MICHIGAN DEPARTMENT OF ENVIRONMENTAL QUALITY

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INTEROFFICE COMMUNICATION

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July 16, 2018

To: File for 1,2-Diaminocyclohexane (CAS No. 694-83-7)

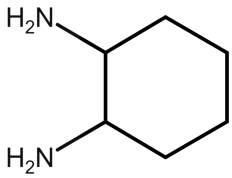
From: Michael Depa, Air Quality Division, Toxics Unit

Subject: Screening Level Derivation

The initial threshold screening level (ITSL) for 1,2-diaminocyclohexane is 2 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 1,2-diaminocyclohexane. The ACGIH has not derived a TLV.

Figure 1. Molecular Structure of 1,2-Diaminocyclohexane



Molecular Formula: C6-H14-N2
Molecular Weight: 114.191
Vapor pressure was reported as 1,2-diaminocyclohexane: 0.407 mmHg at 25°C (ChemIDplus, 2018).

Groups of ten male Crl:CD*BR rats were exposed to 0, 10, 49 and 240 mg/m³ of 1,2-diaminocyclohexane by inhalation (nose-only) for six hours/day, five day/week, for two weeks. (ECHA. 2018). This report was cross-referenced to an unpublished report by DuPont Company (1993). Inhalation was of an aerosol-vapor mixture. The aerosol size (mass mean aerodynamic diameter; MMAD) was reported as ranging from 2.6 to 5.8 micrometers (µm).

Five animals of each treatment group as well as control animals were observed for a 14-day post-exposure recovery period. Immediately after the two-week exposure, all treatment group rats showed dose dependent nasal lesions, which consisted of inflammation and necrosis of the nasal mucosa. After the two-week recovery period none of the nasal lesions were observed in any test material exposed rats.

As reported by the authors:

Low dose group:
- nasal lesions, which were considered to be of minimal severity.
- minimal inflammation and necrosis in the larynx/pharynx region in 1 out of 5 rats.

Mid dose group:
- nasal lesions, which were considered to be of mild severity;
- minimal inflammation and necrosis in the larynx/pharynx region in 1 out of 5 rats.

High dose group:
- nasal lesions, which were considered to be of moderate severity.
- minimal to moderate inflammation and necrosis in the larynx/pharynx region in 2 out of 5 rats.
- minimal to mild inflammation of the tracheal muscle in 2 out of 5 rats

There were no adverse effects observed in any of the test groups with respect to the hematologic, clinical chemical, urinalysis, and body weight parameters measured. As expected from its chemical basicity, inhaled test material produced respiratory tract irritation in exposed rats. However, the lesions (inflammation /necrosis) observed occurred only in the upper respiratory tract (mainly the nose, larynx, and pharynx), were moderate at the highest concentration tested, and were decreased in severity at the lower test concentrations. Nasal effects observed in the 49 mg/m^3 group were mainly mild and those in the 10 mg/m^3 group were minimal. The observed effects were completely reversible after a two-week recovery period even at the 240 mg/m^3 concentration. Although a no-adverse-effect concentration was not determined in this study, the respiratory (mainly nasal) effects observed at the lowest tested concentration (10 mg/m^3) were considered minimal and reversible. Because effects on the respiratory tract were seen in all concentration groups tested and these effects were clearly dose related, a no-observed-adverse-effect-level (NOAEL) could not be determined. The lowest-observed-adverse-effect-level (LOAEL) of this study was identified as 10 mg/m^3.

Other Information

Various agencies have established exposure limits for 1,2-diaminocyclohexane (see Table 1). However, since the toxicological basis of these limits was not available, there was no information with which to judge their efficacy to protect human health, especially sensitive individuals. Consequently, they were not used to derive a screening level.

Table 1. Exposure Limits (EPA, 2018)

Limit Value	Concentration Units	Description of Limit	Reference
564	µg/m³	1/2-Hour Average	a
188	µg/m³	24-Hour Average	a
350	mg/m³	1 hour Critical Air MEG	b
60	mg/m³	1 hour Marginal Air MEG	b
10	mg/m³	1 hour Negligible air MEG	b
1.9	mg/m³	PAC-1 (Mild)	c
21	mg/m³	PAC-2 (Irreversible)	c
120	mg/m³	PAC-3 (Life threatening)	c

[a] Ontario (Canada) Ministry of the Environment (OMOE, 2018) Jurisdictional Screening Level (JSL) List for use in assessing air contaminants (as reported by EPA, 2018).
[b] US Army Military Exposure Guidelines (MEGs) for Short-Term exposures to chemicals in ambient air for various military exposure scenarios during deployments (APHC, 2018).
[c] US Department of Energy (DOE, 2018): current data set of Protective Action Criteria (PAC) values. These are Emergency exposure limits which are essential components of planning for the uncontrolled release of hazardous chemicals.

Derivation of ITSL

Because the duration of the inhalation study (EPA, 2018) was 28 days, the equation described in Rule 232(1)(d) was modified by changing the 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.

The ITSL was calculated as:

ITSL = LOAEL/(20 x 100 x UF) x unit conversion

Where the Uncertainty Factor (UF) is to extrapolate from a LOAEL to a NOAEL. This UF was decreased from 10 to 3 because the nasal effects were considered mild and reversible.

ITSL = (10 mg/m³)/(20 x 100 x 3) x 1000µg/mg
ITSL = 1.67 µg/m³ ≈ 2 µg/m³ (rounding to one significant figure)

The ITSL for 1,2-diaminocyclohexane is 2 µg/m³ with annual averaging time (averaging time is specified in Rule (232(2)(c)).

References

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