MICHIGAN DEPARTMENT OF ENVIRONMENTAL QUALITY

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INTEROFFICE COMMUNICATION

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July 16, 2018

To: File for Triethoxy(3-isocyanatopropyl)silane (CAS No. 24801-88-5)

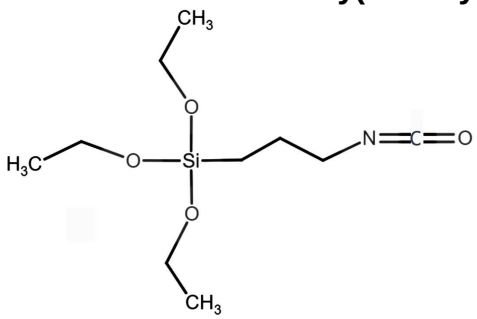
From: Michael Depa, Air Quality Division, Toxics Unit

Subject: Screening Level Derivation

The initial threshold screening level (ITSL) for triethoxy(3-isocyanatopropyl)silane (synonym 3-Isocyanatopropyltriethoxysilane) is 0.08 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 (EPA) Integrated Risk Information System (IRIS), ECHA (European Chemical Agency) Registration, Evaluation, Authorization and Restriction of Chemicals (REACH), Registry for Toxic Effects of Chemical Substances (RTECS), American Conference of Governmental and Industrial Hygienists (ACGIH) Threshold Limit Values (TLVs), EPA Acute Exposure Guideline Levels (AEGLs), National Institute for Occupational Safety and Health (NIOSH) Pocket Guide to Hazardous Chemicals, Agency for Toxic Substances and Disease Registry (ATSDR) Minimal Risk Levels (MRLs), U.S. EPA Provisional Peer Reviewed Toxicity Values (PPRTVs) for Superfund, International Agency for Research on Cancer (IARC) Monographs, California Office of Environmental Health Hazard Assessment (OEHHA), Chemical Abstract Service (CAS) - SciFinder (1967 – May, 2018), National Library of Medicine (NLM) Toxline, and National Toxicology Program (NTP) Status Report. The EPA has not established a reference concentration for Triethoxy(3-isocyanatopropyl)silane. The ACGIH has not derived a TLV.

Figure 1. Molecular Structure of Triethoxy(3-isocyanatopropyl)silane



Molecular Formula: C10-H21-N-O4-Si
Molecular Weight: 247.4g
Vapor pressure was reported as triethoxy(3-isocyanatopropyl)silane: 2 Pa (0.015 mmHg) at 20°C.

Oral Toxicity

A well reported repeated dose 90-day oral toxicity study, conducted in the main according to the current guideline for that endpoint and in accordance with GLP, identified a systemic NOAEL value of 200 mg/kg bw/day in male and female rats; mortality, clinical observations and liver effects were evident at 600 mg/kg bw/day. No effects on reproductive organs, oestrus cycle or sperm parameters were evident at the highest tested dose of 600 mg/kg bw/day. This study would have only limited potential to detect all possible reproductive effects (ECHA, 2018).

A well reported study conducted according to generally accepted scientific standards and in accordance with GLP reported maternal toxicity (increased incidences of mortality, clinical observations, and slight decreases in body weight gain and food consumption) at 600 mg/kg bw/day. The occurrence of maternal toxicity was accompanied by slight fetal toxicity (increased minor skeletal variations). No significant maternal or developmental effects were observed at 20 or 100 mg/kg bw/day. The maternal and developmental NOAEL were 100 mg/kg bw/day (ECHA, 2018).

Acute Inhalation Toxicity

As reported by Union Carbide (1992) the lethal concentration fifty percent (LC50) was 360 mg/m³ (95% confidence interval: 152 – 748 mg/m³).

Subacute Inhalation Toxicity

Groups of 5 male and 5 female Wistar rats were exposed to 1.8, 4.9, and 18.1 mg/m³ for 6 hr/day, 5 days/wk for 31 days (20 exposure days)(ECHA, 2018). The target concentrations were: 1.5, 5 and 15 mg/m³. Additional rats were kept for a 14-day recovery study. **Results:** At 18.1 mg/m³ the authors reported slight breathing abnormalities during exposure days 7-17. Significantly reduced body weights were observed in both sexes at mid (4.9 mg/m³) and high (18.1 mg/m³) concentrations. The reduced body weights were fully reversed during the recovery period in females, but males retained non-statistically significant evidence of this effect. Food consumption was reduced in males at 18.1 mg/m³, which was fully reversed after 14-days recovery. Significantly reduced thrombocytes were seen in females at 18.1 mg/m³. This reduction was reversed after 14-day recovery period. Reduced urinary volume and concomitantly increased creatinine content in males at 18.1 mg/m³. After the 14-day recovery period the urinary volume was comparable with controls. **Histopathology in the respiratory tract: Nasal passages:** Concentration-related effects were seen in all exposure groups with increased severity and progression of effects from anterior to posterior sections of the nasal passages. Effects comprised of focal erosion/ulceration and severe epithelial degeneration at 18.1 mg/m³. At 4.9 mg/m³ similar changes were seen in the anterior sections with more moderate effects in the middle and posterior sections. Minimal changes in the most anterior sections were seen in females exposed to 1.8 mg/m³. These changes had considerably decreased after 14-days recovery. **Larynx:** Effects were seen at 4.9 and 18.1 mg/m³ including epithelial degeneration and hyperplasia, squamous metaplasia and mononuclear cell infiltrates. One male was slightly affected at 4.9 mg/m³. These changes had considerably decreased after 14-days recovery. **Trachea and lungs:** The authors reported adverse lung effects only at 18.1 mg/m³, which included tracheal epithelia hyperplasia, epithelial degeneration/regeneration and mononuclear cell infiltrates. At 18.1 mg/m³ the lungs showed very slight or slight epithelial degeneration/regeneration. These changes had reversed after 14-days recovery. The Lowest Observed Adverse Effect

Level (LOAEL) was identified as 1.8 mg/m³ (0.0018 mg/l) based on very slight respiratory lesions in females only, that were, "[S]ignificantly reduced after the 14-day recovery." A No Observed Adverse Effect Level was no identified in this study.

Derivation of ITSL

Since the study duration was 28 days, the equation described in Rule 232(1)(d) was modified by changing the default uncertainty factor of "35" to "20", because Rule 232(1)(d) was designed for a 7-day inhalation study, and the duration of the study used to calculate the ITSL is 28 days in duration. The lowering of the uncertainty factor from 35 to 20 reflects an increase in the certainty when extrapolating from a short-term exposure study to a long-term health-based screening level.

***7-day exposure**:* Rule 232(1)(d):

ITSL = LOAEL/(*35* × 100 × UF) × (hrs exposed/24 hrs)

28-day exposure: Modified Rule 232(1)(d):

ITSL = LOAEL/(*20* × 100 × UF) × (hrs exposed/24 hrs)

The ITSL was calculated as:

ITSL = LOAEL/(20 × 100× UF) × 6hrs/24hrs × unit conversion

Where the Uncertainty Factor (UF) is 3 for the LOAEL to NOAEL extrapolation where the LOAEL was mild nasal effects, which were reduced in severity after a 14-day recovery period.

ITSL = (1.8 mg/m³)/(20 ×100 × 3) × 6/24 × 1000µg/mg
ITSL = 0.075 µg/m³ ≈ 0.08 µg/m³ (rounding to one significant figure)

The ITSL for triethoxy(3-isocyanatopropyl)silane is 0.08 µg/m³ with annual averaging time (averaging time is specified in Rule (232(2)(c)).

References

ECHA. 2018. Registration Dossier for Triethoxy(3-isocyanatopropyl)silane (EC number 246-467-6). European Chemical Agency (ECHA). Regulation (European Commission) No 1907/2006 Registration, Evaluation, Authorization and Restriction of Chemicals (REACH) First published: 30-Jan-2016. Last modified: 04-May-2018. https://echa.europa.eu/registration-dossier/-/registered-dossier/16621/1

Union Carbide (1992). Initial Submission: Range-Finding Toxicity Studies of Sllane. 36-65(Gamma-Isocyanopropyltriethoxysllane) With Cover Letter. Dated 08/26/92. EPA/OTS; Doc #88-920009398. Downloaded from the National Technical Reports Library (NTRL) https://ntrl.ntis.gov/NTRL/ on May 8, 2018.