronics cleaning, production of insulating foam, mobile air conditioning, and sterilization.

Montreal Protocol

The increase in CFC production prompted officials in the United Nations Environment Programme (UNEP) to develop and promote a multilateral response to stratospheric ozone depletion. These efforts resulted in the development of an international agreement -- the 1985 Vienna Convention To Protect the Ozone Layer -- which provided the framework for the eventual adoption of the Montreal Protocol on Substances That Deplete the Ozone Layer. The Montreal Protocol was signed in 1987, ratified in the U. S. in 1988, and became effective worldwide on January 1, 1989. To date, 64 nations, 28 of which are developing countries, have ratified the Protocol.

The Montreal Protocol, as initially ratified, requires a freeze in production and consumption, at 1986 levels, of the following chemicals:

CFC-11	Trichlorofluoromethane
CFC-12	Dichlorodifluoromethane
CFC-113	1,1,2-trichloro-1,2,2,-trifluoroethane
CFC-114	1,2-Dichlorotetrafluoroethane
CFC-115	Chloropentafluoroethane

The freeze is to be followed by a phased-in reduction to 80 percent of 1986 levels beginning in mid-1993 and 50 percent beginning in mid-1998. The Protocol also limits the production and consumption to 1986 levels of halons 1211, 1301, and 2402, beginning in 1992. These reductions are to be accomplished by allocating production and consumption allowances to firms that produced and imported these chemicals in 1986, based on their 1986 levels of activity.

On August 12, 1988, under the authority of the Clean Air Act, EPA promulgated regulations to implement the reductions called for in the Montreal Protocol (53 FR 20566).

London Amendments to the Montreal Protocol

Scientists measuring stratospheric ozone have concluded that the amount of global ozone in northern hemisphere mid-latitudes has decreased 1.7 to 3 percent from 1969 to 1986, with the lowest levels occurring in winter. This decrease is two to three times greater than had been predicted by atmospheric models. Several extensive scientific investigations also produced evidence that CFCs led to decreases in stratospheric ozone during the spring months in the area over the Antarctic pole (sometimes called the Antarctic ozone "hole").

Scientists believe that the naturally occurring atmospheric concentration of chlorine is 0.7 part per billion (ppb). When the Antarctic ozone hole was first observed in the mid 1970s, the chlorine concentration equalled approximately 2.0 ppb; it is currently at 3.0 ppb. EPA has concluded that levels of chlorine and bromine in the atmosphere will continue to increase measurably despite the reductions in CFCs required by the Montreal Protocol. Concentrations of chlorine are predicted to exceed 8 ppb by the year 2075.

Based on these assessments, the U.S. and other Parties to the Montreal Protocol determined that further restrictions, including controls on other chlorinated compounds and an eventual phaseout of CFCs, were warranted.

In June 1990, the Parties met again in London to formally amend the Montreal Protocol to include more stringent provisions. Under the revised Protocol:

- o all fully halogenated CFCs and carbon tetrachloride will be phased-out by 2000,

- o halons will also be phased-out by 2000 with exemptions for essential uses, and

- o methyl chloroform will be phased-out by 2005.

In addition, the Parties issued a non-binding declaration calling for HCFCs to be used only when other alternatives are not feasible, with phaseout by 2020 if possible, but no later than 2040. These restrictions are based on a series of recently completed scientific, economic, and technological assessments prepared by the Parties to the Protocol.

Clean Air Act Amendments

In November 1990, the Clean Air Act was amended to include a number of provisions that will eliminate the production of CFCs, halons, carbon tetrachloride, and methyl chloroform by the turn of the century. One key provision requires EPA to set "Lowest Achievable Emission Levels" for CFCs in the air-conditioning and refrigeration sectors and prohibits venting of HCFCs in these sectors within the next two years. In addition, the new Clean Air Act requires recycling of all refrigerants in mobile air-conditioning within the next five years.

INTERIM REPORTS

To increase the public's knowledge of the potential CFC replacement chemicals, EPA has been working to characterize the human health and environmental risks associated with the major substitutes for CFCs and halons. In late 1989, EPA released a draft strategy document, "CFC Substitutes Human Health and Environmental Effects Program," that outlined the Agency's approach to this task. Several offices within EPA, primarily the Office of Toxic Substances (OTS), the Office of Air and Radiation (OAR), and the Office of Water (OW), were involved in the creation of the strategy document.

A focal point of the strategy was the creation of interim reports which should help provide the public with an early indication of the health and environmental impacts of major chemical alternatives to the ozone depletors. Chemicals are selected for assessment in the interim reports based on projected use volumes and the potential for significant increases in exposures and releases, rather than because of specific toxicity problems associated with the chemicals.

The interim reports are to be based on data available at the time of publication, rather than being comprehensive documents. Although the data in the interim reports can be expected to change in these fast-moving fields, EPA believes that industry and the public should have access to the information as it becomes available. Where data for a particular chemical are not available, EPA relies on closely related chemicals and scientific judgment to estimate hazard and exposure factors. EPA will prepare future reports as new data on these chemicals become available or as other substitutes or exposure scenarios are identified.

This first interim report focuses on eight hydrofluorocarbons (HFCs) and hydrochlorofluorocarbons (HCFCs) as substitutes for the CFCs. These chemicals are:

HCFC- 22	Chlorodifluoromethane (CAS # 75-45-6)
HCFC-123	2,2-Dichloro-1,1,1-trifluoroethane (CAS # 306-83-2)
HCFC-124	1-Chloro-1,2,2,2-tetrafluoroethane (CAS # 2837-89-0)
HFC -125	Pentafluoroethane (CAS # 354-33-6)
HFC -134a	1,1,1,2-Tetrafluoroethane (CAS # 811-97-2)
HCFC-141b	1,1-Dichloro-1-fluoroethane (CAS # 1717-00-6)
HCFC-142b	1-Chloro-1,1-difluoroethane (CAS # 75-68-3)
HFC -152a	1,1-Difluoroethane (CAS # 75-37-6)

For purposes of this report, the term "hazard" refers to the potential for human health or environmental effects because of the inherent toxicity of a chemical. "Exposure" addresses potential exposures to: workers who manufacture, process, or use HFCs/HCFCs; the general population exposed to releases from industrial sites; and consumers of products that contain HFCs and HCFCs.

The HFCs and HCFCs have a variety of use applications. The major uses addressed in this document include: mobile air conditioning, refrigeration, foam insulation, electronics and metal cleaning, and sterilization. A separate EPA report entitled "Aqueous and Terpene Cleaning Interim Report" presents EPA's assessment of the aqueous and terpene cleaners as substitutes for CFC-113 and methyl chloroform, another ozone-depleting chemical, in metal and electronics applications. Additional chemical and process alternatives exist for the CFCs, methyl chloroform, halons, and other ozone-depleting substances. These alternatives warrant a similar review, but due to time constraints and lack of information on their use, they could not be included in this report. EPA will broaden the scope of the next Interim Report to include additional CFC alternatives. In the meantime, developers and users of CFC substitutes should consider the following:

- In developing and using alternatives to the CFCs, care must be taken that in solving one problem we do not create another. Any chemical or process that takes a significant portion of the market should be capable of being used in a safe and environmentally acceptable manner.

- In general, when making decisions about how to replace the ozone-depleting chemicals, EPA encourages industry to first consider a preventive approach that will reduce overall use of chemicals through toxics use reduction, alternative processes, or conservation. In situations where these options do not exist, industry should avoid replacing ozone depletors with chemicals that possess known hazards and that cannot be used in a safe manner. EPA also cautions industry to be prudent in choosing any chemical for which there is a lack of hazard information and encourages those actions which would reduce exposure and release to the environment.

As mentioned above, this interim report is based on information that is currently available. In all cases, EPA did not possess a full data set in terms of hazard and exposure information for the HFCs and HCFCs. An industry consortium known as the Program for Alternative Fluorocarbon Toxicity Testing (PAFT) is currently involved in conducting a series of toxicity tests on some of the HFCs and HCFCs which will greatly increase the amount of information on the possible health effects associated with the chemicals. In terms of the exposure assessment, the lack of actual data on the HFCs and HCFCs is largely due to the fact that most of these chemicals have not been used in commerce, and exposure measurements have not been taken during their actual use. Where data did not exist, EPA relied on closely related chemicals and scientific judgment, where appropriate, to estimate the anticipated exposures and environmental releases of the HFCs and HCFCs in the given use scenarios. EPA will update this assessment when additional toxicity and exposure data are available.

Despite its limitations, there are several conclusions that can be drawn from this preliminary assessment. These findings are summarized below. This information should be provided to formulators, users, and the workforce handling these substitutes.

OVERALL FINDINGS OF THIS ASSESSMENT

The interim assessments evaluated the available information on the toxicity of the substitutes, as well as the potential exposure levels to workers, consumers, and the general population from the manufacture, formulation, and use of these chemicals. Because many of these chemicals are not yet produced or used and are still undergoing toxicity testing, the assessment necessarily rests on incomplete data and therefore, should not be interpreted

as a final judgment. Nonetheless, the results of these preliminary analyses indicate that HFCs and HCFCs can be used in a manner safe to workers, consumers, and the general population, given appropriate technological changes and exposure control practices in some applications.

In reaching this conclusion, we must emphasize the interim nature of these assessments in two respects. First, as more and better information becomes available on the toxicity of the alternatives and their likely exposures, a more definitive assessment can be conducted. Second, the data used in these analyses are, in many cases, limited, and assumptions are often based more on analogy than direct measurement. As new equipment is developed that utilizes these chemicals, and as work practices are modified to facilitate use of the substitute chemicals and to meet the needs of the new Clean Air Act Amendments to control emissions, exposures are likely to be reduced. We urge all companies and workers involved with the production and use of CFC substitutes to take reasonable efforts to ensure that exposures to these chemicals are controlled while additional data are being developed.

Following are some general conclusions regarding toxicity and exposure for the HFCs and HCFCs.

Toxicity

Based on existing laboratory studies, the HCFCs and HFCs, as well as the CFCs, have generally low toxicity, with both classes of compounds exhibiting low acute toxicity. However, compared to the CFCs, a class of compounds generally recognized as chemically inert and biologically inactive, the HCFCs and HFCs exhibit a greater potential for systemic effects. In general, the available testing indicates that observed effects, including transient central nervous system effects, developmental and maternal toxicity, and liver toxicity, occur only at relatively high exposure levels in animal studies. Available carcinogenicity studies on three of these substances do not provide evidence of a carcinogenic potential in humans; carcinogenicity studies are ongoing or planned for four other compounds. Section 2 of this report discusses compound-specific toxicity information.

Exposure

To gain perspective on the potential risks associated with the use of the HFCs and HCFCs, the Agency conducted several assessments to estimate exposures to the general population (primarily ambient air releases), consumers, and workers. The results of these preliminary analyses are summarized below by exposure category.

General Population

The ambient exposure analysis considered releases to all media, but quantified the fate and transport of emissions to the ambient air only, the predominant exposure pathway. The results of the ambient air analysis indicate that exposure levels resulting from the manufacture and use of the HFCs and HCFCs will pose low exposure to the general population.

Consumer

The results of the consumer exposure analysis demonstrate that consumer exposures are expected to be low. The Agency is still awaiting ongoing exposure testing that is being performed by industry to better characterize household emissions from foam insulation, a large use that the Agency was unable to quantify at this time. The consumer assessment will be revised once these data become available.

Occupational

The Agency estimated exposures in several occupational settings, including: chemical manufacturing; foam blowing; commercial air conditioning and refrigeration; mobile air conditioner manufacture and service; sterilant carrier use; and electronic and metal cleaning. Because most of the CFC substitutes are not currently used in these sectors, only a limited amount of occupational exposure data were available. Therefore, the Agency used the exposure information from existing CFC applications and modeling techniques to predict HFC and HCFC exposure levels. Data limitations precluded consideration of the extent to which occupational exposures could be reduced by equipment and technology changes that are required for use with the CFC substitutes. Preliminary use-specific exposure results are presented in Section 3.

The Agency recognizes the limitations inherent in the occupational exposure analysis, in particular the reliance on existing CFC data to predict exposures for the HCFCs and HFCs. However, the results of this preliminary analysis can guide future exposure studies that should be undertaken to better understand the potential exposures and risks resulting from the use of the HFCs and HCFCs.

Traditionally, exposures to the CFCs have been relatively high, compared to other industrial chemicals, because of the well-known low biological activity of these compounds. Since the HFCs and HCFCs are more reactive biologically, exposure levels similar to those associated with the CFCs are likely to be inappropriate in some circumstances. The results that follow identify industrial settings in which control strategies, different from those currently employed, may be needed.

The preliminary findings of the occupational exposure analysis indicate that exposures to the HFCs or HCFCs in mobile air conditioner manufacture and service and as a sterilant carrier are expected to be low when taking into account the current understanding of the toxicological characteristics of the CFC substitutes. The proposed Clean Air Act Amendments will require mandatory recycling in mobile air conditioner servicing in the long term (next five years), which will further reduce exposures.

Estimated exposures in HFC/HCFC manufacture, foam blowing, commercial refrigeration servicing, and electrical and metal cleaning, could be relatively higher, especially under worst-case conditions. For industrial chillers, as an example, the modeled results indicate significant levels of exposure--both under mid-range and worst-case operating conditions. While there is considerable uncertainty in these exposure estimates, the available data suggest that changes in current workplace practices and controls may be needed to ensure that occupational exposures in these industrial sectors are reduced.

Available information indicates that a number of changes already under consideration by industry could reduce exposures. In the case of chillers, for example, the HCFCs are <u>not</u> "drop-in" replacements for the existing chemicals (a simplifying assumption made in the exposure analysis because of data limitations). As industry develops new equipment for use with these substitutes, the need to reduce exposures should be considered. Again, the requirements of the anticipated Clean Air Act Amendments also contain several requirements, such as mandatory recycling in mobile air conditioner and commercial refrigeration servicing, that will further reduce exposures. More information is needed to better characterize occupational exposures, including the effectiveness of new equipment designs, controls, and workplace practices in reducing exposure. Information on potential exposures, releases, exposure-limiting equipment designs, and workplace practices should be made available to chemical users and the workforce.

Degradation

This assessment summarizes recent data related to chemical degradation of the CFC substitutes. The HFCs and HCFCs are considered as acceptable substitutes for the CFCs because of their greater reactivity and, thus, shorter environmental lifetimes. This characteristic inevitably makes these chemicals subject to some degradation in certain uses.

For example, preliminary laboratory data suggest that under stress conditions, small quantities of HCFC-123 can degrade to HCFC-133a and other halogenated compounds of toxicological

concern. Research to develop better information related to degradation under actual use conditions and the employment of possible stabilizers, is underway and will be evaluated as it becomes available. These data will facilitate further analysis of any potential environmental and health impacts.

ONGOING ACTIVITIES

This interim report does not present an analysis of the risks posed by use of specific CFC substitutes. However, it does provide an initial indication of situations in which exposures--if maintained at levels similar to those observed with the CFCs--could be inappropriate. These results highlight where additional information and control strategies, different from those currently employed, could be needed.

The Agency is awaiting the receipt of additional exposure and toxicity data that can be used for risk characterization purposes. One of the largest activities underway is the conduct of new toxicity testing. This program, known as the Program for Alternate Fluorocarbon Toxicity Testing (PAFT), was initiated voluntarily by the CFC producers worldwide to enhance the toxicity database on the substitutes. EPA has begun to receive preliminary results from PAFT; the completion of other tests will occur over the next two to three years. Table 2-3 identifies the specific testing agreement and the schedule for completion of these tests.

Once new exposure and toxicity data are received, EPA will refine the information contained in this document. The Agency will continue to address numerous issues, especially those related to the interpretation and use of the toxicity testing results for risk characterization purposes. Key issues will include the relevance of the effects seen in animals to humans and the appropriate methodologies for extrapolating from animal studies to human exposures. In anticipation of this work, submission of new data and comments on the information contained in this document will be of great value.

OUTLINE OF THIS REPORT

Section 2, Hazard Assessment, presents a summary of EPA's hazard assessment for the eight HFCs/HCFCs. The term "hazard" refers to the potential for human health or environmental effects because of the inherent toxicity of a chemical.

Section 3, Occupational Exposure, examines the processes by which the HFCs and HCFCs are produced and used, and estimates potential occupational exposures of workers through inhalation during manufacture and use of the HFCs and HCFCs.

Section 4, Consumer Exposure, presents EPA's estimates of the likely exposure to consumers from use of products containing HFCs and HCFCs.

Section 5, General Population Exposure, presents EPA's estimates of likely industrial releases of the HFCs and HCFCs into the environment and discusses exposure to the general population from these releases.

More complete assessments of the human health and ecotoxicity effects of the HFCs and HCFCs can be found in EPA's support documents. A list of these support documents and other references can be found at the end of this report. Additional copies of this document and the EPA support documents can be obtained through:

TSCA Assistance Information Service
U.S. Environmental Protection Agency
Office of Toxic Substances (TS-799)
Washington, D.C. 20460

Telephone: (202) 554-1404

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2. HAZARD ASSESSMENT

This section discusses the health hazard information available for the eight potential CFC substitutes, identifies data gaps where possible and discusses the Agency testing strategy for this class of chemicals. Because of the physical properties and uses of these chemicals, the main route of human exposure is through inhalation.

It should be noted that this section only assesses the hazard information and does not provide an analysis of risks posed by use of specific CFC substitutes. "Hazard" is defined in this report as the intrinsic toxicity of a substance. "Risk" is the probability that a substance will produce harmful effects under specified conditions under which it is used. Depending on the conditions under which it is used, a toxic substance may pose lower risk than a relatively nontoxic one.

In general, toxicity studies are designed to dose at levels that induce some effects. As a result, it is rare for such toxicity testing to show no effects at all. Thus, interpretation of toxicity testing results must take into account the nature of the effects observed and the doses at which they occurred. In the case of the HFCs and HCFCs, testing was performed at dosage levels that ranged from 300 ppm to 700,000 ppm, representing a fraction of the total air volume ranging from 0.03 percent to 70 percent. Most of the dosage levels used for testing the HFCs and HCFCs are very high relative to other chemicals that have been tested.

Section 2.1 presents a synopsis of currently available hazard information on five HCFCs (HCFC-22, HCFC-123, HCFC-124, HCFC-141b, and HCFC-142b) and three HFCs (HFC-152a, HFC-134a, and HFC-125). A comprehensive review of available data can be found in the hazard assessment support document. To develop an understanding of the similarities and differences of the hazards of the HCFCs and HFCs compared to the currently used CFCs, a brief review of the toxicological profiles of the major CFCs is provided in Section 2.2.

Since there is virtually no available health hazard information of the HCFCs and HFCs in humans, the hazard

evaluation is based mainly on animal toxicity data. There is very limited information available on the pharmacokinetics and metabolism of these chemicals. By analogy to CFCs (as reviewed by the World Health Organization, WHO, 1987), the HCFCs and HFCs are likely to be readily absorbed by the lungs during inhalation exposure. Most of the chemical that is absorbed is expected to be eliminated unchanged in the expired air. Available data on HCFC-22 and HFC-134a indicate that these chemicals are likely to undergo very limited metabolism (0.2% and 0.05%, respectively). Further evidence for some degree of metabolism comes from the finding of a dose-dependent urinary excretion of fluoride in a chronic toxicity study with HFC-152a at high exposure concentrations (10,000 and 25,000 ppm). In addition, a metabolite common to both HCFC-123 and halothane (2-bromo-2-chloro-1,1,1-trifluoroethane) was found bound to rat liver proteins following acute exposure to either HCFC-123 or halothane. Details of the review of the metabolism data can be found in the hazard assessment support document.

The health endpoints discussed in section 2.1 include acute toxicity, cardiac sensitization, neurotoxicity, subacute/subchronic/chronic toxicity, mutagenicity, oncogenicity, developmental and reproductive toxicity. Considerations are given to the EPA's Risk Assessment Guidelines in the evaluation of these various health endpoints. In a number of cases, the information presented for some of these endpoints is preliminary or incomplete. Additional toxicity studies are either ongoing or being planned for some of these chemicals. Once additional toxicity data are received, the Agency will be able to provide a more complete assessment of the potential adverse effects of these chemicals in humans.

A description of the testing program by the PAFT industry consortium is provided in Section 2.3. The Agency identified additional toxicity testing to more fully characterize the potential neurotoxicity, reproductive toxicity and oncogenicity for some of these chemicals. The Agency has used structure activity relationships (SAR) analysis as a predictive tool in identifying chemicals with toxicologic concern for additional testing needs, rather than recommending tests for all endpoints for all 8 chemicals. Considerations are given to the chemical reactivity of the compound (i.e., the number of halogen substituents, the position and the kind of halogen substituents) as well as information available on metabolism and possible mechanisms of action. PAFT has agreed to sponsor these additional toxicity studies as proposed by the Agency. Tentative dates for the availability of the results of these toxicity tests are also provided in this section.

These chemicals are not expected to be found in water at significant levels and therefore are not likely to pose risk to aquatic organisms. However, information on their potential

aquatic toxicity can be found in the hazard assessment support document.

2.1 SUMMARY OF TOXICITY STUDIES

2.1.1 SUMMARY OF TOXICITY STUDIES OF HCFC-22

HCFC-22 has very low acute toxicity. Its lethal concentration ranges from 277,000 to 300,000 ppm in mice and rabbits (Sakata et al., 81).

Cardiac sensitization is seen in an epinephrine challenge test with HCFC-22 in dogs at a concentration of 50,000 ppm and in mice at 400,000 ppm. No epinephrine-induced cardiac arrhythmias were seen in monkeys at concentrations as high as 100,000 ppm (series of studies by Aviado, Smith, Belej, et al., 74; 75).

HCFC-22 has been tested in chronic inhalation toxicity studies in rats and mice (Tinston et al., 81a; 81b). No overt toxicity was seen in rats and mice exposed to HCFC-22 up to 50,000 ppm. In the rat study, the only reported changes were a decrease in body weight gain in high-dose males, increased body weight gains in females of all exposure groups (1000; 10,000; and 50,000 ppm), and increases in the weights of the liver, kidney, adrenal, and pituitary glands in high-dose females. In the mouse study, high-dose animals were reported to be hyperactive. No definition of hyperactivity or scoring criteria were given. No systemic effects were seen in rats and mice at 10,000 ppm.

Mixed results have been reported in the Salmonella/mammalian microsomal assay (Ames assay) with HCFC-22. In one study, HCFC-22 was mutagenic in strain TA1535 (Koops, 77a; Longstaff et al., 84). In another Ames assay, HCFC-22 tested negative (Barsky, 76). HCFC-22 was tested in the BHK-21 cellular transformation assay (Longstaff et al., 84). It was reported to be negative; however, no conclusions can be drawn about its activity in this test system since no data were reported to support this claim. HCFC-22 did not induce mutation at the hypoxanthine-guanine-phosphoribosyl transferase (HPRT) locus of Chinese hamster ovary (CHO) cells (McCooey, 80). Two in vivo cytogenetic studies and two dominant lethal assays have been conducted. HCFC-22 induces chromosomal abnormalities in the femoral bone marrow of treated rats (Anderson et al., 77b; Anderson and Richardson, 79a) but does not appear to induce dominant lethality in treated male mice (Anderson et al., 77a; Hodge et al., 79c) and rats (Lee and Suzuki, 81), although an erratic response pattern was noted in mice.

Although HCFC-22 induces chromosomal aberrations in femoral bone marrow, it does not appear to induce chromosomal aberrations in germ cells of males as evidenced by the negative dominant

lethal studies. There is no indication that HCFC-22 induces gene mutation in mammalian cells as evidenced by a negative CHO assay. On the basis of the data presented, HCFC-22 in all probability does not present a mutagenic hazard to man. No further testing for heritable genetic effects is recommended. Results in the cellular transformation assay do not relate to heritable mutagenic effects and do not indicate the need for further testing.

Available epidemiological data are inadequate to evaluate the carcinogenicity of HCFC-22 in humans. There is limited evidence for the carcinogenicity of HCFC-22 in laboratory animals. HCFC-22 caused small increases in fibrosarcomas (most of which involved the salivary glands) and Zymbal gland tumors in male rats at a high concentration (50,000 ppm). In this study, no tumorigenic responses were observed at lower exposure concentrations in male rats (1000 and 10,000 ppm). Further, no increased incidence of tumors was found in female rats and mice of both sexes when exposed to similar concentrations (Tinston et al., 81a; 81b). HCFC-22 was also tested in another chronic inhalation study in rats (Maltoni et al., 82; 88). No tumors were found at the two dose levels tested (1000 and 5000 ppm). This study is considered to be limited because the maximum tolerated dose (MTD) appears not to have been reached. In a limited gavage study where animals were exposed for only one year (Longstaff, 82; Longstaff et al., 84), HCFC-22 did not induce tumors in rats at a dose of 300 mg/kg/day.

The potential maternal and developmental toxicity of HCFC-22 has been evaluated in four studies in rats (Culik et al., 76; Culik and Crowe, 78; Palmer et al., 78a) and one study in rabbits (Palmer et al., 78b). No maternal or developmental toxicity was observed in the rabbit study at exposure concentrations up to 50,000 ppm. However, HCFC-22 was found to cause maternal toxicity in rats as evidenced by reduced maternal body weight gain at the highest dose tested (50,000 ppm) in the Palmer et al. (78a) study. In addition, non-statistically significant and non-dose-related increases of eye abnormalities (small or missing eyes) were found in the fetuses in three rat studies at all doses tested (first study - 1000 and 10,000 ppm; second study - 500, 1000, and 20,000 ppm; third study - 100, 300, and 10,000 ppm). Palmer et al., (78a) then ran a large study in which there were more than 4000 fetuses from each exposure group. Increases in the same eye abnormalities were seen at all dose levels tested (100, 1000 and 50,000 ppm) but statistical significance ($p < 0.05$) was achieved only at the highest concentration. This large study did not examine fetal abnormalities other than the effects on the eye. Some reviewers have questioned the significance of these findings because of the magnitude of this effect in historical controls. The Agency is not yet in possession of the primary data on historical controls.

Except for the dominant lethal studies cited earlier, the potential for reproductive toxicity of HCFC-22 has not been studied.

2.1.2 SUMMARY OF TOXICITY STUDIES OF HCFC-123

HCFC-123 has low acute toxicity. Its LC_{50} for acute inhalation exposure is between 28,000 and 50,000 ppm in rats (Hall and Moore, 75; Waritz and Clayton, 66; Coate, 76) and Chinese hamsters (Darr, 81), and its dermal LD_{50} is greater than 2 g/kg in rats and rabbits (Brock, 88a; Brock, 88b). Its approximate lethal dose in an acute oral study in rats is 9 g/kg (Henry and Kaplan, 75).

HCFC-123 is a mild ocular irritant (Brittelli, 76a) and produces minimal dermal irritation (Brock, 88c) as demonstrated in skin and eye irritation studies in rabbits.

Based on the results of a dermal sensitization study in guinea pigs (Goodman and Morrow, 75), HCFC-123 is not a dermal sensitizer.

Cardiac sensitization as measured in an epinephrine challenge test is seen in dogs at concentrations of 20,000 ppm and greater (Trochiomowicz and Mullin, 73). Dogs exposed to 10,000 ppm of HCFC-123 for 5 minutes followed by a challenge dose of epinephrine showed some increased heart beat (tachycardia) as well as signs of central nervous system (CNS) depression, but did not exhibit cardiac sensitization.

Signs of CNS depression are consistently seen at concentrations of HCFC-123 of 5000 ppm and greater in acute, short-term, and subchronic inhalation studies in rats.

HCFC-123 has been shown to cause liver toxicity in one short-term and three subchronic studies in rats and in a single subchronic study in dogs. Pathological changes in the liver were found in dogs exposed to 10,000 ppm, but not in those exposed to 1000 ppm (Crowe, 78). In rats, the observed liver effects were not consistent across the studies. Significant dose-related increases in liver weights were reported in all subchronic studies (Crowe, 78; Industrial Biotest Laboratory, 77c; Malley, 90) at doses ranging from 500 to 10,000 ppm and from 5000 to 20,000 ppm in a 4-week study (Kelly, 89). However, mild pathological changes were only found in one study (Industrial Biotest Laboratory, 77c). The preliminary results of the 12 month sacrifice from an ongoing chronic study in rats showed liver weight changes at 5000 ppm but not at lower doses (300 and 1000 ppm). A full characterization of the potential for liver effects will be developed following the receipt of the results of the ongoing chronic study.

HCFC-123 has been tested in vitro in the Salmonella/mammalian microsomal assay (Barsky and Butterworth, 76; Callander, 89) and in vivo in the micronucleus assay (Muller and Hofmann, 88). Both assays were negative. There is no evidence to suggest that HCFC-123 induces either gene or chromosomal mutations and hence no reason to suspect that it might be a germ cell mutagen. No further testing for heritable genetic effects is recommended.

No information on the oncogenic potential of HCFC-123 is available. An oncogenicity/chronic toxicity study on HCFC-123 in rats is underway. EPA has received some information from the 12-month sacrifice as mentioned above. The terminal sacrifice will occur in January 1991. A full report of the results is expected in early 1993.

The maternal and developmental toxicity of HCFC-123 has been evaluated in a range-finding and a final inhalation study in rabbits (Bio/dynamics, 89a; 89b) and two inhalation studies in rats (Culik and Kelly, 76; Industrial Bio-Test, 77). The final rabbit study provides evidence of maternal toxicity following exposure to doses as low as 500 ppm of HCFC-123 as demonstrated by significant reductions in food consumption and body weight gain. There was no statistically significant evidence of developmental toxicity in the final study at doses as high as 5000 ppm. However, higher doses were used in the range-finding study. This study showed dose-related decreases in litter size and fetal body weight (10,000 ppm or greater).

Maternal toxicity was also reported in two rat studies. A significant reduction in maternal weight gain was seen in the study by Industrial Bio-Test (77) when pregnant dams were exposed to 5000 ppm (only dose tested) of HCFC-123. In the second study (Culik and Kelly, 76), pregnant dams exposed to HCFC-123 at 10,000 ppm (only dose tested) showed clinical signs of anesthetic effects. No conclusive evidence of developmental toxicity was reported, but both rat studies are considered inadequate for hazard assessment. This is because both studies suffer from a number of deficiencies including the use of a single dose, a small number of animals, and an inadequate assessment of fetal parameters (e.g., fetal body weight, visceral examination).

Data from a 2-generation reproductive effects study on HCFC-123 and data from developmental toxicity studies on HCFC-124, a structurally similar compound, will be used to better define the potential for developmental toxicity of HCFC-123.

HCFC-123 will be tested in a 2-generation reproductive effects study.

2.1.3 SUMMARY OF TOXICITY STUDIES OF HCFC-124

HCFC-124 has very low acute toxicity. Its LC_{50} for acute inhalation exposure in rats ranges from 230,000 to greater than 360,000 ppm (Hazleton, 76; Kelly, 90).

Cardiac sensitization was seen in an epinephrine challenge test in dogs at concentrations of 25,000 ppm and greater (Mullin, 76). No effect was observed at 10,000 ppm.

Signs of CNS depression have been seen in acute and subacute studies of HCFC-124 at concentrations greater than 50,000 ppm.

HCFC-124 has been shown to cause absolute and relative liver weight changes in rats in a subchronic study (Industrial Biotest Laboratory, 77a). In this study, liver weight changes were seen at 1000 and 5000 ppm. HCFC-124 is being tested in another 90-day subchronic study in rats at 5000, 15,000, and 50,000 ppm. The results of this study should be available for evaluation in mid 1991. The results of this study will be incorporated to more fully evaluate the potential for liver effects of HCFC-124.

HCFC-124 tested negative in the Ames assay (Barsky, 76; Litton Bionetics, 76) and did not induce micronuclei in an inhalation micronucleus assay in mice (Rickard, 90). There is no evidence to suggest that it induces either gene or chromosomal mutations and hence no reason to suspect that it might be a germ cell mutagen. No further testing for heritable genetic effects is recommended.

No information on the oncogenic potential of HCFC-124 is currently available. PAFT plans to conduct an oncogenicity/chronic toxicity study on HCFC-124 in hamsters.

HCFC-124 has not been adequately tested for developmental toxicity. In the only available study (Industrial Biotest Laboratory, 77b), exposure of pregnant rats to 5000 ppm of HCFC-124 (only dose tested) produced a significant increase in resorptions. PAFT has scheduled developmental toxicity studies in rats and rabbits.

HCFC-124 has not been tested for reproductive toxicity. The results of the 2-generation reproductive effects study on HCFC-123 will be used to evaluate the need for further assessment of this end effect for HCFC-124.

2.1.4 SUMMARY OF TOXICITY STUDIES OF HCFC-141b

HCFC-141b has low acute toxicity in inhalation, oral, and dermal studies. Its LC_{50} for inhalation exposure is approximately 60,000 ppm (Doleba-Crowe, 77b; Hardy et al., 89a).

No effects were seen in oral studies at 5000 mg/kg or in dermal studies at 2000 mg/kg (Sarver, 88; Liggett et al., 89; Gardner, 88; Brock, 89b).

HCFC-141b is a mild to moderate eye irritant and produces nil to minimal skin irritation (Brock, 88d; Liggett, 88a; Brock, 89a; Liggett, 88b).

In a study designed to detect epinephrine-induced cardiac sensitization in dogs (Mullin, 77), a marked response was seen at concentrations of 5000 to 20,000 ppm. No response was noted at 2500 ppm. In a second study (Hardy et al., 89b), epinephrine-induced cardiac arrhythmias were induced at concentrations ranging from 9000 to 21,000 ppm in dogs and from 3000 to 10,000 ppm in monkeys.

HCFC-141b was tested for dermal sensitization in 20 female albino guinea pigs (Kynoch and Parcell, 88). No evidence of delayed contact hypersensitivity was found.

Cage-side observations of transient CNS depression (effects occurring only during exposure) were noted at 3200 ppm and greater in rats and 4200 ppm and greater in rabbits in developmental toxicity studies. Because these results could be indicative of neurotoxicity, the PAFT testing program for HCFC-141b (and HCFC-123) will closely examine the effects of CNS depression through more careful testing of these effects (e.g., functional, rather than cage-side observations).

Although exposure to 20,000 ppm of HCFC-141b in a subchronic study in rats resulted in lower body weights, decreased food consumption, decreased responsiveness to stimuli, and increased levels of serum cholesterol, these effects were not accompanied by either gross or histopathological changes (Yano et al., 89; Landry et al., 89). Thus, the overall systemic toxicity of HCFC-141b appears to be low.

HCFC-141b gave mixed results in the Ames assay. It was positive in strain TA1535 in two studies (Hodson-Walker and May, 88b; Russell, 77) and negative in one study (May, 89). No explanation for the differences in test results is available. HCFC-141b does not induce chromosomal aberrations in cultured human lymphocytes (Hodson-Walker, 90b). It does, however, induce aberrations in cultured Chinese hamster ovary (CHO) cells (Hodson-Walker, 90a). This is in agreement with an earlier report (Bootman et al., 88c) in which HCFC-141b was also positive in CHO cells in culture. However, this ability to induce chromosomal effect in vitro is not noted when HCFC-141b is tested in vivo. HCFC-141b has been tested twice in the mouse micronucleus assay (Bootman et al., 88a; Vlachos, 88). It was negative in both assays. HCFC-141b was also negative in the E. coli assay for DNA damage in bacterial cells (Hodson-Walker and

May, 88a) and the in vitro assay for gene mutation at the HGPRT locus in Chinese hamster V79 cells (Bootman et al., 88b).

Given the entire set of test results for HCFC-141b, it is concluded that in spite of the positive response in CHO cells and the mixed results in the Ames assay, HCFC-141b in all probability does not present a mutagenic hazard to exposed individuals. The available mutagenicity data also do not indicate a concern for possible carcinogenicity of this compound because currently available data indicate that genotoxicity test results do not correlate well with rodent carcinogenicity test results for this class of compounds.

There is no information on the carcinogenicity of HCFC-141b. As discussed in the hazard assessment support document, SAR analysis indicates a low oncogenicity potential for HCFC-141b. An oncogenicity/chronic toxicity study on HCFC-141b in rats is underway.

HCFC-141b was tested for developmental toxicity in both rats and rabbits and found to cause developmental effects only at high dose levels. In the rat study (Hughes et al., 88), there were clinical signs of transient CNS depression during exposure at all dose levels (3200, 8000, and 20,000 ppm). However, the observed transient CNS depression was accompanied by changes in body-weight gain and food consumption only at the highest dose tested. Although statistical analyses were not performed on maternal parameters, dams exposed to 20,000 ppm exhibited an 8% reduction in mean body weight and a 44% increase in water consumption. Developmental toxicity was evident after exposure to 20,000 ppm of HCFC-141b as demonstrated by a significant increase in resorptions and a significant decrease in litter size and fetal body weight. In addition, fetuses exposed to 20,000 ppm had increased frequencies of edema, spaces between the bodywall and the organs, subcutaneous hemorrhages, supernumerary liver lobes, and delays in ossification of certain skeletal elements; statistical analyses were not performed.

In the rabbit study (Hughes et al., 89), there were no statistically significant differences in food consumption or maternal body weight between treated and control groups at any dose level (1400, 4200, and 12,600 ppm). There were clinical signs of transient CNS depression during exposure at the mid- and high dose levels. There was no evidence of developmental toxicity at any dose level.

HCFC-141b has not yet been tested for reproductive toxicity. PAFT is scheduled to test HCFC-141b in a 2-generation reproductive effects study.

2.1.5 SUMMARY OF TOXICITY STUDIES OF HCFC-142b

HCFC-142b has very low acute toxicity. Its LC_{50} for 30 minutes of exposure is greater than 300,000 ppm (Lester and Greenberg, 50).

HCFC-142b produced only mild irritation when tested in rabbits (Brittelli, 76b).

Epinephrine-induced cardiac arrhythmias were observed in dogs exposed to HCFC-142b at 50,000 ppm (Mullin, 69a). No effects were noted in monkeys and mice at concentrations up to 100,000 ppm. Noise-induced cardiac sensitization (via release of endogenous epinephrine) was reported in dogs during a 30 second simultaneous inhalation exposure to 800,000 ppm of HCFC-142b (Mullin, 70).

HCFC-142b has not been tested for neurotoxicity. An acute study (Lester and Greenberg, 50) demonstrated signs of neurotoxicity at very high concentrations (loss of postural reflexes at 200,000 ppm; loss of righting reflex at 250,000 ppm; loss of corneal reflex at 300,000 ppm).

The results of a subacute (Moore, 76a) and a subchronic study (Kelly, 76) of HCFC-142b indicate low systemic toxicity. No effects were seen at any dose level tested (high dose = 10,000 ppm in 90-day study in rats and male dogs; high dose = 20,000 ppm in 2-week study in male rats).

Results of a chronic inhalation study (Seckar et al., 86) support the findings of low systemic toxicity of HCFC-142b in the subacute and subchronic studies. No treatment-related toxic effects were noted in an inhalation study in rats at doses up to 20,000 ppm.

HCFC-142b was mutagenic in the Ames assay (Jagannath, 77; Longstaff and McGregor, 78; Longstaff et al., 84). As discussed in the hazard assessment support document, HCFC-142b gave a weak positive response when tested for its ability to induce chromosomal aberrations in the bone marrow of male rats (Pennwalt, 80a). HCFC-142b is considered to be without effect in a dominant lethal assay in rats (Pennwalt, 80b).

HCFC-142b was also tested in both the BHK-21 (Longstaff et al., 84) and the Balb/3T3 systems (Matheson, 78). No conclusions can be drawn about the activity of this compound in either of these test systems although HCFC-142b was reportedly positive in the BHK-21 system.

Although HCFC-142b was positive in the Salmonella assay and is a weak inducer of chromosomal aberrations in femoral bone marrow, it does not appear to induce chromosomal aberrations in

germ cells of males as evidenced by a negative dominant lethal study. On the basis of the data presented, there is no evidence to suggest that HCFC-142b presents a mutagenic hazard to man. No further testing for heritable genetic effects is recommended. Results in cellular transformation assays do not relate to heritable mutagenic events and do not indicate the need for further testing.

In a two-year inhalation study in rats on HCFC-142b (Seckar et al., 86), no statistically significant increase of tumor incidences were reported for any dose level (highest dose tested = 20,000 ppm). The maximum tolerated dose (MTD) might not have been reached in this study. However, HCFC-142b is not expected to be oncogenic because of the negative test results combined with SAR analysis that indicates a low oncogenicity potential for HCFC-142b.

HCFC-142b has not been adequately evaluated for developmental toxicity. It has only been tested in one species, rats. The two existing studies in rats are considered limited. No maternal toxicity was seen in these studies. In one study, there is suggestive evidence of developmental toxicity (pre-implantation loss) at 1,000 and 10,000 ppm (Culik and Kelly, 76b). The other study provided only suggestive evidence of developmental toxicity when tested at 2000 and 10,000 ppm (Damske et al., 78).

Except for the dominant lethal study cited earlier, the potential for reproductive toxicity of HCFC-142b has not been studied.

2.1.6 SUMMARY OF TOXICITY STUDIES OF HFC-152a

HFC-152a has very low acute toxicity. Lethal concentrations range from 383,000 to 500,000 ppm depending on the length of exposure (Moore, 75; Lester and Greenberg, 50; Limperos and Zapp, 51). Test animals showed lack of coordination, labored breathing, unresponsiveness to sound, and dose-responsive narcosis at concentrations of 175,000 ppm and greater.

HFC-152a is a weak cardiac sensitizer. Epinephrine-induced cardiac arrhythmias were seen at 150,000 ppm but not at 50,000 ppm in dogs (Mullin, 69b). No effect on the cardiovascular system of monkeys and dogs was seen at concentrations up to 200,000 ppm in the absence of an epinephrine challenge dose. Rats did have arrhythmias at concentrations of 50,000 ppm and greater, but rats are not considered to be a good model for evaluating the cardiotoxicity of halogenated hydrocarbons in humans (from a series of studies by Aviado, Smith, Belej et al., 74; 75).

Signs of CNS depression have been noted in acute inhalation studies in rats at high concentrations (175,000 ppm and greater) (Moore, 75; Lester and Greenberg, 50; Limperos and Zapp, 51). In a 2-week study (Moore, 76b), narcosis and unresponsiveness to sound were noted at 100,000 ppm.

Results of a chronic study in rats (McAlack, 82) indicate that HFC-152a has low systemic toxicity. At 25,000 ppm, animals had symptoms that were indicative of a mild reversible alteration in the renal structure of males and females and a slight interference in renal function in females. There was also an increased incidence of swollen ears, ocular/nasal discharge and wet/stained perinea in both males and females, and an increased incidence of wet/stained body and face in females. These symptoms may be indicative of chronic low level irritation or stress. No effects were seen at 10,000 ppm.

HFC-152a was negative when tested in the Ames assay (Koops, 77b). No conclusions can be drawn about the activity of HFC-152a in the Drosophila melanogaster sex-linked recessive lethal (SRL) assay (Foltz and Fuerst, 74; Garrett and Fuerst, 74) because the available information is inadequate to draw conclusions. There is no evidence to indicate a concern that HFC-152a may induce heritable effects in man. No further testing for heritable genetic effects is recommended.

HFC-152a was non-carcinogenic in a 2-year inhalation study in rats with a high dose of 25,000 ppm (McAlack, 82).

No statistically significant evidence of maternal or developmental toxicity was seen in a study of HFC-152a in rats (Culik and Kelly, 80). There was a dose-related trend in the incidence of two skeletal anomalies. Although this finding is suggestive of developmental toxicity, it should be noted that no statistically significant effects were seen at 50,000 ppm. HFC-152a has not been tested in a second species.

HFC-152a has not been tested for reproductive toxicity.

2.1.7 SUMMARY OF TOXICITY STUDIES OF HFC-134a

HFC-134a has very low acute toxicity. Lethal concentrations range from 567,000 to 750,000 ppm in rats (Silber and Kennedy, 79a; Rissolo and Zapp, 67).

The cardiac sensitization potential of HFC-134a was evaluated in a standard epinephrine challenge test (Mullin and Hartgrove, 79). HFC-134a is a weak cardiac sensitizer. Epinephrine-induced cardiac arrhythmias were seen at doses of 75,000 ppm and greater in dogs. No response was noted at 50,000 ppm.

Signs of transient CNS depression have been seen in acute studies (Silber and Kennedy, 79a; Rissolo and Zapp, 67) and in a developmental toxicity study (Lu and Staples, 81) at 100,000 ppm in rats. In a 90-day inhalation study on HFC-134a (Hext, 89), female rats exhibited decreased brain weights at 10,000 and 49,500 ppm which were not dose related (2.77 and 2.63%, respectively). This statistically significant change was not accompanied by either positive histopathological findings following the usual staining of brain and peripheral nervous system (PNS) sample tissue or by transient CNS depression. Four-week recovery animals from the subchronic study and 12-month sacrifice animals from an ongoing chronic study showed no similar decrease in brain weight. Four-week recovery animals from the subchronic study were negative for all histopathological findings. While EPA agrees that the available histologic reports were negative, adequate details of the evaluation were not provided as to which brain regions were examined. EPA is awaiting more specific information from ongoing studies to fully evaluate the potential neurotoxicity of this compound.

In subacute studies (14 days and 28 days) in rats (Silber and Kennedy, 79b; Riley et al., 79), the only pathological changes noted were in the lung indicative of focal interstitial pneumonitis after exposure to 50,000 or 100,000 ppm of HFC-134a. Some changes in organ weights (liver, kidney, gonad) were seen in the 28-day study at 50,000 ppm. Increased liver weight was also seen at 10,000 ppm in males. None of the organ weight changes were associated with altered gross or microscopic pathology.

Other than the brain weight changes noted above, little or no systemic toxicity was observed in rats following inhalation exposure for 13 weeks to HFC-134a (Hext, 89). Body weight and organ weight changes and changes in urine, blood biochemistry, and hematology parameters were observed but were not dose-related or consistent with time.

HFC-134a was tested three times for its ability to induce gene mutation in the Ames assay (unpublished study submitted to EPA, 76; Taylor, 78; Callander and Priestley, 90). Results were consistently negative. HFC-134a was also nonmutagenic when tested in an assay for micronucleus formation in the femoral bone marrow of treated mice (Muller and Hofmann, 89) and appears to be negative in the dominant lethal assay (Hodge et al., 79a). The results of the chromosomal aberrations assay are inconclusive (Anderson and Richardson, 79b). In addition, HFC-134a did not induce unscheduled DNA synthesis (UDS) in rat hepatocytes in vivo (Trueman, 90). There is no evidence to suggest that HFC-134a induces either gene or chromosomal mutations and hence no reason to suspect that it may induce heritable effects in man. No further testing for heritable genetic effects is recommended.

HFC-134a did not induce tumors in a limited oral bioassay (animals were exposed for only one year) (Longstaff et al., 84); however, this study is inadequate to assess the oncogenic potential of HFC-134a because of the short duration of exposure and the use of only one dose level. SAR analysis for HFC-134a predicts a low potential for oncogenic activity because fluorine generally has lower biological activity than other halogens. PAFT is conducting a chronic inhalation study in rats.

Three inhalation studies have been conducted on the potential maternal/developmental toxicity of HFC-134a; two were conducted in rats (Lu and Staples, 81; Hodge et al., 79b) and one in rabbits (Wickramaratne, 89a; 89b). One rat study with a small sample size (n = 7 or 14) demonstrated maternal toxicity after exposure to 100,000 ppm (reduced response to noise stimuli, uncoordinated movements) or 300,000 ppm (significant reduction in food consumption and body weight gain, no response to noise stimuli, severe tremors, uncoordinated movements) of HFC-134a. Developmental toxicity was also evident after exposure to 300,000 ppm of HFC-134a as demonstrated by a significant reduction in fetal body weight and a significant increase in the incidence of several skeletal variations. No statistically significant effects were seen at 30,000 ppm. The second rat study, which used a much larger sample size (n = 29 to 30), provided no statistically significant evidence of maternal toxicity after exposure to doses as high as 50,000 ppm of HFC-134a. Developmental toxicity was evident after exposure to 50,000 ppm as demonstrated by a significant reduction in fetal body weight and a significant increase in the incidence of several skeletal variations.

In the rabbit study, maternal toxicity was evident after exposure to 10,000 ppm or more as demonstrated by a statistically significant reduction in food consumption and body weight gain. Developmental toxicity was also evident after exposure to 10,000 ppm or 40,000 ppm. Exposure to 10,000 ppm or more resulted in a statistically significant dose-related increase in the fetal incidence, but not the litter incidence, of unossified 7th lumbar transverse processes.

There was a dose-related increase in the incidence of gaseous distention of the stomach. Although the incidence at 40,000 ppm (12.7%) was only slightly outside the range for historical controls (2.3 - 11.5%), the difference when evaluated by number of fetuses was statistically significant. When evaluated by numbers of litters, this statistical change is not apparent. This effect was seen in 7/23, 7/18, 7/21, and 9/23 litters in the control, 1400, 4200, and 12,600 ppm groups, respectively. Gaseous distention can be caused by gasping air. The reason(s) for the increase is unclear but could be indicative of non-random handling of the animals or lung problems. No maternal or developmental effects were seen at 2500 ppm.

HFC-134a has not been tested for reproductive toxicity. Decreased gonad weights were noted in a 28-day study at the highest dose tested (50,000 ppm) (Riley et al., 79); however, the significance of this finding is unclear because no effect on the gonads (either pathological or weight changes) was noted in the subchronic study (Hext, 89) at similar dose levels.

2.1.8 SUMMARY OF TOXICITY STUDIES OF HFC-125

HFC-125 has very low acute toxicity. Its LC_{50} via inhalation is reported to be 700,000 ppm (Vogelsberg, 90).

No other toxicity data on HFC-125 are available. The potential for adverse effects from exposure to HFC-125 can be evaluated by drawing on an analogy between HFC-125 and HFC-134a. Details of these studies are presented in the review of HFC-134a.

2.2 TOXICOLOGICAL COMPARISON WITH RELATED CHEMICALS

A direct comparison of chlorinated hydrocarbons, CFCs and HCFC/HFCs provides a meaningful and useful basis for evaluating the HCFCs as a physicochemically-related class of compounds and for developing (1) individual hazard assessments and (2) a strategy of identifying individual toxicity testing requirements. A detailed discussion of the toxicity of chlorinated hydrocarbons and CFCs is beyond the scope of this report; however, some generalization in regard to biological effects of each of these groups of compounds can be made based on SAR analysis. In general, effects from chlorinated hydrocarbons occur at lower levels and are more severe than are seen with either CFCs or HFCs/HCFCs.

2.2.1 CHLORINATED HYDROCARBONS

The short chain saturated chlorinated hydrocarbons are important solvents and feedstocks.

Overall, this class of compounds is of low acute toxicity. High concentrations may produce renal and hepatic dysfunction and pulmonary irritation. Most chemicals in this class are moderate cardiac sensitizers and are known to produce CNS depression. The liver is often a target organ for chronic toxicity.

Depending on the degree of halogenation, stereochemical considerations, and metabolism to genotoxic intermediates, some compounds in this class are genotoxic, mutagenic and/or carcinogenic. The predictive power of mutagenicity tests for these compounds is limited.

2.2.2 CHLOROFLUOROCARBONS

The following section provides a description of toxicity data for CFC-11, CFC-12, and CFC-113. These three compounds are the most significant chlorofluorocarbons in current use, from the point of view of production as well as widespread use. This class of compounds came into commercial production at a time when toxicological testing requirements were limited by today's standards. Thus, many of the available studies may not be adequate to fully characterize important endpoints. However, under the conditions of human exposure, no striking examples of chronic toxicity have emerged. The data support a broad comparison for a variety of toxic effects of the major CFCs with the chlorinated hydrocarbons. In general, it can be shown that the CFCs are less toxic.

Both CFC-11 and CFC-12 have relatively low acute toxicity (inhalation LC_{50} is greater than 100,000 ppm in animals). Alterations in both pulmonary compliance and resistance have been observed in humans following exposure to CFC-11 and CFC-12 (Clayton, 67). In comparison to the chlorinated hydrocarbons, the CFCs exhibit generally lower acute toxicity.

Cardiotoxicity has been studied in greatest detail with both CFC-11 and CFC-12. Both compounds have been observed to produce an increase in heart rate and decrease in blood pressure in monkeys (at 50,000 ppm), arrhythmias, and increases in vagal-heart acetylcholinesterase activity in an isolated preparation (Young and Parker, 75; Doherty and Aviado, 75). Many of the observed effects can be blocked by treatment with a beta-adrenergic blocker. It was also noted that CFC-11 sensitizes cardiac muscle to the effects of epinephrine, while CFC-12 exhibits either minor sensitization potential or no effect on epinephrine activation of cardiac muscle. These are effects common to halogenated hydrocarbons.

In terms of hepatotoxicity, CFC-12 has been studied in both continuous (90-day) and repeated exposures (8h/5 days/6 weeks) at 4000 ppm in rats, monkeys, rabbits, and guinea pigs. Following both continuous and repeated exposures at very low concentrations (100 ppm), only the guinea pigs exhibited extensive liver damage. However, the fact that no liver pathology was noted in any of the other species, taken together with the authors' acknowledgement that the guinea pig has an inherent susceptibility in continuous exposure studies suggest that these agents, unlike the chlorinated hydrocarbons, are not directly hepatotoxic, and that the guinea pig response appears to be an allergic response (Prendergast et al., 67; Maltoni et al., 88).

As reported by WHO (89), CFC-11, CFC-12 and CFC-113 have been tested for developmental toxicity. In addition, CFC-12 and CFC-113 were tested for reproductive effects. Although some of

these studies may be limited by today's standards and thus not all results are conclusive, none of the studies showed evidence of reproductive or developmental toxicity. Therefore, it appears that CFCs would have low potential for toxicity in this category.

CFC-12 has been studied for potential neurotoxicity. In humans, motor skills were affected (20,000 ppm); in rats, anesthetic effects were observed at 400,000 ppm (Azar et al., 72). These findings indicate the apparent anesthetic effect that has been observed throughout with CFCs, HFCs, and HCFCs (see below). Epidemiological evaluation of the human exposure experience reveals no associated neurotoxicity or behavioral effects with chronic exposure to general anesthetics, but no systematic testing of this endpoint has been done in animals.

With regards to carcinogenicity, chronic inhalation studies with either CFC-11 or CFC-12 (at 5000 ppm) were conducted in both rats and mice and reported no significant incidence of tumors (Prendergast et al., 67; Maltoni et al., 88). This is a low dose, not likely to be a maximum tolerated dose (MTD). Long-term oral carcinogenicity studies of CFC-11 and CFC-12 have given negative results (WHO, 89). CFC-113 was evaluated in a chronic study at a well-defined MTD of 20,000 ppm and also produced no increased tumor incidence (Wood, 85).

CFC-11 and CFC-12 are negative for mutagenicity in the Ames assay with and without activation in TA98, TA1538, TA100, and TA1535 strains (Longstaff et al., 84). There are no chromosomal damage studies for these compounds. It should be noted that many mutagenicity assays provide inconsistent data and poor reproducibility with a variety of halogenated hydrocarbons.

2.2.3 HYDROFLUOROCARBONS AND HYDROCHLOROFLUOROCARBONS

HCFCs and HFCs share common physicochemical features, and toxicity tests produce similar qualitative results. While actual data gaps are apparent, extrapolation within the matrix is possible and affords a rational basis for developing a toxicity testing strategy. Several general observations are evident for HCFCs and HFCs.

All appear to be of low acute toxicity and are generally significantly less acutely toxic than either the halogenated hydrocarbons or the CFCs. Only HCFC-123 and HCFC-141b exhibit LC_{50}'s in the 50,000 ppm range. All others range from 100,000 to 700,000 ppm.

All HCFCs appear to be weak cardiac-sensitizers (with epinephrine) as described for CFCs.

Two chemicals induce some effects on the liver. Both HCFC-123 and HCFC-124 cause liver weight changes but only HCFC-123 has been found to cause some pathological changes at high exposure levels (10,000 ppm in dogs). The HCFCs are, thus, similar to the CFCs and exhibit little marked potential for frank liver toxicity, unlike the chlorinated hydrocarbons.

Some of the HCFCs and HFCs cause maternal toxicity as evidenced by a decrease in food consumption and body weight gain. Developmental effects are also seen at dosages that equal or are greater than the maternally toxic dose. A consideration of SAR and available data for compounds such as dibromochloropropane, halothane, and HCFC-133a suggest the reproductive system as a potential target for HCFCs. The class of HCFCs, thus appear to have a somewhat greater potential for reproductive and developmental toxicity than do the CFCs.

Like the chlorinated hydrocarbons and CFCs, all HCFCs and HFCs appear to cause CNS depression much like the general anesthetics. At the present time, they have not been adequately studied in animals.

There is not an abundance of carcinogenicity data on the HFCs or HCFCs. The available carcinogenicity data on three compounds (HCFC-22, HFC-152a, and HCFC-142b) do not provide evidence of a significant carcinogenic potential in humans although some studies are limited. SAR analysis suggests a low carcinogenic potential for HFCs and some HCFCs (e.g., HCFC-141b and HCFC-142b).

It should be noted again that many mutagenicity assays provide inconsistent data and poor reproducibility with this class of compounds. While the HCFCs are sometimes positive in the Ames assay, HFCs are all negative in the Ames assays. Because of the same technical difficulties a general comparison with the CFCs is not easily made. No clear picture emerges from the results of the available genotoxicity assays.

2.3 TESTING STRATEGY

After all of the currently available animal studies were reviewed, the Agency developed a testing strategy to fill data gaps. Instead of testing all compounds for all possible adverse effects, analogies between individual chemicals are used to address some toxicological endpoints.

The CFC producers initiated the Program for Alternative Fluorocarbon Toxicity Testing (PAFT) in 1988 to develop a comprehensive, common toxicology data base to support the manufacture, introduction and use of alternatives by

manufacturers internationally. This is the first time that an industry, representing companies from around the world, has voluntarily joined to evaluate the toxicology of limited production or research chemicals. The status of the PAFT testing program is presented in Table 2-1. Table 2-2 lists the participating PAFT companies. The program is divided into three parts. PAFT I is investigating and reviewing the toxicology of HCFC-123 and HFC-134a; PAFT II, HCFC-141b; PAFT III, HCFC-124 and HFC-125.

In designing the PAFT programs factors considered were safety, an urgent need for toxicology information, availability of the compounds in amounts sufficient to sustain long-term tests, the economic future of these alternatives, and the availability of space for inhalation studies in qualified toxicology laboratories. Additionally, consideration was given to the testing requirements in the United States, Europe, and the Far East.

The program integrates past and present toxicological information to enable an evaluation of health effects including elements of acute, subchronic, developmental and chronic inhalation studies, genotoxicity studies, oncogenicity studies and environmental studies. Most of the tests in PAFT I and PAFT II, excluding the chronic studies, have been completed and work is underway on the PAFT III program.

PAFT studies in progress and schedules for completion are listed in Table 2-3. Studies already submitted to the Agency are listed in Table 2-4.

EPA evaluated the PAFT testing program and identified additional testing needs for neurotoxicity and reproductive toxicity. EPA also asked for a change in the oncogenicity testing program for HCFC-123 and HCFC-124.

TABLE 2-1 STATUS OF TESTING PROGRAM

	HCFC-22	HCFC-123	HCFC-124	HCFC-141b	HCFC-142b	HFC-152a	HFC-134a	HFC-125
[a]Acute	T	T	T	T	T	T	T	T
[a]CSens	T	T	T	T	T	T	T	NT
[a]Neuro	NT	P	NT	O	NT	NT	NT	NT
[a]Subchr	T	T	O	T	T	T	T	P
[a]Muta	T	T	T	T	T	T	T	P
[a]Onco	[b]T	O	P	O	T	T	O	NT
[a]Devel	T	[c]T	O	T	[d]T	[e]T	T	P
[a]Repro	NT	P	NT	P	NT	NT	NT	NT

As discussed in Section 2.3, testing for neurotoxicity and reproductive effects will be conducted on two compounds, HCFC-123 and HCFC-141b. The need for testing additional compounds will be evaluated when the results of these studies are available.

T = tested for this endpoint; NT = not tested for this endpoint; P = testing planned for this endpoint; O = testing ongoing for this endpoint

[a] Acute = acute toxicity; CSens = cardiac sensitization; Neuro = neurotoxicity; Subchr = subchronic toxicity; Muta = mutagenicity; Onco = oncogenicity in at least one species; Devel = developmental toxicity in two species; Repro = 2-generation reproductive effects study

[b] HCFC-22 has been tested for oncogenicity in rats and mice

[c] tested in rats and rabbits, test results inconclusive in rats. The results from the reproductive effects study in rats will be used to determine the need for further testing for developmental toxicity in rats.

[d] tested in one species only, test results inconclusive. The potential for developmental toxicity for HCFC-142b can be evaluated by comparison to that of HCFC-141b.

[e] tested in one species only. The potential for developmental toxicity for HFC-152a can be evaluated by comparison to that of HFC-134a.

TABLE 2-2 PAFT COMPANIES

1.	AKZO Chemical	Holland
2.	Allied-Signal	USA
3.	Asahi Glass	Japan
4.	ATO Chem, NA	USA
5.	ATO Chem, SA	France
6.	Central Glass	Japan
7.	Daikin	Japan
8.	Du Pont	USA
9.	Hoechst	Germany
10.	ICI	England
11.	Kali Chemi	Germany
12.	Montefluos	Italy
13.	Rhone-Poulenc ISC Div.	France
14.	Showa Denko	Japan
15.	Solvay & CIE	Belgium
16.	Ulsan Chemical	Korea

Neurotoxicity testing is needed for this class of compounds because signs of CNS depression are consistently seen in the available studies (acute, subacute, subchronic, and developmental toxicity studies). EPA selected HCFC-123 and HCFC-141b for neurotoxicity testing because they are the most acutely toxic of the eight compounds, and signs of CNS depression were seen at lower exposure levels in the existing studies for these two compounds than for the other compounds. In addition to the effects noted in animal studies with various HCFC compounds, the support for neurotoxicity for this class of compounds is also based on human evidence suggesting possible impairment of psychomotor and cognitive performance associated with inhalation exposure to CFC-11 (trichlorofluoromethane), CFC-12 (dichlorodifluoromethane), and CFC-113 (1,2,2-trichloro-1,1,2-trifluoromethane) (as reviewed by WHO, 1987).

EPA considers it necessary for HCFC-123 to be tested in a 2-generation reproductive effects study. Positive findings of reproductive effects in HCFC-133a assays, similarities evident by SAR analysis, and suggestive results in existing developmental toxicity studies prompt this decision. To fully characterize the potential reproductive hazards of the class of HCFCs, EPA also designates HCFC-141b to be tested for this effect.

As discussed in the hazard assessment support document, SAR analysis identified HCFC-123 and HCFC-124 as having the greatest potential for oncogenic activity. In order to account for differences in species sensitivity, HCFC-123 and HCFC-124 will be tested for oncogenicity in different species. Genotoxicity test results do not correlate well with rodent carcinogenicity test results for this class of compounds. Therefore, additional genotoxicity testing is not expected to contribute to an understanding of the carcinogenic potential of these compounds.

EPA will reevaluate any additional testing needs, if necessary, based on its analysis of the entire testing package.

TABLE 2-3
PAFT STUDIES IN PROGRESS, SCHEDULED OR CURRENTLY UNDER DEVELOPMENT AS PROVIDED BY PAFT ON 8/23/90

PAFT I	
HCFC-123	
Chronic Study Initiated	Jan. 1989
Terminal Sacrifice	Jan. 1991
Final Report	1st quarter 1993
Inhalation Reproduction Study	
Tentative Start	Jan. 1991
Tentative Completion of In-Life	Mar. 1991
Final Report	1st quarter 1993
Neurotoxicology Evaluation	
Tentative Start	Jan. 1991
Terminal Sacrifice	Apr. 1991
Final Report	1st quarter 1993
HFC-134a	
Chronic Study Initiated	Oct. 1989
Terminal Sacrifice	Nov. 1991
Final Report	4th quarter 1993

TABLE 2-3 (cont)

PAFT II

HCFC-141b

Chronic Study	Initiated	Jan. 1990
	Terminal Sacrifice	Jan. 1992
	Final Report	1st quarter 1994
Inhalation Reproduction Study		
	Tentative Start	Jan. 1991
	Tentative Completion of In-Life	Mar. 1992
	Final Report	1st quarter 1993
Neurotoxicology Evaluation		
	Initiated	Jan. 1990
	In-Life Completion	June 1990
	Final Report	1st quarter 1991

PAFT III

HCFC-124

Subchronic Inhalation		
	Study Initiated	May 1990
	In-Life Completion	Aug. 1990
	Final Report	2nd quarter 1991
Rat Teratology		
	Study Initiated	May 1990
	In-Life Completion	Aug. 1990
	Final Report	2nd quarter 1991
Rabbit Teratology		
	Tentative Start	Jan. 1991
	In-Life Completion	Feb. 1991
	Final Report	2nd quarter 1992
Chronic Study	Dates not yet determined	

HFC-125 — No studies have been placed yet. Identification of a source for the test compound is completed. Completion of a subchronic inhalation and two species teratology is estimated by 4th quarter 1992. HFC-125 will also be tested in a battery of mutagenicity assays.

TABLE 2-4 PAFT STUDIES SUBMITTED TO EPA

PAFT I		
	HCFC-123	An Inhalation Range-Finding Study to Evaluate the Toxicity of CFC 123 in the Pregnant Rabbit
		Primary Dermal Irritation Study with HCFC 123 in Rabbits
		Acute Dermal Toxicity Study of HCFC 123 in Rabbits
		Acute Dermal Toxicity Study of HCFC 123 in Rats
		An Inhalation Developmental Toxicity Study in Rabbits with HCFC 123
		A 4-Week Inhalation Study with HCFC 123 in Rats
		HCFC 123: Ames Assay using Strains TA98, 100, 1535, 1537, 1538 with and without Metabolic Activation
		Haskell Laboratory Report "Subchronic-Inhalation Toxicity: 90-Day Study with HCFC 123 in Rats"
		HCFC 123 Micronucleus Test in Male and Female NMRI Mice after Inhalation
	HFC-134a	HFC 134a - Embryotoxicity Inhalation Study in the Rabbit
		HFC 134a: Teratogenicity Inhalation Study in the Rabbit
		HFC 134a: 90-Day Inhalation Toxicity Study in the Rat
		HFC 134a - Teratogenicity Study in the Rat (Comments only)
		HFC 134a: In vivo Micronucleus Assay Conducted by Hoechst
		HFC 134a - An Evaluation Using the Salmonella Mutagenicity Assay (CTL/P/2422)

TABLE 2-4 (cont)

	HFC 134a Assessment for the Induction of Unscheduled DNA Synthesis in Rat Hepatocyte In vivo
	HFC 134a: An Evaluation in the In vivo Cytogenetic Assay in Human Lymphocytes
PAFT II	
HCFC-141b	Skin Irritation in Rabbits of HFC 141b
	Primary Eye Irritation Study with HFC 141b in Rabbits
	Acute Oral Toxicity Study with HFC 141b in Male Rats
	Acute Dermal Toxicity Study of HFC 141b in Rabbits
	Mouse Bone Marrow Micronucleus Assay of HFC 141b
	Irritant Effects on the Rabbit Eye of 4874-89 (HFC 141b)
	Irritant Effects on Rabbit Skin of 4874-89 (HFC 141b)
	Acute Dermal Toxicity to Rats of 4874-89 (HFC 141b)
	HFC 141b: 2-Week Inhalation Toxicity Study in the Rat
	PWC 4874-789 Acute Inhalation Toxicity Study in Rats ($-Hour Exposure)
	1,1-Dichloro-1-fluoroethane: 4-Week Inhalation Toxicity Study with Fischer 344 Rats
	1,1-Dichloro-1-fluoroethane: 13-Week Inhalation Toxicity Study with Fischer 344 Rats
	Delayed contact Hypersensitivity in the Guinea Pig with 4874-89 (HFC 141b)

TABLE 2-4 (cont)

	HCFC-141b - Assessment of Mutagenic Potential in Amino-Acid Auxotrophs of Salmonella typhimurium and E. coli including the First Amendment
	A Study of the Effect of HCFC 141b on the Pregnancy of a Rat
	A Study of the Effect of HCFC 141b on the Pregnancy of the Rabbit
	Acute Oral Toxicity to Rats of PWC 4874-89
	Acute Inhalation Toxicity of FC141b in Rats
	Acute Dermal Toxicity of FC 141b in Rats
	Acute Oral Toxicity Studies of FC 141b in Rats
	HCFC 141b: Cardiac Sensitization in Monkeys and Dogs
	HCFC 141b: Final Report - Preliminary Pharmacokinetics
	Determination of Acute Toxicity of HCFC 141b to Daphnia magna
	Determination of Acute Toxicity of HCFC 141b to Brachydanio rerio
	Exposure of Cultured Human Lymphocytes to Vapors of HCFC 141b
	Effects of HCFC 141b on Chromosome of Culture Chinese Hamster Ovary Cells

2.4 DEGRADATION OF HCFCS AND HFCS

The HCFCs and HFCs are considered as acceptable substitutes for the CFCs because of their greater reactivity and, thus, shorter environmental lifetimes. This characteristic would tent to make these chemicals subject to some degradation in certain uses. Industry has provided EPA with the results of a review of published and unpublished information on the decomposition of HCFCs and HFCs. This information suggests that

HCFC-123 can decompose to HCFC-133a depending on such factors as temperature, the presence of metals, the presence of organic materials (such as oil), and pH. Other halogenated hydrocarbons, including halogenated butenes, were also reported.

A variety of toxicity studies of HCFC-133a were run in the 1970s (see hazard assessment support document, Appendix A). HCFC-133a was found to be toxic and industry dropped their interest in the compound as a commercial product. HCFC-133a was carcinogenic in a rat study where 300 mg/kg/day was administered orally for one year (Longstaff et al., 84). Animals were held until week 125 and then examined. HCFC-133a has also been tested in a series of dominant lethal assays in mice (Hodge et al., 79d; 80; Kilmartin et al., 80). HCFC-133a caused reduced fertility and sperm abnormalities at 100 ppm and greater.

There are great uncertainties regarding the levels of HCFC-133a that would form under actual conditions of use and storage. Most of the currently available data were generated under stress conditions. Industry has provided EPA with screening test results designed to examine the compatibility of HCFC-123 with various materials present in large refrigeration systems, rigid foams, and solvent applications. Some of these conditions probably exceed those that would be encountered in practice, and, in general, it was under these conditions that the highest levels of HCFC-133a were found as breakdown products.

Research to develop better information related to degradation under actual use conditions and the employment of possible stabilizers, is underway and will be evaluated as it becomes available. In particular, tests are being conducted to determine the extent to which decomposition products form over longer periods of time during use. The potential for adverse health effects from exposure to HCFC-133a and other decomposition products will be evaluated when potential exposures are characterized.

3. OCCUPATIONAL EXPOSURE

This section characterizes potential occupational exposures resulting from routine use of the eight HFCs and HCFCs. Potential exposures resulting from accidental releases of HFC/HCFCs are not addressed in this document. Although numerous other chemicals and/or alternative technologies having the potential for replacing CFCs have been identified, an assessment of these alternatives is beyond the scope of this document. The information presented in this report is contained in a draft document titled, "Occupational Exposure and Environmental Release Data for Chloroflourocarbons (CFCs) and their Substitutes, (PEI, 1990).

The following occupational exposure scenarios are addressed in this section: manufacture, foam blowing, refrigeration, mobile air-conditioning, sterilant carrier, and metal and electronics cleaning. As can be seen from Table 3-1, these scenarios correspond to uses that account for the great majority of CFC consumption. Table 3-2 provides a summary of potential uses for the eight HFCs and HCFCs as described in recent United Nations Environment Programme (UNEP) documents.

Occupational exposure assessments require information on: the populations exposed; worker activities leading to exposure; routes of exposure; and the frequency, duration, and levels of exposure. Providing there is a complete and representative set of information, a comprehensive exposure assessment would relate worker activities to exposures and present the range and the distribution of monitoring data. In the case of the above HFCs and HCFCs (except for manufacturing and to a limited extent for certain foam blowing operations) there were no personal monitoring data available to characterize potential exposures, primarily because these chemicals are not currently in significant commercial use.

TABLE 3-1 EXISTING CFC U.S. CONSUMPTION SUMMARY, 1985

USE	CFC consumption, million kilograms				
	CFC-11	CFC-12	CFC-113	CFC-114	CFC-115
Foam blowing	68	16	None	3.5	None
Refrigeration(1)	8	47	None	0.5	5
Mobile air conditioning	None	44	None	None	None
Sterilant carrier	None	22	None	None	None
Electronics and Metal Cleaning	None	None	69	None	None
Aerosol Use	4	8	Unknown	Unknown	None
TOTAL	80	137	69	4.0	5

Source: EPA, 89a
Note:

(1) Refrigeration includes both commercial refrigeration and air conditioning

TABLE 3-2 LIKELY HCFC AND HFC SUBSTITUTES FOR CFC USES

USE	HCFC22	HCFC123	HCFC124	HFC125	HFC134a	HCFC141b	HCFC142b	HFC152a
Foam blowing	X	X				X	X	
Refrigeration (1)	X	X	X	X	X	X	X	X
Mobile air conditioning	X		X		X		X	X
Sterilant carrier		X	X			X		
Electronics Metal Clean		X	X			X		

An "X" indicates the HCFC or HFC may possibly be a CFC substitute for the use noted. A blank space indicates no information was found indicating that this HCFC or HFC may be a CFC substitute for the use noted.

Sources: UNEP, 89a; UNEP, 89b; UNEP, 89c; UNEP, 89d.

Note:

(1) Refrigeration includes both commercial refrigeration and air conditioning

Two techniques were used to estimate the range of possible exposure levels: a surrogate approach, based on existing CFC personal inhalation monitoring data, and modeling. For each of these analytical approaches, both mid-range and outerbound occupational exposures were estimated based on available information, including information on the existing CFCs. Mid-range exposures are presented to provide a sense of what likely or average exposures may potentially be. The Agency has a high degree of confidence that potential exposures are likely to be less than the outerbound level presented; there is more uncertainty in the estimates of the mid-range values. The two techniques used to estimate exposure are discussed below, followed by a summary of key data sources used in these analyses.

3.1 SURROGATE APPROACH

Data on the existing CFCs offer some promise as surrogate information to assess potential exposures to the substitutes because of the similarities in their use patterns as well as their physical/chemical properties relative to the HFCs and HCFCs. Some physical and chemical properties of the HFCs and HCFCs are presented in Table 3-3.

The use of existing CFC exposure data as a surrogate method for quantifying exposures to the HFCs/HCFCs has several important limitations that must be noted:

- First, only a limited amount of data was found on the existing CFCs and it may not be representative of typical workplace exposures. A significant proportion of the data was collected by NIOSH in response to complaints. Therefore, there may be some biases associated with this data.

- Second, since the HFCs and HCFCs will not be "drop-in" substitutes in most cases, industry will need to design new equipment. The higher cost of the substitutes and anticipated State and Federal regulations, such as the Amendments to the Clean Air Act, will move industry towards developing new equipment that will minimize releases of HFC/HCFCs to the workplace and the environment. Because EPA does not possess actual data which show the effect of potential technological changes on the actual workplace exposures, reductions could not be quantified in the surrogate approach.

- Third, the exposures to the substitutes, (particularly the outerbound exposures) may effectively be reduced if threshold limit values (TLVs) or other recommended or required exposure limits are established which are below those currently in place for the existing CFCs.

TABLE 3-3 SELECTED PHYSICAL CHARACTERISTICS OF THE HFCs/HCFCs

Characteristics	HCFC-22	HCFC-123	HCFC-124	HFC-125
Formula	$CHClF_2$	CF_3CHCl_2	CF_3CHClF	CF_3CHF_2
Appearance	colorless	colorless	colorless	colorless
Odor	ethereal	ethereal	odorless	ethereal
Physical State	gas	liquid	gas	gas
Molecular Weight	87	153	137	120
Vapor Pressure, mmHg	10,995	688	3155	9309[b]
Boiling Point, °C	-40.8	27.9	-10.2	-48.5
Water Solubility[a]	0.300	0.39	1.71	0.094

TABLE 4-3 continued

Characteristics	HFC-134a	HCFC-141b	HCFC-142b	HFC-152a
Formula	CF_3CH_2F	CCl_2FCH_3	$CClF_2CH_3$	CHF_2CH_3
Appearance	colorless	colorless	colorless	colorless
Odor	ethereal	ethereal	ethereal	faint
Physical State	gas	liquid	gas	gas
Molecular Weight	102	117	101	66
Vapor Pressure, mmHg	4965	517	2260	4018
Boiling Point, °C	-26.5	32.0	-9.8	-25.8
Water Solubility[a]	0.15	0.5[b]	0.5	1.7

[a] Water solubility in lb/100 lb H_2O at 25°C.

[b] Estimated by a duPont representative.

Source: Modified from PEI, 1990.

3.2 MODELING

The modeling technique used in this assessment has been used in the past by EPA to develop risk management decisions. The model chosen uses a mass balance approach coupled with assumptions regarding the size and duration of releases, room size, and the extent of ventilation to estimate worker exposures in enclosed spaces. Engineering judgment was used to estimate typical ranges and distributions of possible values of the model input variables. A Monte Carlo selection technique was used to calculate corresponding distributions of potential exposures.

In this analysis, modeling was used to estimate potential worker inhalation exposures to CFC substitutes during manufacture and servicing of commercial refrigeration and air conditioning systems and also during the charging and servicing of mobile air conditioners. The model used requires estimates of five key parameters. The distributions of possible values for two of these parameters, air exchange rate, and mixing factor were assumed to be the same for each exposure scenario modeled. The distribution of possible values for the remaining three parameters; room volume, duration of release and emission mass were varied depending on the exposure scenario being evaluated. The ranges of values chosen for the air exchange rates and mixing factors assumed are given below.

Model Input Parameter	Range
Air exchange rate(air changes/hour)	1 - 10
Mixing Factor(dimensionless)	0.3 - 1.0

These ranges of model input parameters are believed to be representative of current industrial ventilation practices. The ranges of possible values for the other three model input parameters are given in Sections 3.7 and 3.8.

There is considerable uncertainty whether the modeled exposures are truly representative of future CFC substitute exposures. This uncertainty originates predominantly in assumptions used for model input variable values such as amounts of CFC substitutes released into the workplace and ventilation rates of enclosed spaces where exposures occur. In addition, the extent to which future differences in work practices and equipment design will reduce substitute exposures is unknown. Attempts were made to recognize the potential exposure reduction of CFC substitute recycling and release prohibitions in the modeling used to estimate the occupational exposures.

3.3 DATA SOURCES

The major sources of data on occupational exposure cited in the PEI report include:

- A database maintained by the Occupational Safety and Health Administration (OSHA) which contains records on 1400 chemicals regulated by OSHA and monitored (mostly for enforcement purposes) since 1981.

- Information from National Institute of Occupational Safety and Health (NIOSH) studies such as Health Hazard Evaluations (HHEs) and Industry Wide Surveys (IWSs).

- Information voluntarily submitted to the EPA in conjunction with responses to requests for information under Section 114 of the Clean Air Act.

- Information voluntarily submitted to the Agency by manufacturers and users of CFCs and their substitutes during the development and review of this document.

- Modeling techniques which were used to predict potential exposure levels in the absence of data.

The above data sources only contained data on exposures through inhalation. It should be noted that the majority of the personal inhalation monitoring data were taken in response to complaints and the extent that they accurately characterize potential exposures without any biases is not known. Therefore there is no way of knowing whether these data are truly representative of actual CFC exposures. This uncertainty is further compounded by the use of existing CFC data as surrogates for CFC substitutes for many exposure scenarios.

No data on dermal exposure were found. However, the high volatility of CFCs and many of the substitutes are expected to significantly limit any dermal exposure. For this reason, dermal exposures are not addressed in this analysis.

3.4 SUMMARY AND CONCLUSIONS

Tables 3-4 and 3-5 summarize the results of this preliminary assessment which are described in more detail in the following sections by end use. The results presented here rely heavily on the limited data set for existing CFCs.

TABLE 3-4: ESTIMATED POTENTIAL WORKPLACE EXPOSURES FOR CFC SUBSTITUTES FOR SCENARIOS WHERE MONITORING DATA IS AVAILABLE(1)

SCENARIO	NUMBER OF SITES	NUMBER OF WORKERS		8 HR-TWA INHALATION EXPOSURE		15 MINUTE PEAK EXPOSURES
		PER SITE	TOTAL	Mid-range (ppm)	Outerbound (ppm)	(PPM)
MANUFACTURE	<11	50-145	550 TO 1600	10	100	<1000
FOAM BLOWING						
Rigid	<85	2-10	170-850	20	500	<5000
Flexible	<144	2-10	288-1440	5	55	<550
STERILANT CARRIER	6,000	5	30,000	--	3(2)	15(3)
ELECTRONICS CLEANING	6,700(4)	3	20,100	20	1000	<10,000
METAL CLEANING	12,200(4)	3	36,600	10	1000	<10,000

NOTES

1. Dermal exposures are expected to be minimal for each scenario.
2. Exposure was based on PEL for Ethylene Oxide.
3. 10 minute exposure.
4. The number of sites assumed to be the same as the number of operating units.

TABLE 3-5: ESTIMATED POTENTIAL WORKPLACE EXPOSURES (1,2) FOR CFC SUBSTITUTES BASED ON MODELLING TECHNIQUES

SCENARIO	NUMBER OF SITES	NUMBER OF WORKERS		8 HR-TWA INHALATION EXPOSURES		15 MINUTE PEAK EXPOSURES
		PER SITE	TOTAL	Mid-range (ppm)	Outerbound (ppm)	(PPM)
REFRIGERATION SERVICING (3,7)						
Retail Food Storage	305,000(6)	1-2	1220-2440	20	71	497
Cold Storage Warehouses	76,000(6)	1-2	300-600	20	48	325
Chillers	25,000(6)	1-2	100-200	66	171	1179
Industrial Process Coolers (5)	>1,000,000(6)	1-2	8500-25000	14(8)	42(8)	313(8)
MOBILE AIR-CONDITIONING (4)						
Manufacture	64	20	1280	53	105	158
Servicing	329,000	1-5	329,000 - 1,654,000	7	21	26

NOTES

1. Dermal exposures are expected to be minimal for each scenario.
2. Emission masses for servicing scenarios take into account recycling required by 1990 Clean Air Act
3. Refrigeration exposures were based on modelling using HCFC-22 as a model compound except for chillers which used HCFC-123
4. Mobile air-conditioning exposures were based on modeling using HFC-134a as a model compound.
5. This scenario includes ice machines, skating rinks, and chemical plant and refinery process coolers.
6. The number of sites was assumed to be the same as the number of services per year.
7. Refrigeration includes both commercial refrigeration and air conditioning.
8. These estimates are for servicing of medium sized ice-machines which make up the bulk of this category.

Additional data characterizing actual HFC/HCFC use and exposures would improve this assessment. Exposure monitoring studies of actual worker activities associated with the use of HFCs/HCFCs are particularly needed to reduce the uncertainties associated with the current exposure characterization. There are several important issues that must be considered when developing plans for monitoring studies to gain additional data. To ensure that monitoring data collected is representative of actual potential exposures, the variables that affect the measured exposures should be characterized and known to be within the bounds of what may reasonably be expected to occur in actual practice. The major variables that are expected to affect exposures include:

- Worker activities and work practices.
- Quantities and rates of HFC/HCFC used and potentially released.
- Technologies and equipment used.
- Engineering controls that limit exposures such as ventilation rates.
- Personal protective equipment.
- Physical/chemical properties such as vapor pressures and molecular weights. If existing CFCs are used to simulate the HFCs and HCFCs, then they should have properties that are similar.
- Concerns regarding the relatively greater toxicity of the substitutes.

Plans for obtaining monitoring data must also address the issue of how many measurements are necessary to fill the perceived data gaps. EPA would like the opportunity to meet with industry to discuss specific monitoring protocols before any data are collected.

3.5 MANUFACTURE

HFCs and HCFCs will be manufactured by chlorinating and/or fluorinating volatile chlorinated solvents in continuously operating, contained systems.

Because manufacturing plans are still being developed by industry, the potential number of manufacturing sites and production volumes for the eight HFCs and HCFCs are unknown. Based on the average plant capacity data for the existing CFCs, an average daily throughput for a CFC substitute may be 32,200

kg/site-day. It is assumed that the potential total number of manufacturing sites will be similar to the number used to manufacturing current CFCs, which is 11. This number probably overstates the future markets for HFCs/HCFCs, given their relatively high costs and the availability of other non-HFC/HCFC substitutes.

No information was found on the number of workers potentially exposed at existing or substitute CFC manufacturing sites. It is estimated that 50 to 145 workers per site could be exposed. Therefore, the total number of workers exposed is estimated at 550 to 1600.

Workers could potentially be exposed during quality control sampling, packaging and shipping, and maintenance activities. Workers may be exposed for up to 8 hours per day, 250 days per year.

Workers at CFC manufacturing facilities typically do not use personal protective equipment (PPE) to limit inhalation of CFCs under normal operating conditions. However, the use of toxic gases such as chlorine in the CFC manufacturing process requires a substantial amount of engineering controls that effectively limit exposure to those chemicals. In some instances, these controls also serve to limit exposure to CFCs.

Occupational exposures to HFCs and HCFCs are expected to be similar to the existing CFCs because of their similar physical and chemical properties. Personal monitoring data found for CFCs, HFCs, and HCFCs (8-hour TWA) are displayed in Table 3-6. It is not known whether this data set is representative of all CFC or CFC substitute manufacturing operations. However, it is believed that outerbound 8-hour TWA exposures to the HFCs and HCFCs can be expected to be below 100 ppm, if controls that are commonly found in existing CFC manufacturing environments are used. The geometric mean of 8-hour exposure data currently available indicate that mid-range exposures could be less than 10 ppm.

No short-term exposure data for the CFCs, HFCs, or HCFCs were found. EPA investigations into occupational exposures to other volatile chlorinated compounds during use in metal and electronics cleaning and dry cleaning operations indicate that 15-minute ceiling exposures can be an order of magnitude greater than 8-hour data. Based on these data, outerbound short-term exposures are estimated to be less than 1000 ppm. There is a high degree of uncertainty in this estimate due to the difference in activities that may result in peak exposures.

TABLE 3-6 PERSONAL INHALATION MONITORING DATA (8 HOUR TWA) FOR THE MANUFACTURE OF CFCS, HFCS, AND HCFCS

CFC	No. of sites	No. of samples	Range ppm	Geo. Mean ppm	Data Sources
CFC-11	2	29	0.7 - 90.7	6.4	NIOSH 114 letter
CFC-12	1	25	0.1 -159.0	3.3	NIOSH
CFC-113	2	15	0.1 -108.0	5.0	NIOSH 114 letter
CFC-115	1	12	0.1 - 34.0	0.9	NIOSH
HCFC-22	2	18	0.01- 11.0	0.6	NIOSH 114 letter
HCFC-123	1	5	0.2 - 10.8	0.9	114 letter
HCFC-141b	1	6	0.1 - 2.7	0.5	114 letter
HCFC-142b	1	6	0.1 - 3.7	0.5	114 letter
HFC-152a	1	3		1.5	NIOSH

3.6 FOAM BLOWING

Currently, CFC-11 and CFC-12 are used as blowing agents in the manufacture of rigid and flexible polyurethane (PUR) foams. CFC-11, CFC-12, CFC-113, and CFC-114 are also used as blowing agents in the production of other foams such as phenolic, polypropylene, polyethylene, PVC, and polystyrene foams. Foam production processes using HCFCs are expected to be technologically similar to those that currently use existing CFCs. HCFC-22, HCFC-123, HCFC-141b, HCFC-142b may be used in future foam blowing processes. It should be noted that the new Clean Air Act bans the use of HCFCs in non-insulating foams in three years. There is no information indicating that HFCs will be used in foam blowing.

3.6.1 RIGID PUR FOAMS

Rigid PUR foams are produced by four different processes: in the form of laminated boardstock; as bunstock; by pour-in-place/ injection; or by spray technology. There are an estimated

85 facilities operated by 55 firms that are major producers of rigid polyurethane foam. Average CFC throughputs were 2500 kg/site-day for CFC-11-based processes and 170 kg/site-day for CFC-12-based processes based on 1985 data.

The number of exposed workers for rigid foams is estimated to range from two to ten workers per site with the lower estimate for sprayed foam and the higher estimate for boardstock, bunstock, or slabstock plants. The total number of workers exposed is estimated to be 170 - 850.

Worker activities in the various foam manufacturing processes include: formulation of polyol and polyisocyanate solutions, sampling, monitoring foam machines and foam lines, and cutting and stacking foam. The presence of isocyanates in the work area, some of which have OSHA Permissible Exposure Limits (PELs) less than 1 ppm, may be a factor that minimizes exposure to CFCs and their substitutes. Workers may perform these activities for up to 8 hours per day for up to 250 days per year. No personal protective equipment is known to be routinely used to limit inhalation exposure to CFCs during foam manufacture.

There were 103 personal inhalation measurements for the manufacture of rigid foam using CFC-11 with a geometric mean of 18.3 ppm. These monitoring data are presented in Table 3-7, along with monitoring data for flexible foam. It is not known whether these data are representative of all foam blowing operations and, in particular, operations that may use HCFCs. However, considering the existing CFC data, mid-range exposures to HCFCs can be expected to be less than 20 ppm during rigid foam manufacturing, provided that engineering controls and operating practices similar to those used in existing CFC operations are used to limit exposure. Outerbound exposures to HCFCs are expected to be less than 500 ppm.

Limited short-term exposure data for rigid and flexible foam production were found and are displayed in Table 3-8. Because none of these data exceeded the maximum 8-hour measurements noted in Table 3-7, it was assumed that they were not representative of worst-case, short-term exposures. EPA investigations into occupational exposures to other chlorinated volatile compounds during use in metal and electronics cleaning and dry cleaning operations indicate that 15-minute exposures can be up to an order of magnitude greater than 8-hour data. Based on the 8-hour data and the results of the chlorinated volatile investigations outerbound, short-term occupational exposures are estimated to be about 5000 ppm for rigid foam. There is a high degree of uncertainty in this estimate because of the significant differences in activities that may lead to peak exposures.

TABLE 3-7 PERSONAL INHALATION MONITORING DATA (8 HOUR TWA) FOR FOAM BLOWING

Process	CFC	No. of Sites	No. of Samples	Range ppm	Geo. Mean ppm	Data Sources
Rigid Foam	CFC-11	16	103	0.2 - 540	18.3	NIOSH OSHA Industry
Rigid Foam	CFC-12	1	1	0.07		NIOSH
Flex. Foam	CFC-11	3	46	0.05 - 55.2	1.4	NIOSH OSHA

TABLE 3-8 15-MINUTE PERSONAL INHALATION MONITORING DATA FOR FOAM BLOWING

Process	CFC	No. of Sites	No. of Samples	Range ppm	Geo. Mean ppm	Data Sources
Rigid Foam	CFC-11	2	5	11.0 - 310.0	44.0	NIOSH OSHA
Rigid Foam	CFC-12	1	1	44.0		NIOSH
Flex. Foam	CFC-11	1	5	0.07 - 0.12	0.09	NIOSH OSHA

3.6.2 FLEXIBLE PUR FOAMS

Flexible PUR foams are produced by two main processes in the form of molded foam articles or slabstock. There are an estimated 105 facilities producing flexible polyurethane slabstock and 39 facilities operated by 28 firms producing flexible polyurethane molded foam. In 1985, an average facility using CFC-11 in flexible slabstock production had a CFC throughput of 435 kg/site/day. An average facility using CFC-11 in flexible molded foam production had a throughput of 325 kg/site-day in 1985.

It is expected that many producers of flexible foams will not convert their processes to HCFC blowing agents because of their high cost and the availability of cheaper alternatives. The number of sites using HCFCs as blowing agents for flexible

foams are expected to be much less than the number of sites currently using CFCs.

The number of exposed workers for flexible foams is estimated to range from two to ten workers per site. The lower estimate corresponds to sprayed-foam plants while the higher estimate is associated with boardstock, bunstock, or slabstock plants. The total number of workers exposed is estimated at 288 - 1440.

Worker activities in the various foam manufacturing processes are: formulation of polyol and polyisocyanate solutions, sampling, monitoring foam machines and foam lines, and cutting and stacking foam. The presence of isocyanates in the work area, some of which have OSHA Permissible Exposure Limits (PELs) less than 1 ppm, may be a factor that minimizes exposure to CFCs and their substitutes. Workers may perform these activities for up to 8 hours per day for up to 250 days per year.

No personal protective equipment is known to be routinely used to limit inhalation exposure to CFCs during foam manufacture.

There were 46 personal inhalation measurements for the manufacture of flexible foam using CFC-11, with a geometric mean of 1.4 ppm. These data are presented in Table 3-7. Considering the existing CFC data, mid-range exposures to HCFCs can be expected to be less than 5 ppm for flexible foam manufacture, provided that engineering controls and operating practices similar to those used in existing CFC operations are used to limit exposure. Based on available data, outerbound exposures to HFCs and HCFCs are expected to be less than 55 ppm for flexible foam. Outerbound short-term occupational exposures are estimated to be about and 550 ppm for flexible foam production.

3.7 COMMERCIAL REFRIGERATION AND AIR CONDITIONING

CFC-11, CFC-12, CFC-114, and CFC-115, as well as HCFC-22, are currently used as refrigerants in retail food storage, cold storage warehouses, chillers, industrial process refrigeration, as well as in other minor uses. Chillers are defined, for the purposes of this report, as the cooling systems used in commercial air conditioning applications. The four major applications account for a vast majority of the total CFC consumption for commercial refrigeration and air conditioning. The substitutes that may be used in the future include HCFC-123, HCFC-124, HFC-125, HFC-134a, and HFC-152a, as well as continued use of HCFC-22. Equipment for cold storage warehouses, chillers, and industrial process refrigeration can be either inside or outside of a building. Retail food storage equipment is always inside.

The greatest potential for occupational exposures to CFCs or their substitutes when used as refrigerants occurs during servicing. Currently, prior to servicing, a portion of a refrigeration system's charge may be vented to the atmosphere in an uncontrolled fashion resulting in exposure to workers. Recharging vented units may also lead to similar exposures. However, there are several factors that will change current worker exposures patterns including: the use of new equipment designs, which are essential as the CFC substitutes are not drop-in replacements; mandatory recycling under the Clean Air Act Amendments, and a prohibition on the venting of CFC substitutes, also under the Clean Air Act Amendments.

3.7.1 RETAIL FOOD STORAGE

Retail food storage refrigeration systems are used to refrigerate food (e.g., frozen foods and dairy products) and beverages in display cases or cabinets. These types of systems are located in convenience stores, small independent grocery stores, and large supermarkets. The average refrigerant charge is about 130 kilograms. There are approximately 305,000 retail food storage units currently operating. Servicing is estimated to occur once per year for each unit.

3.7.2 COLD STORAGE WAREHOUSES (CSWs)

Refrigeration systems are employed in CSWs to provide long-term storage during the distribution process of items such as meats, produce, dairy products, and other perishable foods. CSW refrigeration systems include both coolers and freezers. A typical unit is charged with 11,400 kg of refrigerant. There are an estimated 18,900 CSWs currently operating that use CFCs or HCFCs. CSW units are reported to be serviced four times per year.

3.7.3 CHILLERS

A chiller is a critical part of air conditioning systems used to cool large buildings, hospitals, and schools. The chiller system consists of a central refrigeration unit that "chills" a secondary fluid (e.g., water or brine), which is circulated through remote heat exchangers to cool air. Typical refrigerant charge quantities can vary from 65 to 1200 kilograms. 100,000 chillers are currently in operation. Each system may receive service once every four years.

3.7.4 INDUSTRIAL PROCESS REFRIGERATION

Industrial process refrigeration systems are used for a wide variety of purposes ranging from storing volatile liquids to maintaining ice rinks. Process refrigeration may be used in facilities such as refineries, chemical plants, dairy and meat packing plants, and ice making plants. The refrigerant may provide cooling directly to the surface to be cooled or be used to cool a secondary working fluid. These systems may contain refrigerant charges that range in size from one to several thousand kilograms. It is estimated that more than 1 million industrial process refrigeration units may currently be in service. Servicing is estimated to occur two to three times per year.

3.7.5 SERVICING

Assuming one to two workers are exposed during each servicing, each service takes an entire working day, and each service employee works 250 days/year, the total number of workers exposed per year for each application is estimated to be:

retail food storage	1220 - 2440
cold storage warehouses	300 - 600
chillers	100 - 200
industrial process refrigeration	8500 - 25000

No personal protective equipment or engineering controls are known to be routinely used to limit inhalation exposure to CFCs during servicing of refrigeration units.

Only six 8-hour personal exposure measurements were found for workers to CFCs during refrigeration servicing. These data are presented in Table 3-9. This data set is not extensive enough to draw conclusions regarding 8-hour exposures. In addition, no short-term CFC substitute exposure data were found for workers servicing commercial refrigeration and air conditioning equipment. Therefore, modeling estimates of exposures were made using HCFC-22 as a representative compound for retail food storage, cold storage warehouses and industrial refrigeration. HCFC-123 was used as a representative compound to estimate occupational exposures related to servicing of chillers.

The ranges of values of exposure scenario-specific model inputs used to estimate exposures during commercial refrigeration and air conditioning servicing were:

	Room Volume (m^3)	Emission Mass (kg)	Duration of Release(min)
Retail Food Storage	500-10,000	0.91-3.65	5-30
Cold Storage Warehouses	250-1,000	0.23-0.68	5-30
Chillers	250-1,000	1.25-5.0	5-30
Industrial Process Refrig.	250-1.000	0.45-0.90	5-30

The room volume range chosen for retail food was intended to encompass the sizes of typical retail food stores. The room volume ranges for the other applications were intended to encompass the sizes of small compressor rooms. The ranges of emission masses used in the modeling were based on assuming that a portion (generally less than 5% for the above scenarios) of a cooling system's refrigerant charge is vented during servicing. These estimates of emission mass assume some portion of the refrigerant charge is recycled. Emissions into the workplace were assumed to last from 5 to 30 minutes.

Mid-range and outerbound exposures were modeled to be:

	8-hour TWA Mid-range ppm	8-hour TWA Outerbound ppm	15-minute Outerbound ppm
Retail Food Storage	20	71	497
Cold Storage Warehouses	20	48	325
Chillers	66	171	1179
Industrial Process Refrig.	21	71	476

TABLE 3-9 PERSONAL INHALATION MONITORING DATA (8 HOUR TWA) FOR SERVICING OF REFRIGERATION UNITS[a]

CFC	No. of Samples	Range ppm	Data Source
CFC-12	2	0.7	OSHA
CFC-115	2	1.6 - 2.2	NIOSH
HCFC-22	2	0.8 - 1.4	NIOSH

[a] Each line of data represents measurements at a single site.

A recent Finish (Antti, 1990) paper included data on short-term HCFC-22 exposures experienced during refrigerator repair work. The exposures presented ranged from 1300 to 10,000 ppm. The duration of the exposures were cited to be 70 to 150 minutes.

3.8 MOBILE AIR-CONDITIONING

Currently, CFC-12 is the only CFC used in mobile air-conditioning. HCFC-22, HCFC-124, HCFC-142b, HFC-134a, and HFC-152a may be used in the future.

3.8.1 MANUFACTURING

Mobile air conditioners (MACs) are refrigeration systems that are installed in motor vehicles to provide cooling in the passenger area. MACs are installed in automobiles, light-duty trucks, heavy-duty trucks, and buses during vehicle manufacture as original equipment.

There are 64 vehicle manufacturing sites in the U.S. where MACs are installed in vehicles. In 1985, U.S. production of motor vehicles was approximately 11.7 million vehicles. A typical charge of CFC-12 in MACs is approximately 1 kilogram.

It is estimated that up to 20 workers per manufacturing site will be involved in this activity. The total number of workers potentially exposed to CFC substitutes during MAC manufacture is estimated to be 1280.

The process for charging MACs with HFCs/HCFCs during vehicle manufacture is expected to be similar to existing operations. Although HFCs and HCFCs are comparable with the current MAC systems, some necessary modifications prevent them from being drop-in substitutes. MAC compressors will have to be redesigned to compensate for efficiency losses resulting from the inherent chemical properties of the HFCs and HCFCs. Use of substitutes may also require the development of alternate compressor oils and hose material. Increased costs of refrigerants may result in greater emphasis on recovery and recycle systems prior to servicing or disposal of motor vehicles.

No 8-hour TWA monitoring data were found for charging MAC units at auto manufacturing sites. However, monitoring data were found for the charging of refrigerants to household refrigerators at assembly plants, which is a similar operation. Personal inhalation exposures of CFC-12 in this study ranged from 0.7 to 4.9 ppm. The same model used to estimate exposures in refrigeration servicing was used to predict 8-hour mid-range and outerbound exposures of 53 and 105 ppm respectively. HFC-134a was the modelled substitute.

For modeling purposes, MAC manfacturing room volumes were assumed to be 5,000 to 20,000 m^3. The emission mass range was based on an analogy to measured releases during manufacturing of household refrigerators. Emissions to the workplace were assumed to last from 5 to 30 minutes.

No short-term exposure data was found for auto manufacturing sites. The model that was used to predict exposures in refrigeration servicing predicted 15-minute exposures of 158 ppm.

3.8.2 SERVICING

MAC system repairs are performed in factory-authorized shops, independent repair shops, and by the vehicle owner. The number of service sites in the U.S. was estimated in 1986 to be 329,000. The number of MACs serviced per site per year may range from 11 for a fleet maintenance shop to 170 for a new car/truck dealer.

The number of workers servicing MACs is estimated to be from 1 to 5 per site. The total number of workers potentially exposed to HFCs/HCFCs during MAC servicing is estimated to range from 329,000 to 1,654,000.

Prior to servicing, MAC units are frequently vented to the atmosphere in an uncontrolled manner. Recharging, after servicing, is performed manually. The recharging is usually accomplished by connecting a pressurized container of refrigerant to the MAC. Recharging can also be performed using prepackaged aerosol cans of refrigerant.

Servicing and recharging practices are expected to be modified for the HFCs and HCFCs. It is anticipated that recovery units will be put into service to recover the used refrigerant that had been vented prior to servicing, thereby limiting environmental releases and worker exposure. Some states are enacting recycling legislation, and the anticipated Clean Air Act amendments would require mandatory recycling of MAC refrigerants. These systems would have to purify recovered refrigerant before it could be returned to MAC systems for reuse.

No personal protective equipment are known to be routinely used to limit inhalation to CFCs during the MAC recharging or servicing. Some service sites may have ventilation systems to dilute potential exposures when service is performed in service bays with closed doors.

No data on 8-hour or short term occupational exposures to CFCs or their substitutes were found for MAC service sites. Estimates of occupational exposures during MAC recharging and servicing (venting and recharging) were developed using the same model used in refrigeration servicing. HCFC-134a was the compound used in the modeling. An outerbound modeling estimate of 8-hour exposure with recycling is 21 ppm. An outerbound estimate of 15-minute exposures with recycling is 26 ppm.

For modeling purposes, MAC servicing room volumes were assumed to range from 250 to 10,000 m^3. This range was intended to encompass service facilities that have one to several service bays. The emission mass range was based on information on average release quantities during servicing. These estimates of emission mass assume some portion of the refrigerant charge is recycled. Emissions to the workplace were assumed to last 5 to 20 minutes.

3.9 STERILANT CARRIER

Currently, CFC-12 is the only CFC used as a sterilant carrier. In this application, CFC-12 is used as a flame suppressant carrier for ethylene oxide, which is used to destroy bacteria, viruses, and fungi present on contaminated hospital equipment. CFC-12's function is to serve as an inert diluent to reduce the flammability concerns associated with handling pure ethylene oxide. The ethylene oxide/CFC-12 mixture makes contact with the contaminated hospital equipment in sealed vessels. HCFC-123, HCFC-124, and HCFC-141b are potential substitutes for CFC-12 due to similar physical properties.

A 1977 source estimates that there are about 6,000 hospitals in the U.S. that have sterilizers. Most hospitals operate more than one sterilizer. NIOSH National Occupational Hazard Survey (NOHS) data indicate that approximately 30,000 workers in the health care field are potentially exposed to CFC-12 in sterilant use. Based on the above data, there would be an average of 5 workers per site.

Worker activities for sterilization operation include loading, operating, and unloading sterilizers; transferring sterilized articles to aerators; unloading aerators; and putting the articles into a sterilized storage area. There are also workers involved in washing instruments and carts, folding linens, and wrapping and packaging items for sterilization.

Typically, engineering controls are used to limit exposure to ethylene oxide. These include a dedicated local exhaust ventilation that directs air away from areas in which workers function. The only personal protective equipment expected to be used is gloves, which are used when removing sterilized articles.

No exposure data were found for CFC substitutes. A limited amount of personal monitoring data for CFC-12 used as a sterilant was found. Table 3-10 presents a summary of these data. These data are probably not relevant to this assessment because the OSHA PEL for ethylene oxide has recently been reduced to 1 ppm. Using the new OSHA PEL coupled with adjustments for differences in vapor pressures and solution concentrations, exposures to CFC substitutes are estimated to be about 3 ppm.

Short term (15 minute) HFC/HCFC exposures are estimated to be less than 15 ppm. This estimate was developed by considering the recently modified NIOSH Recommended Exposure Limit (REL), which is a 10 minute ceiling, for ethylene oxide and adjusting this value for differences between CFC-12 and ethylene oxide vapor pressures.

TABLE 3-10 PERSONAL INHALATION MONITORING DATA (8 HOUR TWA) FOR CFC-12 USE AS A STERILANT CARRIER[a]

No. of samples	Range ppm	Data Source
3	1.3 - 27.9	NIOSH
1	0.5	NIOSH
4	0.9 - 32.0	OSHA
1	1482.7	OSHA[b]

[a] Each line of data represents measurements at a single site.
[b] This measurement was taken at a facility which has been out of business since 1981.

3.10 ELECTRONICS AND METAL CLEANING

CFC-113 is used in the electronics industry to clean printed circuit (PC) boards and other equipment. It also has applications in a variety of other manufacturing and service industries to degrease and clean metal parts. Although CFC-113 is the only existing CFC which is currently used extensively in these applications, methyl chloroform as well as several other chlorinated solvents are also used. CFC-113 usage has been greatest in areas requiring "precision" cleaning. HCFC-123 and HCFC-141b may be used in the electronics and metal cleaning applications in the future. An azeotrope of these two HCFCs and methanol is particularly promising for PC board cleaning.

There are two major types of cleaning processes in which CFC-113 is used: vapor degreasing and cold cleaning. Vapor degreasers are used primarily in electronics industry applications. There are an estimated 6000 vapor degreasers operated by the electronics industry. An additional 700 units are used to clean other kinds of electronic cleaning operations. Annual CFC-113 consumption in electronics applications is estimated to be 26 million kilograms per year.

There are an estimated 12,200 vapor degreasers and cold cleaning units operated to clean metal parts. This cleaning may be necessary for subsequent assembly, painting, welding, electroplating, and further inspection. Approximately 43 million kilograms of CFC-113 are consumed per year for these uses.

An estimated 3 workers per cleaning unit are potentially exposed to CFC-113 during electronics and metal cleaning operations. Worker activities that may contribute to exposure include transfer of CFC solvent to cleaning equipment, handling of cleaned articles during their removal from the cleaners, and disposal of dirty solvent.

No information was found on personal protective equipment used in solvent cleaning operations. Ventilation is used frequently to limit worker exposure. Engineering controls and operating practices that limit CFC loss, such as keeping equipment sealed, positioning work to minimize drag out, and directing solvent sprays below vapor levels, will also reduce occupational exposures.

Table 3-11 displays pertinent occupational exposure data for CFC-113-based electronics and metal cleaning operations. The geometric means of the data indicate that mid-range or expected likely exposures for PC Board Cleaning can be expected to be less than 20 ppm and less than 10 ppm for metal cleaning. Given the range of the CFC-113 data, workers attending similar HCFC-based operations in the future can be expected to have outerbound 8-hour exposures of less than 1000 ppm.

TABLE 3-11 PERSONAL INHALATION MONITORING DATA (8 HOUR TWA) FOR CFC-113 IN ELECTRONICS AND METAL CLEANING

Process	No. of sites	No. of samples	Range ppm	Geo. Mean ppm	Data Source
PC Boards	16	62	0.04 - 890.0	19.3	NIOSH OSHA Industry
Other Elect. Cleaning	48	144	0.001 - 970.0	8.1	NIOSH OSHA
Metal Cleaning	29	55	0.04 - 730.0	8.3	NIOSH OSHA

Table 3-12 displays short-term data for CFC-113. Short-term exposures to CFC substitutes are hard to gauge with this limited amount of data. EPA has gathered data on worker exposures to methylene chloride during electronics cleaning and trichloroethylene during vapor degreasing. These data indicate that outerbound short-term HFC/HCFC exposures during electronics and metal cleaning should be less than an order of magnitude greater than the 8-hour data or 10,000 ppm.

TABLE 3-12 15 MINUTE PERSONAL INHALATION MONITORING DATA FOR CFC-113 IN ELECTRONICS AND METAL CLEANING

Process	No. of sites	No. of samples	Range ppm	Geo. Mean ppm	Data Source
Other Elect. Cleaning	4	10	3.1 - 330	73.7	NIOSH OSHA

4. CONSUMER EXPOSURE

This section presents a summary of EPA's assessment of the potential exposures to consumers which could occur from the use of the HFCs and HCFCs. Since no exposure data for these chemicals existed, the exposure assessment was based on analogies to present CFC use exposure.

This assessment estimates amounts of individual exposure and the populations exposed for representative scenarios. Because of EPA's mission to safeguard human health, these exposures have been estimated conservatively; that is, the assumptions selected in the estimation process have in some cases tended to drive estimates of exposure to the high end of the range. These exposure and population values are believed to be possible based on the information presently available. In these estimates, it has been assumed that the HFCs and HCFCs will completely replace present CFCs in both the type and extent of use described. The maximum exposures reported are not likely to apply to the entire exposed population.

The consumer product use scenarios discussed in this report are a few of the applications that may cause exposures to CFC substitutes. They were selected because they satisfied at least one of the following conditions: large percentages of CFCs are used in the application; the application was believed to have a greater potential for either short-term high exposures or long-term lower level exposures when compared to other applications; and information useful to the assessment was readily available for the application. Consumer exposure to CFCs, and by analogy HFCs and HCFCs, is estimated for the following scenarios: refrigerated home appliances, motor vehicle air conditioning, and video tape head cleaners. Table 4-1 presents the estimated exposures and the exposed populations.

Two other uses which meet the preceding conditions are rigid closed cell foam insulation and rigid polystyrene foam used in food packaging. Consumer exposures to emissions from foam insulation are not estimated here because an industry-sponsored foam insulation testing program is currently underway which is intended to provide more complete blowing agent emission rate data than that currently available. Consumer exposure is also not estimated here for food packaging, which is subject to Food and Drug Administration regulations.

TABLE 4-1 POTENTIAL CONSUMER INHALATION EXPOSURES TO HFCs/HCFCs

Scenarios	Exposures (mg/yr)	Exposure population sizes[a]
Household Appliances (Normal leakage)		
Refrigerator[b]		
10th percentile house[c]	5.1 or 15.3	12.5×10^6 each
Mean house[d]	2.1 or 6.5	87.5×10^6 each
Freezer[b]		
10th percentile house	10.2 or 20.4	5.5×10^6 each
Mean house	4.3 or 8.6	38.5×10^6 each
Dehumidifier		
10th percentile house	14.7	2.4×10^5
Mean house	6.2	1.7×10^6
(Service emission[e])		
10th percentile	1529	NA
Mean	647	NA
Mobile Air Conditioners (System leakage[f])		
Subcompact	0.76 or 167	7.2×10^6
Compact	1.09 or 218	8.4×10^6
Midsize	1.37 or 240	16.8×10^6
Large	1.61 or 259	13.5×10^6
(Recharging)	865	2.1×10^6
Video Tape Head Cleaners	21	55×10^6

[a] The distribution of the estimated exposed population among the levels of exposure estimated for each scenario is not known. Maximum exposures are not likely to apply to the entire exposed population. Populations estimated for the 10th percentile volume house are one-tenth of the total estimated exposed population. Those estimated for the mean volume house are 70 percent of the total estimated exposed population.

[b] Refrigerators and freezers may have either reciprocating or rotary compressors. The former require less charge and are estimated to have proportionately lower emissions, and the lower estimated exposures shown here.

[c] The 10th percentile house volume equalled 174 m^3.

[d] The mean house volume equalled 411 m^3.

[e] Service emissions are estimated to occur once every 13 years.

[f] System leakage may be in engine compartment or in evaporator case. The latter causes the higher exposures to vehicle passengers shown here.

The range in appliance exposure estimates are due to different house volumes and charge sizes. Differences in motor vehicle air conditioning exposure estimates are from different leak locations and passenger compartment volumes.

Sources of uncertainty for each scenario are as follows:

- In the home appliance scenario, limited information was available for differences in the size and frequency of service releases. Refrigerant reclamation and recycling during servicing would be expected to lower or eliminate the service releases.

- In the automobile air conditioning refrigerant leakage scenario, the chief uncertainties are: the fraction of refrigerant leakages that occur inside the evaporator case versus those outside the case, the actual fraction of the leakage outside the evaporator case that enters the passenger compartment, and data on automobile air exchange rates.

- In the scenario for use of video tape head cleaners, a critical uncertainty is the amount of replacement of the CFC cleaners by new chemicals versus other presently available substitutes, i.e., alcohol.

Data on actual HFC/HCFC exposures to consumers would greatly improve this assessment. Additional information could be gathered as a precursor to field measurements, emissions (chamber) testing, and model development. As an example, representatives of the foam insulation industry are presently pursuing limited emissions testing of their products to assist in data development needs. These steps are discussed further in the consumer exposure support document.

5. GENERAL POPULATION EXPOSURE

This section estimates the potential exposures to the general population from the manufacture and commercial use of the HFCs and HCFCs.

5.1 ENVIRONMENTAL FATE

Because the HFCs/HCFCs are very volatile, they are expected to migrate to the atmosphere as gases. These chemicals pose some ozone depletion and global warming concerns. An extensive discussion of ozone depletion and global warming can be found in Scientific Assessment of Stratospheric Ozone: 1989, Vol I and II, published by the World Meteorological Organization as the Global Ozone Research and Monitoring Project - Report # 20.

5.2 ENVIRONMENTAL RELEASE AND EXPOSURE

The release data information available to EPA at the time of this report was "generic", that is, representative of the HFC/HCFC amounts which may be released for the given activity. These release data are summarized in Table 5-1. Since there is no current data on HFCs and HCFCs, the release estimates are based on current average CFC releases. Actual HFC/HCFC releases may be lower than current CFC releases both in total and per site. This is because new Clean Air Act emission regulations and potentially higher costs of the HFCs and HCFCs are expected to cause more conservative use, more reclamation and recycling, or use of other substitutes. Lack of data makes it impossible to determine what actual reductions in releases may be.

The Toxic Release Inventory was used to estimate releases from manufacturing and electronics and metal-cleaning by type, i.e., stack or fugitive. Other stack/fugitive release estimates were based on a number of other sources and professional judgment.

TABLE 5-1 HFCs/HCFCs AMBIENT RELEASE ESTIMATES

Activity	# sites	Release days/year	Release (kg/site-day) Stack	Fugitive[1]
Manufacture	11	350	93	34
Foam Blowing				
- Rigid	85	250	195	20
- Flexible	144	250	390	45
Mobile Air Conditioning (MAC)				
- Manufacture	64	250	56	
- Servicing	329,000	11 to 170	0.3 to 4.3	
Sterilization	6,000	365	2	2
Electronics and Metal Cleaning				
- PC Board Cleaning	705	250	42	98
- Other Electronics	82	250	36	86
- Metal Cleaning	1,435	250	36	86
Refrigeration				
- Retail Food Storage				
Manuf/Install.	33,200	1		20
Servicing	304,520	1		8
- Cold Storage Warehouses				
Manuf/Install.	1600	1		273
Servicing	18,900	4		76
- Chillers				
Manuf/Install.	4,260	1		28
Servicing	25,000	1		118
Industrial Process Refrigeration				
- Ice Machines				
Manufacture				
Medium	127,112	1		0.15
Large	8	1		2.1
X-large	1	1		32
Servicing				
Medium	1,060,000	3		0.1
Large	150	3		0.6
X-large	20	3		8.5
- Chemical Processing				
Manuf/Install.	182	1		1,436
Servicing	4,000	1		2,240
- Refineries				
Manufacture	2	1		1,436
Servicing	26	1		2,270
- Ice Skating Rinks				
Manufacture	10	1		202
Servicing	200	1		320

[1] These estimates assume unregulated venting and will be lower for HCFC/HFCs based on controls mandated by the Clean Air Act.

Because most of the site locations corresponding to the release data are unknown, the usual exposure estimation technique of utilizing site-specific meteorological and population information to estimate concentrations and the populations exposed at those concentrations was not utilized. Instead, a generic site was selected for its meteorological information only. The ramifications of this selection are discussed in Section 5-2.

Concentration and exposure estimates based on the release estimates are presented in Table 5-2. The concentrations presented were estimated using the EPA Industrial Source Complex Long Term (ISCLT) Dispersion Model. Exposures were calculated from these concentrations using the equation:

$$E = (C \times I)/BW$$

where E is the exposure in mg/kg-day, C is the annual average concentration in mg/m^3, I is the inhalation rate in m^3/day (20 m^3), and BW is the average body weight in kilograms (70 kg). Each exposed individual is assumed to live and work in the same ambient zone of concentration 24 hours a day year-round through a 70 year lifetime. Since this zone could be located near several release sources, the exposed individual's overall exposure could be the sum of multiple exposures, although not necessarily at the maximum concentrations presented here. The probability of multiple exposures is expected to be small.

5.2 UNCERTAINTIES IN RELEASE, CONCENTRATION, AND EXPOSURE ESTIMATES

To make use of these estimates, it is important to understand the uncertainties associated with them. Considerable uncertainty is associated with the release estimates because much of the data were based on analogy to existing CFCs, which will have differences in physical and chemical properties, material quantities, equipment design, and emission controls compared to the HFCs/HCFCs. Since it was not possible to factor in all of the variables, these results may be higher than actual releases.

Since the concentration and exposure estimates were derived from the estimated releases, it follows that there are uncertainties associated with these values as well. There were additional uncertainties associated with the estimation of the concentrations to which people may be exposed. A major source of uncertainty was the need to use a generic site location to evaluate aerial releases because insufficient information was available to select specific release sites. This generic site was selected from an analysis of maximum exposed individual (MEI) concentrations calculated for an identical release from each of 392 sites across the U. S. These MEIs were calculated from ISCLT model runs of statistical wind summaries available for the 392 sites.

TABLE 5-2 POTENTIAL AMBIENT INHALATION EXPOSURES TO HFCs/HCFCs

Activity	Maximum exposure concentration[a] (ug/m^3)	Highest lifetime exposure[b] (mg/kg-d)
Manufacture		
- Stack Release	9.2	2.6×10^{-3}
- Nonstack Release	22.8	6.5×10^{-3}
Foam Blowing, Rigid		
- Stack Release	9.6	2.7×10^{-3}
- Nonstack Release*	9.9	2.8×10^{-3}
Foam Blowing, Flexible		
- Stack Release	19.2	5.5×10^{-3}
- Nonstack Release*	22.3	6.4×10^{-3}
Mobile Air Conditioning (MAC)		
- Manufacture*	26.4	7.6×10^{-3}
- Servicing*	5.3 to 22.9	1.5 (to 6.5) $\times 10^{-3}$
Sterilization		
- Stack Release	0.043	1.2×10^{-5}
- Nonstack Release	0.98	2.8×10^{-4}
Electronics and Metal Cleaning		
- PC Board Cleaning		
- Stack Release	3.2	9.1×10^{-4}
- Nonstack Release*	128	3.7×10^{-2}
- Other Electronics		
- Stack Release	2.7	7.7×10^{-4}
- Nonstack Release*	319	9.1×10^{-2}
- Metal Cleaning		
- Stack Release	2.7	7.7×10^{-4}
- Nonstack Release*	115	3.3×10^{-2}
Refrigeration		
- Retail Food Storage		
- Manuf/Install.*	0.15	4.4×10^{-5}
- Servicing*	0.22	6.3×10^{-5}
- Cold Storage Warehouses		
- Manuf/Install.*	0.88	2.5×10^{-4}
- Servicing*	0.96	2.8×10^{-4}
- Chillers		
- Manuf/Install.*	0.17	4.8×10^{-5}
- Servicing	0.17	4.8×10^{-5}
- Industrial Process Refrigeration		
- Ice Machines		
- Manufacture*		
- Medium	0.001	3.0×10^{-7}
- Large	0.014	4.0×10^{-6}
- X-large	0.21	6.1×10^{-5}
- Servicing*		
- Medium	0.005	1.4×10^{-6}
- Large	0.03	8.6×10^{-6}
- X-large	0.42	1.2×10^{-4}

TABLE 5-2 (cont)

Activity	Maximum exposure concentration[a] (ug/m^3)	Highest lifetime exposure[b] (mg/kg-d)
- Chemical Processing		
- Manufacture	2.8	8.0×10^{-4}
- Servicing	39.9	1.1×10^{-2}
- Refineries		
- Manufacture	2.8	8.0×10^{-4}
- Servicing	39.9	1.1×10^{-2}
- Ice Skating Rinks		
- Manufacture	1.6	4.6×10^{-4}
- Servicing	7.7	2.2×10^{-3}

[a] The concentrations presented were estimated using the EPA Industrial Source Complex Long Term (ISCLT) Dispersion Model.These concentrations are the maximum possible at or beyond site fencelines. Because of data limitations, concentrations for activities marked with an asterisk (*) could not be estimated at the fenceline, but only at some point beyond the fenceline. Because of this, those activities may have larger concentrations between the fenceline and the point estimated than presented here.

[b] The Highest Lifetime Exposure (E) = (C x I)/BW, where:

C = maximum annual average concentration (mg/m^3)
I = inhalation rate (20 m^3/day)
BW = average body weight (70 kg)

Example calculation:

(22.4 ug/m^3 x 1 mg/1000 ug x 20 m^3/d)/70 kg =

6.4×10^{-3} mg/kg-d

Exposures are conservatively assumed to be 24 hours a day, year-round, for a 70 year lifetime.

The effects of this type of use of a generic release site were twofold. First, the meteorological conditions (prevailing winds, etc.) at the site selected were known to cause conservative (i.e., high) maximum concentrations resulting in upper-bound exposure estimates. It is important to note, however, that the maximum concentration for this site in the sensitivity analysis was only about twice the lowest maximum concentration calculated. Second, using a generic release site does not permit an estimate of how many people, if any, are exposed at the estimated air concentrations of the HFCs and HCFCs.

The estimates of model parameters for stack and fugitive releases are obvious sources of uncertainty because they are based on professional judgment assumptions about the facilities at the release point.

Model parameters such as the type of release, release height, and size of release facility are key determinants of downwind ambient air concentrations. For example, a volume fugitive release, which is typically a release from building ventilators, will cause higher ambient air concentrations than an area release of the same size. Also, a stack release at a 30 meter height will have its maximum concentration further from the source than the same release from a 5-meter stack.

The facility fenceline distance estimates were also assumed. These distances are not used in the ISCLT model itself, but are compared to the distances the model predicts that release concentrations will be from the release source. Only those concentrations beyond the assumed fenceline distance are considered available for general population exposure. An additional uncertainty regarding fenceline estimates is that although the exposures presented here were calculated from the maximum concentrations predicted by the ISCLT aerial release model, there were insufficient data available to estimate concentrations within certain distances of assumed building source releases. This means that releases from buildings with fencelines within these distances of unknown concentrations may or may not have larger concentrations than the model could predict. The activities where this occurred are marked in Table 5-2; the concentration values used in these instances are the maximum the model could predict.

It is important to understand that these maximum concentrations are defined by a particular direction as well. For example, the area of maximum concentration for a release might be said to be 200 meters from a source on a westerly heading. In other directions and further away from the source of release, the concentrations will decrease.

5.3. OTHER AMBIENT RELEASES

Direct releases to environmental media other than air are only estimated for HFC/HCFC manufacture, assuming 11 sites and 350 days release per year. The receiving media and release amount, in kg/site-day, are:

water: 0.1
landfill: 0.07
incineration: 21
underground injection: 8.5

Because of the high vapor pressures of the HFCs and HCFCs, any disposal method that is exposed to air is expected to result in volatilization of the substitutes. HFC/HCFC release after

incineration is expected to be <0.1 kg/site-day, assuming a 99.9 percent destruction. Because many of the HFCs/HCFCs are somewhat soluble in water, their underground injection disposal in aqueous materials could lower their volatilization. The possibility of migration of the injected material into groundwater used for drinking water depends on regulation of the injection site. For example, hazardous waste injection sites are segregated from potable groundwater supplies. Present CFCs are federally regulated as hazardous wastes for certain solvent uses or if contaminated with hazardous materials. There may also be additional state regulations. Regulation of HFC/HCFC materials used as CFC substitutes is expected to be similar.

Although HFC/HCFC releases to water, landfill, and incineration may eventually volatilize to air, these release amounts cannot be summed with the air releases previously presented because their release sites may be spatially distant from the manufacturing sites. Because of these uncertainties, and the small sizes of these releases compared to the direct air releases, exposures were not calculated for these releases, or the injection release.

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