MICHIGAN DEPARTMENT OF ENVIRONMENTAL QUALITY

INTEROFFICE COMMUNICATION

February 7, 2017

To : File for Aluminum Chloride (CAS No. 7446-70-0)

From : Mike Depa, Toxics Unit, Air Quality Division

Subject : Initial Threshold Screening Level

The initial threshold screening level (ITSL) for aluminum chloride is 0.1 µg/m³ with annual averaging time.

The following references or databases were searched to identify data to determine the screening level: U.S. Environmental Protection Agency's (EPA's) Integrated Risk Information System (IRIS), the American Conference of Governmental Industrial Hygienists (ACGIH) Threshold Limit Values (TLV), the National Institute of Occupational Safety and Health (NIOSH), the Agency for Toxic Substances and Disease Registry (ATSDR), the California Office of Environmental Health Hazard Assessment (Cal OEHHA), National Library of Medicine's TOXNET and TOXLINE, Toxic Substance Control Act (TSCA) Test Submissions (TSCATS), EPA's Provisional Peer Reviewed Toxicity Values for Superfund (PPRTV), European Chemicals Agency (ECHA) Risk Assessment (REACH) database, Chemical Abstract Service (CAS) SciFinder database and US EPA (epa.gov).

Notable Properties of Aluminum Chloride

1. Aluminum chloride is water soluble (ICSC, 2005)
2. Physical State: Colorless-to-white powder. Turns grey-to-yellow on exposure to moisture. (ICSC, 2005)
3. Anhydrous aluminum chloride reacts violently with water, evolving heat, and gases consisting of hydrogen chloride and steam, as well as aluminum oxide[1] (Al_2O_3) particulates (Grams, 2003)
4. Fumes resulting from exposure of anhydrous aluminum chloride to moisture are corrosive and acidic. (Grams, 2003)

The ACGIH (1991) established a TLV for aluminum chloride based on the amount of hydrolyzed acid, namely hydrochloric acid (HCl; CAS No. 7647-01-0). ACGIH (1991) stated:

> On the basis that 3 mols of hydrochloric acid (HCl), with a TLV of 5 ppm, hydrolyzed from 1 mol of aluminum chloride (AlCl3), a TLV-TWA of 2 mg/m³, as Al, is recommended to provide the same degree of freedom from irritation that is provided by the TLV for HCl.

---

[1] Aluminum oxide (Al_2O_3) (also called "alumina") is exempt from the definition of a Toxic Air Contaminant pursuant to Rule 120(f)(iii) for "aluminum oxide (nonfibrous forms)".

Although it seems reasonable that one molecule of AlCl3 is likely to be as acidic as three (3) molecules of hydrochloric acid (HCl) because of the release of HCl from AlCl3, it was deemed inappropriate to use the TLV of 2 ppm AlCl3 because it was rescinded in 2008 (ACGIH, 2008).

Animal Toxicity Study

Male Sprague-Dawley rats in groups of 50 adults were exposed by inhalation to respirable (less than 10 µm) dusts of aluminum chloride (1.83 + 0.7 mg/m^3) and filtered air alone over a period of five months, the exposures being six hours daily for five working days per week (Finelli, 1981). There was a 63 day post-exposure period as well as several interim sacrifices (10 rats per month at 2, 3, 4, and 5 months of exposure and 10 rats at 63 days post-exposure). In a summary of the study provided by REACH (2017) the results of the study were as follows:

No significant differences in body weights compared to controls
*****Significant increase in liver weight relative to body weight of aluminum chloride-exposed rats after the third month of exposure (an increase of 9.4 percent over controls)
*****Significant increase in kidney weight relative to body weight of aluminum chloride exposed rats after the fourth month of exposure (9 percent)
No difference in lung weights compared to controls
**Lysozyme levels in lavage fluid showed higher levels compared to controls, "which appeared to be time dependent"
Lysozyme activities decreased significantly on cessation of exposure to aluminum chloride
Glucose-6-phosphate dehydrogenase levels were not affected by exposure
**Enhanced alkaline phosphatase activity in aluminum chloride-exposed rats, that was exposure time-dependent, and was also reversible
^{125}I-albumin (radioactive iodine was injected in the tail and measured in lavage) leakage through the alveolar wall was not affected by exposure to aluminum chloride

*Considered to be an adverse effect of exposure

**Unknown relevance to the certitude of adverse effect, yet indicative of unhealthful

Derivation of the Screening Level

The study by Finelli (1981) was used to quantitate inhalation health risk of AlCl3. The effects observed are shown above and included statistically[2] increased organ-to-body weight ratios of both liver and kidney. Because it was not reported that the organ-to-body weight ratios returned to normal after a 63-day post-exposure period, it was assumed that the elevated values remained statistically elevated. Lung effects were limited to evaluation of lavage fluids, yet there were statistically elevated increases in lysozyme and alkaline phosphatase activity. These enzyme increases returned to normal after the recovery period. There were several limitations that add significant uncertainty to the derivation of a screening level, including: no histopathology was performed in the study, only one dose level was used, and the single dose used in the study was identified as an adverse effect level. It is better to have more than one dose

[2] Level of statistical significance was not reported, only that the levels were "significant", and that they were an "increase" over control values.

where the higher dose is an effect level and the lower dose is a no-observed-adverse-effect-level (NOAEL). Nonetheless, the study was adequately reported, and described a minimum, yet appropriate amount of detail allowing for a Point of Departure (POD) for quantitative chemical risk assessment. The study by Finelli (1981) identified a lowest-observed-adverse-effect-level (LOAEL) of 1.83 mg/m³, which was used as the POD as follows:

$LOAEL_{ADJ}$ = LOAEL x hours exposed per day x days exposed per week.
$LOAEL_{ADJ}$ = 1.83 mg/m³ x 6/24 x 5/7
$LOAEL_{ADJ}$ = 0.326 mg/m³

There was no information available to calculate a dosimetric adjustment factor (DAF). Normally a Human Equivalent Concentration (HEC) is derived from the duration adjusted dose (ADJ). A default DAF of 1 was used in this case, which assumes dose equivalency between animal and human. Because of the uncertainty in this assumption a full 10-fold uncertainty factor was used for extrapolation between animals and humans (see UF1 in equation below).

Applying uncertainty factors (UFs), a Reference Concentration was calculated:

RfC = ($LOAEL_{ADJ}$)/(UF1 x UF2 x UF3 x UF4)

Where UF1 is 10 for animal to human extrapolation
UF2 is 10 for sensitive individuals
UF3 is 10 for LOAEL to NOAEL
UF4 is 3 for subchronic to chronic extrapolation

RfC = (0.326 mg/m³)/(10 x 10 x 10 x 3) x 1000µg/mg
RfC = 0.108 µg/m³, or ~ 0.1 µg/m³, rounded to 1 significant figure

The UF4 of 3 for subchronic to chronic was justifiably decreased from 10 because the Finelli (1981) study duration was five months, and a typical subchronic study is three months in duration. Also, the thousand-fold combined uncertainty factor of animal-to-human, sensitive individuals, and LOAEL-to-NOAEL (10 each) was reasoned to account for at least some residual uncertainty for subchronic-to-chronic extrapolation.

The ITSL of 0.1 µg/m³ was derived pursuant to Rule 229(2)(b). The averaging time was set at annual, based on the nature of the study and the screening level calculation that was used to extrapolate from subchronic to chronic (life-time) exposure.

References:

American Conference of Governmental and Industrial Hygienist (ACGIH) (1991) Aluminum. Documentation for Threshold Limit Values and Biological Exposure Indices. Cincinnati, OH.

American Conference of Governmental and Industrial Hygienist (ACGIH) (2008) Aluminum Metal and Insoluble Compounds. Documentation for Threshold Limit Values and Biological Exposure Indices. Cincinnati, OH.

Finelli, H.V. 1981. Summary from REACH of European Chemical Agency. Dossier for Aluminum Chloride. Taken from: Finelli VN, Que Hee SS, & Niemeier RW (1981) Influence of exposure to aluminium chloride and fluoride dusts on some biochemical and physiological parameters in rats. In: Brown SS & Davies DS ed. Organ-directed toxicity chemical indices and mechanisms (IUPAC). New York, Pergamon Press, pp 291-295.

Grams, G. W. 2003. Aluminum Halides and Aluminum Nitrate. Kirk-Othmer Encyclopedia of Chemical Technology. Published Online: 14 FEB 2003. DOI: 10.1002/0471238961.0112211307180113.a01.pub2. Copyright © 1999-2016 John Wiley & Sons, Inc.
http://onlinelibrary.wiley.com/doi/10.1002/0471238961.0112211307180113.a01.pub2/abstract <accessed December 21, 2016>

ICSC (2005) Aluminum Chloride (Anhydrous). International Chemical Safety Cards (ICSC) Number 1125. Peer-Review Status: 20.04.2005 Validated