

MICHIGAN DEPARTMENT OF ENVIRONMENTAL QUALITY

INTEROFFICE COMMUNICATION

TO: HFC-227ea file (CAS # 431-89-0)

FROM: Gary Butterfield

SUBJECT: Screening level for HFC-227ea

DATE: March 27, 2006

The chemical with manufacturer's name HFC-227ea is also known with the proper chemical name as 1,1,1,2,3,3,3-heptafluoropropane. This material has a molecular weight of 170 g/mol. The melting point is -131C and the boiling point is -15C. The vapor pressure of this material is 453 kPa (which converts to 3400 mmHg) at 25C.

HFC-227ea can be used as a refrigerant, blowing agent, pharmaceutical propellant, and a fire extinguishing agent. It is not an ozone depleting agent. It is quite unreactive in the atmosphere and has been excluded from the list of volatile organic compounds by EPA (Nov 29, 2004 69FR69290-8). Because the carbon fluoride bond is so strong, there is little free radicals generated. Therefore this compound does not deplete stratospheric ozone. However, it is a global warming gas with an atmospheric life time of 42 years.

The following references or databases were searched to identify data to determine the screening level: U.S. Environmental Protection Agency (EPA) Integrated Risk Information System (IRIS), National Institute for Occupational Safety and Health (NIOSH) Registry for Toxic Effects of Chemical Substances (RTECS), American Conference of Governmental and Industrial Hygienists (ACGIH) Threshold Limit Values (TLVs), Michigan Department of Environmental Quality (DEQ) library, International Agency for Research on Cancer (IARC) Monographs, Chemical Abstract Service (CAS) Online (1968 - November 2004), National Library of Medicine (NLM) - Toxline, and National Toxicology Program (NTP) Status Report.

There were no published toxicity studies available for this compound. The DuPont MSDS identifies several unpublished studies that could provide the basis for setting a screening level. These include an acute LC50 study, a 14-day inhalation study, and a 90-day inhalation study. The DuPont MSDS technician, who was contacted, was not able to provide copies of any of these studies.

As part of the Australian Industrial Chemicals Notification and Assessment Scheme (NICNAS) documents are prepared that include an assessment of impacts on public health, occupational health and the environment on chemicals being imported to Australia. One of those documents is for HFC-227ea. In this document, summaries of the acute inhalation study (WIL Research Labs 1992) and the 90-day study (Naas 1994), which are cited in DuPont's MSDS, were obtained.

In the acute study, groups of 5 male and 5 female CrI:CD/BR rats were exposed to 788696 ppm (or 5480 g/m³) of HCF-227ea for 4 hours. The NICNAS document states that the acute study was conducted according to OECD guidelines for acute inhalation toxicity testing. There was a 14-day observation period following the exposure. No deaths occurred during this study.

In the 90-day study (Naas 1994), groups of 12 Sprague-Dawley rats of each sex were exposed to 0, 139, 348 or 731 mg/L (or 0, 20000, 50000 or 105000 ppm) for 6 hours a day, 5 days per week for 13 weeks. The NICNAS document states that this study was conducted according to US EPA's Toxic Substance Control Act's health effects testing guidelines, the OECD Guidelines for Subchronic Inhalation Toxicity Studies, and the Japanese Ministry of International Trade and Industry Guidelines. There were no treatment related increases in incidence of clinical observations, body weight changes, hematology parameters, serum chemistry, ophthalmology lesions, organ weights values, or histological findings. The highest dose, 731 mg/L, was considered to be the NOAEL.

It is generally considered to be better using more chronic data when establishing a screening level, in order to illuminate the possible long term effects of exposure. Therefore, the above 90-day study provides the best basis upon which the ITSL can be set. There is also an acute inhalation study (WIL Research Labs 1992) can be used to support the above 90-day based screening level, as the resulting ITSL based on the acute study is similar to the above longer term, 90-day screening level. Following EPA's RfC methodology the ITSL can be calculated as follows.

$$\text{NOAEL}_{(\text{ADJ})} = 731 \text{ mg/L} \times 6/24 \times 5/7 = 130 \text{ g/m}^3$$

Where HFC-227ea can be considered to be a Category 3 gas, with a ratio of blood to gas partition coefficient unknown and assumed to be 1.

$$\text{NOAEL}_{(\text{HEC})} = 130 \text{ g/m}^3 \times 1 = 130 \text{ g/m}^3$$

$$\text{RfC} = (130 \text{ g/m}^3)/(10 \times 10 \times 10) = 130 \text{ mg/m}^3$$

$$\text{ITSL} = 130,000 \text{ ug/m}^3$$

An uncertainty factor of 10 was used for each factor of animal-to-human, sensitive individual, and subchronic-to-chronic.

An annual averaging time will be used with the above ITSL of 130,000 ug/m³. The lack of any adverse effects at all dose levels in the subchronic inhalation study, coupled with the development of an acute based ITSL (see below) supports the use of this averaging time.

Many times there is a concern for adverse effects from possible high level acute exposures to chemicals that have screening level set with long term averaging time. When available, a screening level with a short term averaging time can be used to evaluate those concerns. A study by Emmen et al (2000) provides data that can be used to develop a one hour averaging time screening level. In this study a group of eight (4 male and 4 female) human volunteers were exposed for 1 hour to concentrations between 1000 and 8000 ppm, which converts to concentrations of 6950 to 55600 mg/m³. There were no adverse effects from the 1 hour exposure on the ECG, central nervous system, blood pressure, lung function, blood samples (hematology and serum chemistry), or respiratory tract irritation. There have been some reports of cardiac sensitization in lab animals, and increased pulse rates in human volunteers occurring at very high exposure levels. The 8000 ppm exposure in the Emmen et al study are much lower than the studies with cardiac effects, and provides the best basis for establishing a short term screening level. An uncertainty factor of 10 for sensitive individuals will be applied to the 8000 ppm (or 55600 mg/m³) concentration to obtain the one hour ITSL of 5,560 mg/m³ or 5,560,000 ug/m³.

References:

Emmen et al. 2000. Human safety and pharmacokinetics of the CFC alternative propellants HCF 134a (1,1,1,2-tetrafluoroethane) and HCF 227 (1,1,1,2,3,3,3-heptafluoropropane) following whole body exposure. *Reg Toxicol Pharmacol* 32:22-35.

Naas DJ. 1994. A 90-day inhalation toxicity study of FM-200 in rats. WIL Research Labs, Ashland Ohio project # WIL-12318.

NICNAS. 1999. Australia: National Industrial Chemical Notification and Assessment Scheme - heptafluoropropane (HCF-227ea). File No.: EX/5 (NA/164).

WIL Research Labs, Ashland Ohio. 1992. An acute inhalation toxicity screen of FM-200 in rats. WIL project # WIL-12248.

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