MICHIGAN DEPARTMENT OF ENVIRONMENTAL QUALITY

INTEROFFICE COMMUNICATION

TO: Hydrogen fluoride file (CAS # 7664-39-3)

FROM: Gary Butterfield

SUBJECT: Screening levels for hydrogen fluoride

DATE: November 24, 2009

The following references or databases were searched to identify data to determine the screening level: U.S. EPA Integrated Risk Information System (IRIS), Registry for Toxic Effects of Chemical Substances (RTECS), American Conference of Governmental and Industrial Hygienists (ACGIH) Threshold Limit Values (TLVs), National Institute for Occupational Safety and Health (NIOSH) Pocket Guide to Hazardous Chemicals, Environmental Protection Bureau Library, International Agency for Research on Cancer (IARC) Monographs, National Library of Medicine (NLM), Health Effects Assessment Summary Tables (HEAST), Agency for Toxic Substances and Disease Registry (ATSDR) and National Toxicology Program (NTP) Status Report.

A limited CAS and NLM on-line searches were conducted July 13, 2009, covering publications from recent periods, 2003 to 2009, as several agencies (ATSDR, ACGIH, CalEPA & OEHHA) have also recently published "screening level" values and were considered to have adequately evaluated the older studies. No significant, recently published studies were located during the literature search. Therefore, the key studies used by the other agencies will also be used by the AQD to establish the screening levels. The EPA has classified hydrogen fluoride as a Hazardous Air Pollutant (HAP). The EPA has not established a reference concentration (RfC) or reference dose (RfD) for hydrogen fluoride. There is an EPA RfD for fluorine (soluble fluorides); however, it is not considered appropriate to utilize the oral RfD for inhalation ITSL development. ATSDR (2003) has set an acute MRL of 0.02 ppm. The ACGIH has set a TWA TLV of 0.5 ppm and STEL of 2 ppm to avoid eye, skin, and upper and lower respiratory tract irritation.

Physical/chemical properties:
Hydrogen fluoride is a colorless vapor at temperatures above its boiling point (19.4C or 67F) and a fuming liquid at lower temperatures. The melting point is -83C. The vapor pressure is 917 mmHg at 25C. The molecular weight of hydrogen fluoride is 20.01g/mol. The molecular formula is HF. Hydrogen fluoride is highly soluble in water and alcohol.

Effects to humans:
The primary adverse effects to humans from exposure to hydrogen fluoride include dermal, eye, and respiratory irritation and/or burning. These symptoms are generally associated with acute exposures. Exposure to hydrofluoric acid is of special concern as discovery of the burn may not

occur immediately, providing more time for the hydrofluoric acid to penetrate deeper into the subdermal layers (Patty's Industrial Hygiene & Toxicology, 1994) and potentially cause more severe burns. Also, for the chronic lower level exposure situations, the observation that exposure to other forms of fluorides (e.g., particulate or gaseous) would likely result in effects on bone density (fluorosis) as Collings et al. (1951) reported similar absorptions of the various forms of fluorides.

The toxicity of hydrogen fluoride or hydrofluoric acid has been widely studied, and it is beyond the scope of this screening level justification memo to describe all of the studies. A comprehensive overview of animal and human studies can be found in several other sources, including ATSDR (2003), and Patty's Industrial Hygiene and Toxicology (1994). Key human exposure studies have been utilized to set screening level values by other agencies, and were considered in setting these screening levels.

The chronic ITSL is being set at 14 ug/m^3 with an annual average, a value that is equal to the inhalation reference exposure level (REL) reported in the chronic toxicity summary of fluorides (including hydrogen fluoride) published in 2003 by the California Office of Environmental Health Hazard Assessment (California OEHHA, 2003). The key study described in this document was Derryberry et al. (1963), which involved occupational exposure of fluoride (via inhalation) to 74 male workers and increased bone density. In their documentation California obtained and published Derryberry's raw data. A statistical evaluation of the raw data by OEHHA personnel revealed a statistically significant relationship between air fluoride concentrations, and minimal bone density increases. A no observed adverse effect level (NOAEL) and lowest observed adverse effect level (LOAEL) for skeletal fluorosis of 1.07 and 1.89 mg F/m^3 or 1.13 and 1.98 mg HF/m^3, respectively. California reports that a benchmark dose $BMCL_{05}$ concentration (0.37 mg F/m^3 or 0.39 mg HF/m^3) was identified via application of USEPA benchmark dose software (see the attached appendix). The benchmark concentration $BMCL_{05}$ was adjusted for work day and week exposure duration [0.39 mg HF/m^3 x ($10m^3/20m^3$ x 5/7) = 0.14 mg/m^3] and an intraspecies uncertainty factor of 10 was applied to arrive at their REL of 14 µg HF/m^3. The REL is being adopted as the AQD chronic ITSL because methods followed by Cal EPA are the same RfC type methods that would be used by AQD. The averaging time for the chronic ITSL is going to be set at annual rather than 24-hour, which is normally used with RfC type calculations, because an acute ITSL for hydrogen fluoride is also being set as described in the following paragraph. It could be noted that ACGIH 2005 states that "Grade I fluorosis results in no medically recognized dysfunction". However, the lack of comprehensive health effects examinations of persons exposed to hydrogen fluoride and the potential greater susceptibility of children to the effects of fluorides are areas of uncertainty, which suggest utilization of the more conservative (i.e., lower) OEHHA REL compared to other agency screening levels. Support for AQD use of this REL as a screening level also comes from EPA's 2002 NATA, which used of this value in their evaluation, with the lack of an available EPA RfC for hydrogen fluoride.

The establishment of an acute ITSL, with one hour averaging time, for hydrogen fluoride is considered appropriate when taking into consideration possible high exposures to hydrogen fluoride. Several agencies have set short term limits for hydrogen fluoride exposure, including Cal EPA, ATSDR, AEGL and ACGIH. Many of these short-term exposure limits are based on the same key study (Lund et al 1997, 1999). The AQD is adopting the one-hour REL of Cal EPA OEHHA, 2008 as the methods used to develop their short term REL is similar to what the AQD would follow when setting an acute ITSL. This set of key studies by Lund et al included a set of approximately 20 to 23 male volunteers who were exposed for one hour to hydrogen fluoride concentrations that ranged from 0.2 to 5.2 mg HF/m^3. In Lund et al (1997), the study participants were evaluated for blood fluoride concentration, eye and airway symptoms, and

pulmonary function testing before, during, and after the one-hour hydrogen fluoride exposure. The Lund et al (1999) study looked at changes in bronchoalveolar lavage (BAL) before and after the one-hour exposure for effects. Statistically significant differences in symptomatic evaluations were not observed at concentrations below 2.5 mg/m^3 in the Lund et al 1997 as reported by the authors. Therefore, the range 2.5 to 5.2 mg/m^3 was selected as the LOAEL. The 2.4 mg/m^3, the upper end of the NOAEL middle concentration range (0.7-2.4 mg/m^3) was selected as the NOAEL. An intraspecies uncertainty factor of 10 was applied to the NOAEL to arrive at the acute reference exposure level of 240 µg/m^3 with one hour averaging. The Lund et al 1999 study also provides support for this NOAEL/LOAEL by finding increases of lymphocytes and CD3 positive cells (as a possible indication of inflammation reaction) at middle and high dose levels. The AQD is setting the acute ITSL equal to the above derived REL value, 240 µg/m^3 with one-hour averaging.

References:

Agency for Toxic Substances and Disease Registry (ATSDR). 2003. Toxicological profile for fluorides, hydrogen fluoride, and fluorine.

American Conference of Governmental industrial Hygienists (ACGIH). 2005. Threshold Limit Value (TLV) for hydrogen fluoride.

California Office of Environmental Health Hazard Assessment (OEHHA). 2003. Chronic toxicity summary of fluorides (including hydrogen fluoride).

California Office of Environmental Health Hazard Assessment (OEHHA). 2008. Acute toxicity summary for hydrogen fluoride.

Collings GH, Fleming RBL, and May R. 1951. Absorption and excretion of inhaled fluorides. A.M.A. Arch. Ind. Hyg. 4:585-590.

Derryberry et al. 1963. Fluoride exposure and worker health – the health status of workers in a fertilizer manufacturing plant in relation to fluoride exposure. Arch. Environ. Health 6:503-514.

Lund et al. 1997. Exposure to hydrogen fluoride: an experimental study in humans of concentrations of fluoride in plasma, symptoms, and lung function. Occup. Environ. Med 54:32-37.

Lund et al. 1999. Increased CD3 positive cells in bronchoaveolar lavage fluid after hydrogen fluoride inhalation. Scand J Work Environ Health 25:326-334.

Patty's Industrial Hygiene and Toxicology. 1994. Chemical summary for hydrogen fluoride (HF). Volume II, part F, p4454-4465.

GB:lh

Appendix

BMDS output

Derryberry et al (1963) - minus the highest dose group, see Cal EPA

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    Probit Model. (Version: 3.1;  Date: 05/16/2008)
   Input Data File: C:\USEPA\BMDS21\Data\lnp766439Setting.(d)
   Gnuplot Plotting File:  C:\USEPA\BMDS21\Data\lnp766439Setting.plt
                                        Mon Nov 16 08:18:15 2009
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 BMDS Model Run
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   The form of the probability function is:

   P[response] = Background
            + (1-Background) * CumNorm(Intercept+Slope*Log(Dose)),

   where CumNorm(.) is the cumulative normal distribution function

   Dependent variable = Col3
   Independent variable = Col1
   Slope parameter is not restricted

   Total number of observations = 4
   Total number of records with missing values = 0
   Maximum number of iterations = 250
   Relative Function Convergence has been set to: 1e-008
   Parameter Convergence has been set to: 1e-008

   User has chosen the log transformed model

                 Default Initial (and Specified) Parameter Values
                   background =           0
                    intercept =    -1.81915
                        slope =     1.30491

           Asymptotic Correlation Matrix of Parameter Estimates

 ( *** The model parameter(s)  -background have been estimated at a boundary point, or have
been specified by the user, and do not appear in the correlation matrix )

              intercept        slope
 intercept            1        -0.94
     slope        -0.94            1
```

Parameter Estimates

Variable	Estimate	Std. Err.	95.0% Wald Confid Int Lower CL	Upper CL
background	0	NA		
intercept	-1.9793	0.581606	-3.11922	-0.839372
slope	1.459	0.643525	0.197714	2.72028

NA - Indicates that this parameter has hit a bound
implied by some inequality constraint and thus
has no standard error.

Analysis of Deviance Table

Model	Log(likelihood)	# Param's	Deviance	Test d.f.	P-value
Full model	-25.7525	4			
Fitted model	-26.5016	2	1.4983	2	0.4728
Reduced model	-29.7989	1	8.09283	3	0.04413

AIC: 57.0033

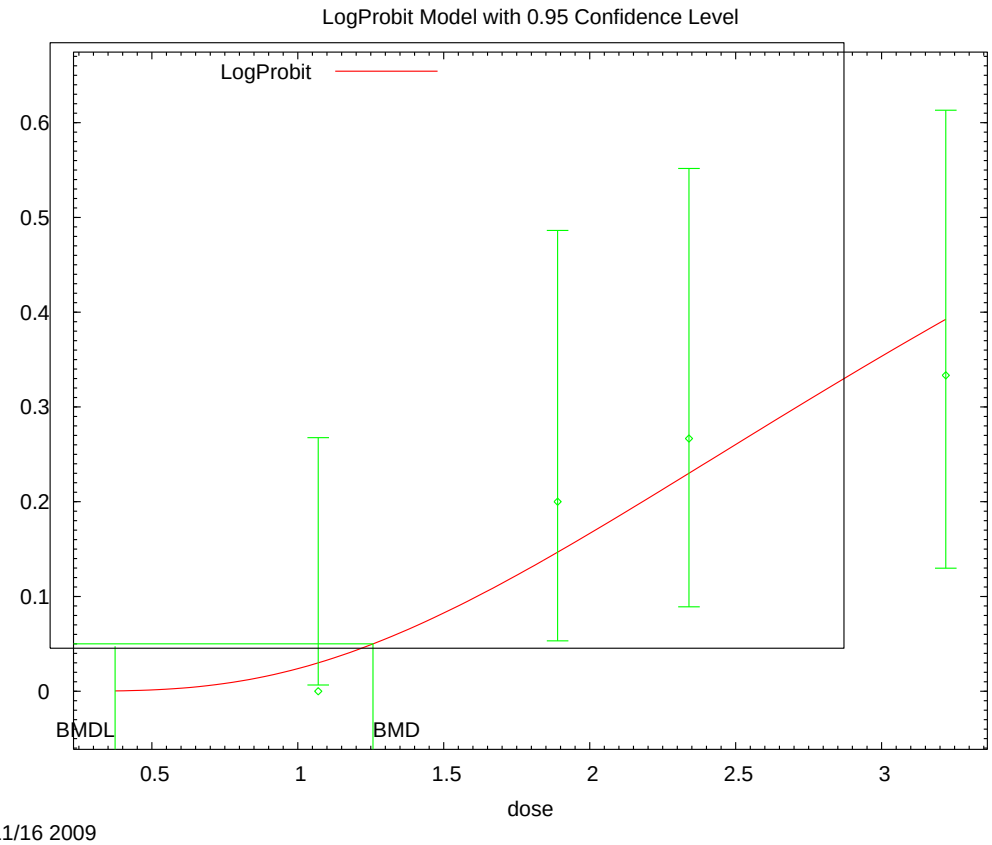
Goodness of Fit

Dose	Est._Prob.	Expected	Observed	Scaled Size	Residual
1.0700	0.0300	0.420	0.000	14	-0.658
1.8900	0.1467	2.201	3.000	15	0.583
2.3400	0.2300	3.450	4.000	15	0.338
3.2200	0.3924	5.885	5.000	15	-0.468

Chi^2 = 1.11 d.f. = 2 P-value = 0.5751

Benchmark Dose Computation

Specified effect = 0.05
Risk Type = Extra risk
Confidence level = 0.95
BMD = 1.25763
BMDL = 0.374011



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