MICHIGAN DEPARTMENT OF ENVIRONMENTAL QUALITY

INTEROFFICE COMMUNICATION

TO: File for Vinylidene fluoride (CAS # 75-38-7)

FROM: Robert Sills, AQD Toxics Unit Supervisor

SUBJECT: Vinylidene fluoride ITSL change in the averaging time from 24 hrs to annual

DATE: September 8, 2015

The current ITSL for vinylidene fluoride (30 ug/m^3) has a justification (attached) dated November 6, 2003. The averaging time (AT) assigned at that time was 24 hours, as per the default methodology (Rule 232(2)(b)). The current file review concludes that the AT may appropriately be set at annual, based on the nature and duration of the key study and the ITSL value derivation, as allowed under Rule 229(2)(b). Therefore, the AT is being changed from 24 hours to annual at this time.

MICHIGAN DEPARTMENT OF ENVIRONMENTAL QUALITY

INTEROFFICE COMMUNICATION

November 6, 2003

TO: Vinylidene fluoride file (CAS # 75-38-7)

FROM: Gary Butterfield

SUBJECT: Screening level for vinylidene fluoride

Vinylidene fluoride is a gas with a molecular weight of 64.03 g/mol. Vinylidene fluoride is also commonly known as 1,1-difluoroethylene and VF2. The melting point is -144 degrees Celsius. The boiling point is -86 degrees Celsius.

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 - May 2003), National Library of Medicine (NLM) - Toxline, and National Toxicology Program (NTP) Status Report.

NIOSH has established an REL of 1 ppm and a ceiling limit of 5 ppm for vinylidene fluoride. The OEL by NIOSH is much lower than the ACGIH TLV value of 500 ppm TWA. There is no STEL value for vinylidene fluoride adopted by ACGIH.

The CAS and NLM on-line literature searches were conducted on May 5, 2003. There were some hits found during the literature searches for this chemical. Many acute studies were available in published journal articles. Some of these acute studies evaluate metabolism and PBPK. Many of the longer-term studies have not been published in publicly available journal articles. However, copies of those unpublished, longer-term studies are available from EPA's ToSCA library.

A chronic mouse inhalation study was conducted by Biodynamics for CMA in 1991. Groups of CD-1 mice were exposed six hours per day five days per week for 18 months to 0, 600, 2505 or 10018 ppm (converts to 0, 1570, 6560 or 26250 mg/m^3). The main focus on this study was potential oncogenicity effects of vinylidene fluoride. However, no significant histopathology was reported in this study. The incidence of neoplasms was similar in all exposed groups, and determined by the authors to not be toxicologically significant. The authors reported that no carcinogenic effects were observed. Due to the emphasis of this study being placed on finding carcinogenic effects, there is some concern that subtle nasal cavity lesions, like those in the TNO studies (see below), may have been over looked.

Several 90-day inhalation toxicity studies have been conducted with vinylidene fluoride. These studies include: Litton Bionetics Inc. (1984); TNO/CIVO Institute (1986); TNO (1987a) and TNO (1987b).

In the 90-day study conducted by Litton Bionetics, Inc. (1984), groups of F344 rats were exposed 6 hours a day, five days a week to 0, 500, 1500, 5000, 15000 or 50000 ppm (converts to 0, 1310, 3930, 13100, 39300 or 131000 mg/m3). Adverse effects were found in all of the dose levels from this study. Changes in liver and kidney organ weights, as well as hemorrhaging in the nasal cavity were the effects observed in dosed animals. The authors concluded that the NOAEL is less than 500 ppm.

In the 90-day study conducted by TNO/CIVO Inst. (1986), groups of Sprague-Dawley rats were exposed 6 hours a day, five days a week to 0, 1000, 7000, or 40000 ppm (converts to 0, 2725, 18160, or 104700 mg/m3). Histopathology changes in the vomeronasal organ (in the nasal cavity) occurred at all exposure levels, a NOAEL was not identified.

In the second 90-day study conducted by TNO (1987a and b), groups of Sprague-Dawley rats were exposed 6 hours a day, five days a week to 0, 250, 1000 or 7000 ppm (converts to 0, 655, 2620 or 18340 mg/m3). There were no adverse effects observed at the 250 and 1000 ppm exposure levels.

The lower concentrations from several of these studies provide the basis for identifying the NOAEL of 250 ppm. This is based on other studies that found adverse effects at higher concentrations - 500 ppm in LBI's NTP study, and TNO's 1986 study where nasal cavity pathology was observed at 1000 ppm. The TNO's 1987 study did not find adverse effects at the 250 ppm or the 1000 ppm dose levels. However, when considering all of these studies, the highest overall NOAEL is 250 ppm.

Using the EPA's RfC methodology and the NOAEL of 250 ppm, a screening level can be calculated as follows.

NOAEL = 250 ppm = 655 mg/m^3
NOAEL(adj) = 655 mg/m^3 x 6/24 x 5/7 = 117 mg/m^3
NOAEL(hec) = 117 mg/m^3 x 0.23 = 27 mg/m^3
pseudo RfC = (27 mg/m^3)/(10x10x10) = 27 ug/m^3 rounded to 30 ug/m^3

The dosimetric adjustment factor (DAFr) of 0.23 was used in the above NOAEL(hec) calculation. This is based on VF2 being a category 1 gas - effects in upper respiratory tract (extrathoracic), indicating VF2 is a highly reactive gas even though it is only slightly water soluble. Standard minute volumes and extra-respiratory surface areas were used to calculate a DAFr of 0.23 for a 350 gram rat.

$$DAFr = \frac{(0.24\ L/min)/(15\ cm^2)}{(13.8\ L/min)/(200\ cm^2)} = 0.23$$

The standard uncertainty factors of 10 each were used in the above RfC calculation for: animal-to-human, sensitive individuals, and subchronic-to-chronic.

Based on R232(1)(a) the screening level is calculated as follows.

ITSL = pseudo-RfC = 30 ug/m^3 with 24 hour averaging

As additional support, this screening level based on the pseudo-RfC is very similar to the screening level that would have been derived based on the OEL from the NIOSH's REL of 1 ppm (or 2.6 mg/m^3). This REL would have resulted in an ITSL of 26 ug/m^3 with 8 hour averaging by using R232(1)(c).

Additional calculations using Bench Mark Dose Software (BMDS) were also conducted for comparison purposes to the above (old methodology) RfC. The BMDS was run with 6 different models - gamma, multistage, quantal linear, weibull, probit, and logistic. The data used in the models was from the TNO 1987a and 1987b studies. The LBI 1984 study did not report individual animal pathology results, making this study of no use in the BMDS modeling. There was quite a wide range in the possible RfCs obtained from the various models. All of the possible RfCs were higher (50 ug/m^3 and greater) than the RfC calculated from the old methodology above. Not knowing which model is most appropriate upon which to base the RfC, lead to adoption of the ITSL being set to the old methodology RfC of 30 ug/m^3.

References:

Biodynamics. 1991. An inhalation oncogenicity study of vinylidene fluoride in the mouse (FINAL REPORT) (VOLUME I-VII). EPA NTIS/OTS0538077

Litton Bionetics, Inc. 1984. Thirteen-week subchronic study in F344 rats vinylidene fluoride (FINAL report for NTP). EPA NTIS/OTS0523847

TNO CIVO INTSTITUTE. 1986. Subchronic (13-WEEK) inhalation toxicity study on vinylidene fluoride in rats (FINAL REPORT). EPA OTS NTIS/OTS0522774

TNO. 1987a. Subchronic 13 WEEK inhalation toxicity study of vinylidene fluoride in weanling and young adult rats. EPA/OTS OTS0510697.

TNO. 1987b. Subchronic (13-WEEK) inhalation toxicity study of vinylidene fluoride in weanling and young adult rats (Appendix Parts A & B). EPA/OTS OTS0523834