MICHIGAN DEPARTMENT OF ENVIRONMENTAL QUALITY

INTEROFFICE COMMUNICATION

TO: Aluminum potassium fluoride file (CAS # 60304-36-1)

FROM: Gary Butterfield

SUBJECT: Screening level for Aluminum potassium fluoride

DATE: June 12, 2006

Aluminum potassium fluoride is a white powder material at ambient temperatures. It is known by the manufacturer name of Nocolok flux. The molecular formula is $AlKF_4$ for the powder. The molecular weight is 142 g/mol. The water solubility is 4.6 g/L. The melting point is 570 degrees Celsius. This material decomposes at 700 degrees Celsius, with the release of hydrogen fluoride.

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 - Jan 2006), National Library of Medicine (NLM) - Toxline, and National Toxicology Program (NTP) Status Report.

The CAS and NLM on-line literature searches were conducted on January 31, 2006 to evaluate recent published literature. There were no published mammalian toxicity studies found under this CAS number. There has been several unpublished toxicity studies conducted by Netherlands Organisation for Applied Scientific Research (TNO). One of those four-week rat inhalation studies was available from EPA's ToSCA website, TNO (2003). This available study was a follow-up study to some earlier TNO studies that were conducted at higher dose levels, which caused more severe effects, as was summarized in this available study's introduction.

Several possible ways to determine a screening level for this material were considered. There is an ACGIH TLV for aluminum and fluorides available (ACGIH (2001)). The key study identified in the TLV documentation for fluoride is Derryberry et al (1963), where workers were exposed to hydrogen fluoride during fertilizer manufacturing. This study found that workers exposed to 3.38 mg/m^3 were found to develop fluorosis (indicated by increased bone density). This study also reported that the workers exposed to 2.64 mg/m^3 did not have fluorosis. Result of this study lead the TLV committee to set the TLV for fluorides at 2.5 mg/m^3. The ACGIH TLV for soluble aluminum is 2 mg/m^3. The basis for the soluble aluminum TLV is not related to aluminum toxicity, and not considered to be a good basis for setting a screening level. A MSDS for Nocolok flux was obtained from Solvay Chemicals, one of the manufacturers of potassium aluminum fluoride, and which has listed a company occupational exposure limit (OEL) of 0.1 mg/m^3 for this material. The company MSDS does not give details on how this exposure limit was derived; however, it is

interesting to note that the company set it's own OEL significantly lower than the ACGIH TLV's for fluoride and aluminum.

The Derryberry et al (1963) data on fluorosis in workers was further studied by California EPA while setting their chronic REL for fluoride exposure (CalEPA (2003)). The workers were evaluated by CalEPA for air concentration of fluoride exposure, and worker urinary fluoride levels versus occurrence of fluorosis. Breaking the group of Derryberry et al 74 workers into five groups of 14 or 15 workers, it was discovered that the lowest exposed group, based on urinary fluoride, had an average airborne exposure of 1.07 mg/m^3, and was the only group without an increased incidence of fluorosis. The next higher urinary exposure group, with airborne exposure of 1.89 mg/m^3, was considered to be the fluorosis LOAEL. CalEPA went on to use this evaluation in Benchmark Dose Software. The BMC_{05} was calculated to be 0.37 mg/m^3 using the log doses and the Probit model. Adjusting the BMC_{05} for workers being exposed during the work day (10 of 20 m^3) and 5 of 7 days a week resulted in an adjusted dose of 0.13 mg/m^3. Using an uncertainty factor of 10, for sensitive individuals, CalEPA came up with a chronic REL value of 13 ug/m^3 or 16 ppb for fluorides. Although this REL for fluorides seems more scientifically based than does the ACGIH TLV for fluorides, it still covers only the fluoride part of the aluminum potassium fluoride molecule. It would be more preferable to use toxicity data on the actual aluminum potassium fluoride material for establishing a screening level.

In the TNO (2003) study, groups of 6 male Wistar rats, 6 weeks old, were exposed to aerosols of aluminum potassium fluoride (>99% pure) at concentrations of 0, 1, 3.1, 10.3 or 103.5 mg/m^3 for 6 hrs/day, 5 days/week for 4 weeks – a total of 20 exposures. The aerosol had a MMAD that was reported to be between 1.4 and 2.5 um, with geometric standard deviation of 1.7 to 2.4. The authors reported that the lowest dose level had minimal adverse effects observed in some of the animals. These histopathological effects included alveolar macrophage accumulation, and the presence of cellular debris in the alveolar lumina. These effects were interpreted by the authors to be signs of impaired or insufficient clearance capacity of the alveolar macrophage. These same effects were observed at the higher dose levels in greater frequency and with a more severe occurrence. Other histopathologic effects were observed at the higher doses, including nasal olfactory epithelium necrosis and respiratory epithelium hyperplasia. There also was a trend of increased lung organ weights observed at doses of 3 mg/m^3 and higher. That is to say there was a dose related increase in histopathology changes and organ weights observed in this study. Due to the low dose having minimal adverse effects, the 1 mg/m^3 group is considered by the authors to be a minimal LOAEL. However, the AQD considered the simple accumulation of macrophage to not necessarily to be an adverse effect, but could just be a normal lung response to aerosol exposure. Therefore, the 1 mg/m^3 exposure group was considered to be the NOAEL.

The ITSL can then be calculated from methodology of R232(1)(d), as follows.

$NOAEL = 1\ mg/m^3$

$NOAEL_{ADJ} = 1\ mg/m^3 \times 6/24 = 0.25\ mg/m^3$

$NOAEL_{HEC} = NOAEL_{ADJ} \times RDDR = 0.25 \times 0.48 = 0.12\ mg/m^3$

$$ITSL = \frac{0.12\ mg/m^3}{20 \times 10 \times 3} = 0.2\ ug/m^3$$

A 20-fold uncertainty factor instead of 35 was applied for adjustment of the 4-week duration to a chronic exposure duration. The reduction in this uncertainty factor was appropriate due to the longer duration (4 week versus 7 day) of this study. A 10-fold factor was applied for sensitive individuals. A 3-fold factor was applied for animal to human adjustment. Since the use of RDDR to adjust for differences in dose equivalency between animals and humans reduces the uncertainty of this factor. The RDDR value of 0.48 was determined according to EPA's RfC methodology.

ITSL = 0.2 ug/m^3 with annual averaging

References

ACGIH. 2001. Documentation of the threshold limit values.

California EPA. 2003. Determination of noncancer chronic reference exposure level. See web site at: http://www.oehha.ca.gov/air/chronic_rels/pdf/2ApnA_Fluoride_Final.pdf

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.

Netherlands Organisation for Applied Scientific Research (TNO). 2003. A sub-acute (28-day) inhalation toxicity study with Nocolok flux in male Wistar rats. TNO report V4671/01. EPA ToSCA document 8ehq-0703-14514.pdf