**MICHIGAN DEPARTMENT OF ENVIRONMENTAL QUALITY**

_____

**INTEROFFICE COMMUNICATION**

_____

TO: File for Dimethyl dichlorosilane (CAS # 75-78-5)

FROM: Keisha Williams, Air Quality Division (AQD)

DATE: August 7, 2015

SUBJECT: Screening Level for Dimethyl dichlorosilane

The chronic initial threshold screening level (ITSL) for dimethyl dichlorosilane is 1 µg/m$^3$ (annual averaging time) based on the Michigan Department of Environmental Quality (MDEQ), AQD Rule 336.1232 (1) (d). The ITSL value was originally set on December 17, 1991 at 6.2 µg/m$^3$ (annual averaging time) using an LC50 study, but with review of the literature a more sensitive critical effect was identified. Also, an acute ITSL is being established at this time at 3700 µg/m$^3$ with a 1-hour averaging time.

The following references or databases were searched to identify data to determine the screening level: United States Environmental Protection Agency's (EPA's) Integrated Risk Information System (IRIS), the Registry of Toxic Effects of Chemical Substances (RTECS), the American Conference of Governmental Industrial Hygienists (ACGIH) Threshold Limit Values (TLV), National Institute of Occupational Safety and Health (NIOSH) Pocket Guide to Hazardous Chemicals, MDEQ Library, International Agency for Research on Cancer (IARC) Monographs, Chemical Abstract Service (CAS) Online (1992- June 2015), National Library of Medicine (NLM), Health Effects Assessment Summary Tables (HEAST), National Toxicology Program (NTP) Status Report, EPA Aggregated Computational Toxicology Resource (ACToR) Database, EPA TSCATS database, EPA Superfund Provisional Peer Reviewed Toxicity Values, EPA Acute Exposure Guideline Levels for Airborne Chemicals, EPA High Production Volume Database, United States Department of Labor Occupational Safety and Health Administration Permissible Exposure Limits, Spacecraft Maximum Allowable Concentrations, California Office of Environmental Health Hazard Assessments Reference Exposure Levels, Chemical Safety Program Protective Action Criteria, Texas Commission on Environmental Quality Effects Screening Levels, and European Chemicals Agency Registered Substances Dossiers.

## Background Information

Production, uses, and chemical and physical properties

Dimethyl dichlorosilane (DMDCS), also known as dichlorodimethylsilane, has been used to produce silicone goods (NRC, 2012). Chemical and physical properties are given in Table 1.

Table 1. Chemical and physical properties of DMDCS

| |
|---|
| Boiling point: 158°C at 760 mm Hg |
| Chemical Formula: $C_2H_6Cl_2Si$ |
| Color: Colorless |
| Molecular weight: 129.06054 grams/mole |
| Odor description: Pungent |
| Physical state at room temperature: liquid |
| Vapor density: 4.45, where air=1 |
| Vapor pressure: 144 mmHg at 25°C |

Reference: PubChem database, https://pubchem.ncbi.nlm.nih.gov/compound/6398

Regulatory precedence

Several benchmark values have been established to protect against adverse health effects from DMDCS inhalation. As seen in Table 2, these include protective action criteria (PAC), acute exposure guideline levels (AEGLs), emergency response planning guideline (ERPG) values, workplace environmental exposure levels (WEELs) and screening levels used by the Texas Commission on Environmental Quality (TCEQ). The TCEQ is currently reviewing the literature on DMDCS, and their benchmark value may be changed pending this review (TCEQ, 2014). The AEGL value was derived using a human study of hydrogen chloride-induced effects in exercising asthmatics (NRC; 2012; Stevens et al., 1992), "since it is believed that the hydrolysis product, HCl, [of DMDCS] is responsible for the adverse effects" (NRC, 2012).

Table 2. Benchmark values for DMDCS

| Agency | Benchmark Value |
|---|---|
| United States Environmental Protection Agency (EPA) | AEGLs for 1-hour and 8-hour exposures: 4.8 $mg/m^3$ (NRC, 2012; Stevens et al., 1992) |
| TCEQ | Health effects screening levels for long-term exposure: 11 $\mu g/m^3$ and for short-term exposure: 106 $\mu g/m^3$ (TCEQ, 2014)<br>Note that both were derived on 12/20/2010. |
| Chemical Safety Program (based on AEGL 60 minute values) | PAC-1: 4.7 $mg/m^3$<br>PAC-2: 58 $mg/m^3$<br>PAC-3: 260 $mg/m^3$ (Chemical Safety Program, 2012) |
| American Industrial Hygiene Association (AIHA) | ERPG-1: 2 ppm (≈10.6 $mg/m^3$)<br>ERPG-2: 10 ppm (≈52.8 $mg/m^3$)<br>ERPG-3: 75 ppm (≈396 $mg/m^3$) (AIHA, 2014) |
| AIHA | WEEL ceiling value: 2 ppm (≈10.6 $mg/m^3$) (AIHA, 2013) |

Toxicity in humans and interspecies considerations

No epidemiological studies or controlled human studies on the effects of DMDCS were found. Human toxicity from the classes of chemicals to which DMDCS belongs, silanes and organochlorosilanes, have been reported (Sittig, 1981; NIOSH, 1977). These classes have been "reported to be highly toxic by inhalation, ingestion, or skin contact, following an acute exposure. Any of the chlorosilanes can emit a highly irritating, asphyxiating vapor" (NIOSH, 1977).

Since there are no human studies which can be used to derive the ITSL, animal studies will continue to be used for the DMDCS ITSL. No studies were found that compared interspecies responses. However, in the documentation for the AEGL value derivation, hydrogen chloride studies were used to consider interspecies differences (NRC, 2012). With this, it was noted that humans (oral and nasal breathers) as compared to rats (obligatory nose breathers) may be more susceptible to hydrogen chloride-induced toxicity as oral breathing may produce an increased response.

Potential mechanisms of action

Toxicity from DMDCS exposure has largely been equated to hydrogen chloride toxicity. To support this assessment, as summarized in the documentation for the AEGL value, an LC50 study compared ten chlorosilanes (including DMDCS) to hydrogen chloride (NRC, 2012). Groups of 10 animals, five female and five male rats, were used. Effects were evaluated after the 1-hour exposure and during the 14-day recovery period, where the chlorosilane-induced respiratory, ocular, dermal, and gastrointestinal irritation "clinical signs were consistent with hydrogen chloride exposure." Hydrogen chloride toxicity is based on its highly corrosive, reactivity and irritating properties as a strong acid (ACGIH, 2003). It is important to note that every 1 mole of DMDCS can produce 2 moles of hydrogen chloride, so the AEGL value for DMDCS has been molar adjusted to the hydrogen chloride (HCl) AEGL values accordingly. Since irritation from acute exposure has been shown to be a concern, an acute ITSL will be derived at this time.

**Evaluation of Cancer Risk**

No carcinogenicity studies were found. Furthermore, hydrogen chloride has been reported to be "not classifiable as a human carcinogen" (ACGIH, 2003). As a result, DMDCS will not be defined or regulated as a carcinogen at this time.

**Review of Relevant Studies for Non-carcinogen Effects**

Study formerly used to derive the ITSL

The original ITSL (MDNR, 1991) was based on an unpublished LC50 study performed by the toxicology department at Dow Corning Corporation, where the LC50 was determined to be 2341 ppm (approximately 12400 mg/m$^3$) for both male and female rats (Bile et al., 1987). As shown in Equation 1, the previously established ITSL was calculated thusly:

Equation 1.

$$Former\ ITSL = \frac{LC50}{(500\ x\ 100\ x\ 40)} = \frac{12400\ \frac{mg}{m^3}\ x \frac{1000\ \mu g}{mg}}{500\ x\ 100\ x\ 40} = 6.2\ \frac{\mu g}{m^3}, annual\ averaging\ time$$

Study currently used to derive the ITSL for chronic effects

A rat whole body inhalation study was described in the European Chemicals Agency (ECHA) database for registered substances (ECHA, 2015). The study was designed to compare DMDCS-induced respiratory effects to hydrogen chloride-induced effects after subacute exposure for 6 hours per day, 5 days per week for a total of 4 weeks. With n=12 per group (6 male and 6 female), Crl:CD (SD) rats were exposed to DMDCS concentrations of 0, 5 or 25 ppm (approximately 0, 26 and 130 mg/m$^3$ as shown in Equation 2). Several endpoints were

measured including: changes in mortality, body weight, food consumption, organ weights, gross pathology, and non-neoplastic and neoplastic histopathology. Lower mean spleen weights were observed in females exposed to the lowest dose of dimethyl dichlorosilane, and histologic changes in the anterior nasal cavity were also observed at the 5 ppm exposure concentration "with dose-related incidence."

In the "Applicant's summary" section, it was stated that "the effects in the nasal cavity at 5 ppm dichloro (dimethyl) silane were…of minimal severity and of a lower incidence and therefore considered not to be adverse" (ECHA, 2015). However, in the "results and discussion" section, another summary of the results indicated that a no-observable adverse effect level was not identified, and "local irritant effects noted in the nasal cavity at both 5 and 25 ppm…[were dose-related]." As a result, 5 ppm was taken to be the lowest observable adverse effect level (LOAEL). As such, the decreased spleen weight and nasal effects observed at 5 ppm were shown to be the critical effects for DMDCS, and this study summary was used to derive an ITSL using AQD Rules 336.1229 (2) (b) and 336.1232 (1) (d) as shown in Equation 3.

5 ppm is converted to units of µg/m$^3$ as follows in Equation 2:

Equation 2.

$$LOAEL_{units\ of\ \frac{\mu g}{m^3}} = \frac{LOAEL_{units\ of\ ppm}\ x \frac{10^3 ppb}{ppm}\ x\ molecular\ weight_{DMDCS}}{24.45}$$

$$LOAEL_{units\ of\ \frac{\mu g}{m^3}} = \frac{5\ ppm\ x \frac{10^3 ppb}{ppm}\ x\ 129.06054 \frac{grams}{mole}}{24.45} = 26,392.75\ \frac{\mu g}{m^3}$$

Equation 3.

$$ITSL\ for\ chronic\ effects\ = \frac{LOAEL}{20\ x\ 100\ x\ uncertainty\ factor_{LOAEL\ to\ NOAEL}} x \frac{hours\ exposed\ per\ day}{24\ hours\ per\ day},$$

Where: 1) an uncertainty factor of 20 is used to extrapolate from this study's 4-week exposure to chronic exposure instead of the uncertainty factor, 35, that is described in Rule 336.1232 (1) (d) to be used with a 7-day inhalation study; and 2) an uncertainty factor of 3 is used to extrapolate from this study's relatively mild effect at 5 ppm

$$ITSL\ for\ chronic\ effects = \frac{26393\ \frac{\mu g}{m^3}}{20\ x\ 100\ x\ 3}\ x \frac{6\ hours\ exposed\ per\ day}{24\ hours\ per\ day},$$

$$ITSL\ for\ chronic\ effects = \ 1.1\ \frac{\mu g}{m^3} \approx 1 \frac{\mu g}{m^3}, annual\ averaging\ time$$

<u>Study used to derive the ITSL for acute effects</u>

As described above, since acute effects are also a concern from DMDCS exposure, an acute ITSL will be established at this time. The best available data is a human study by Stevens et al. (1992), where the health effects of hydrogen chloride were investigated. Briefly, in this study, 10

asthmatics were exposed to 0.8 or 1.8 ppm (approximately 4,200 or 9,500 µg/m$^3$) of hydrogen chloride for 45 minutes. With evaluations for critical effects of upper respiratory tract symptoms, a no observable adverse effect level (NOAEL) was seen at even the high exposure concentration. This study has been used to derive 1) the MDEQ AQD's acute ITSL for hydrogen chloride, 2) the state of California's Office of Environmental Health Hazard Assessment's acute reference exposure level for hydrogen chloride, 3) the EPA's 60-minute AEGL for hydrogen chloride, and 4) the EPA's 60-minute AEGL for chlorosilanes (MDEQ, 2014; NRC, 2004; NRC, 2014; OEHHA, 2014). While all three agencies use similar methods for benchmark derivation, the 2100 µg/m$^3$ value derived by the MDEQ's AQD and California's OEHHA used exposure duration adjustment considerations that were not made in the EPA's calculation for either hydrogen chloride or chlorosilanes (MDEQ, 2014; NRC, 2004; NRC, 2012; OEHHA, 2014).

Using molar equivalency considerations, the acute ITSL for DMDCS is then calculated as follows in Equation 4:

Equation 4.

$$Acute\ ITSL = acute\ ITSL_{HCl}\ x\ DMDCS molar\ adjustment\ factor,$$

Where: 1) AQD acute ITSL for hydrogen chloride is 2100 µg/m$^3$, 1-hour averaging time, 2) complete hydrolysis of 1 mole of DMDCS gives 2 moles of hydrogen chloride, 3) molecular weight of DMDCS is ≈129.1 grams/mole; and 4) molecular weight of hydrogen chloride is ≈36.5 grams/mole

$$Acute\ ITSL = 2100 \frac{\mu g}{m^3} x \frac{\frac{129.1\ grams}{mole}\ x\ 1\ mole}{\frac{36.5\ grams}{mole}\ x\ 2\ moles} = 3714\ \frac{\mu g}{m^3}$$

$$\approx 3700\ \frac{\mu g}{m^3}, 1\ hour\ averaging\ time$$

**Therefore, the acute ITSL will be 3700 µg/m$^3$, 1-hour averaging time and the chronic ITSL will be 1 µg/m$^3$.**

**References**

ACGIH. 2003. Documentation of the Threshold Limit Values and Biological Exposure Indices. American Conference of Governmental Industrial Hygienists, Cincinnati, OH.

AIHA. 2013. ERPG/WEEL Handbook: WEEL Values (2011). Accessed July 7, 2015. https://www.aiha.org/get-involved/AIHAGuidelineFoundation/WEELs/Documents/2011WEELValues.pdf

AIHA. 2014. ERPG/WEEL Handbook: Current ERPG Values (2014). Accessed July 7, 2015. https://www.aiha.org/get-involved/AIHAGuidelineFoundation/EmergencyResponsePlanningGuidelines/Documents/2014%20ERPG%20Values.pdf

Bile, P.A., G.B. Kolesar, W.H. Siddiqui. 1987. A comparison of acute inhalation toxicity of a series of chlorosilanes with hydrogen chloride in rats. Dow Corning Corporation, Toxicology Department.

Chemical Safety Program. 2012. Protection action criteria (PAC): Chemicals with AEGLs, ERPGs, and TEELs. Accessed July 7, 2015. http://www.atlintl.com/DOE/teels/teel.html

ECHA. 2015. Dichloro(dimethyl)silane, toxicological information, repeated dose toxicity: inhalation, exp key repeated dose toxicity: inhalation. 001. Accessed August 6, 2015. http://apps.echa.europa.eu/registered/data/dossiers/DISS-a134210d-5f49-4176-e044-00144f67d031/AGGR-826a90cd-1d46-4a12-9a63-bf73f72592e6_DISS-a134210d-5f49-4176-e044-00144f67d031.html#AGGR-826a90cd-1d46-4a12-9a63-bf73f72592e6

MDEQ. 2014. Memo from Michael Depa to File for Hydrogen Chloride (CAS No. 7647-01-0). Subject: Development of Screening Level. April 8, 2014. AQD, MDEQ.

MNDR. 1991. Memo from Gary Butterfield to Paul Schleusener. Subject: AAC for dimethyldichlorosilane (75-78-5) for Dow Corning Permit 209-70B. December 17, 1991. AQD, MDNR.

NIH. Dichlorodimethylsilane. Accessed July 7, 2015. https://pubchem.ncbi.nlm.nih.gov/compound/6398

NIOSH. 1977. Profiles on Occupational Hazards for Criteria Document Priorities: Silcone and its Compounds, Report PB-274, 073, Cincinnati, Ohio, pp. 55-61.

NRC. 2012. Acute Exposure Guideline Levels for Selected Airborne Chemicals: Selected chlorosilanes. Volume 11. Washington, D.C.: The National Academies Press.

(References Jean, P.A., R.H. Gallavan, G.B. Kolesar, W.H. Siddiqui, J.A. Oxley, and R.G. Meeks. 2006. Chlorosilane acute inhalation toxicity and development of an LC50 prediction model. Inhalation Toxicology 18(8):515-522.

NRC. 2004. Hydrogen chloride. Pp. 77-122 in Acute Exposure Guideline Levels for Selected Airborne Chemicals. Volume 4. Committee on Toxicology, Washington, DC: National Academies Press.

Stevens, B., J.Q. Koenig, V. Robolledo, Q.S. Hanley, and D.S. Covert. 1992. Respiratory effects from the inhalation of hydrogen chloride in young adult asthmatics. Journal of Occupational and Environmental Medicine. 34 (9): 923-929.)

Sittig, M. 1981. Handbook of Toxic and Hazardous Chemicals. Noyes Publications, Park Ridge, NJ.

TCEQ. 2014. Effects Screening Levels (ESL) Lists Used in the Review of Air Permitting Data: Current ESL List. Accessed July 7, 2015. http://www.tceq.texas.gov/toxicology/esl/list_main.html/#esl_1

KW:lh

**Michigan Department of Natural Resources**

_____

**Interoffice Communication**

_____

Dec 17, 1991

To : Paul Schleusener
Permit Section

From : Gary Butterfield
Toxics Unit

Subject : AAC for dimethyldichlorosilane (75-78-5) for Dow Corning
Permit 209-70B

A literature search was not able to identify any long term studies conducted with dimethyldichlorosilane (CA # 75-78-5). Other acute studies, from foreign publications, as cited in RTECS, identified LC50's reasonably close to the one hour LC50 of 2341 ppm or 12400 mg/m$^3$ reported in the 1987 Dow Corning report.

$$AAC = \frac{12400 \frac{mg}{m^3}}{500\ x\ 100\ x\ 40} = 6.2 \frac{\mu g}{m^3}$$

Based on that one hour LC50, the AAC is 6.2 µg/m$^3$, with annual averaging, as calculated above. If you have any questions about this issue, please feel free to contact me at 373-7061.