MICHIGAN DEPARTMENT OF ENVIRONMENT, GREAT LAKES, AND ENERGY

INTEROFFICE COMMUNICATION

TO: File for diglycol amine (CAS# 929-06-6)

FROM: Keisha Williams, Air Quality Division

DATE: March 26, 2024

SUBJECT: Screening level derivation for diglycol amine (CAS# 929-06-6)

The initial threshold screening level for diglycol amine (CAS# 929-06-6) is 9 µg/m^3 (8-hour averaging time) based on the Michigan Department of Environment, Great Lakes, and Energy (EGLE; formerly Michigan Department of Environmental Quality [MDEQ]), Air Quality Division (AQD), Rule 336.1232 (1) (c) and (2) (a).

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 American Conference of Governmental Industrial Hygienists (ACGIH) Threshold Limit Values (TLV); National Institute of Occupational Safety and Health (NIOSH) Pocket Guide to Hazardous Chemicals; Agency for Toxic Substances and Disease Registry (ATSDR) Minimal Risk Levels, International Agency for Research on Cancer (IARC) Monographs; Health Effects Assessment Summary Tables (HEAST); National Toxicology Program (NTP) Status Report, EPA Superfund Provisional Peer Reviewed Toxicity Values; EPA Acute Exposure Guideline Levels (AEGLs) for Airborne Chemicals; EPA High Production Volume Database; United States Department of Labor Occupational Safety and Health Administration (OSHA) Permissible Exposure Limits (PELs); Spacecraft Maximum Allowable Concentrations (SMACs); California Office of Environmental Health Hazard Assessments Reference Exposure Levels; Texas Commission on Environmental Quality (TCEQ) Effects Screening Levels (ESLs); European Chemicals Agency Registered Substances Dossiers; Chemical Abstract Service (CAS) Online search (search date: April 8, 2016); TSCA database; ACToR database, NLM/TOXLINE database; HAZARDOUS SUBSTANCES DATA BANK (HSDB); Chemical Safety Program Protective Action Criteria; the Organisation for Economic Co-operation and Development (OECD) Screening Information Data Set (SIDS) files; and Deutsche Forschungsgemeinschaft maximale Arbeitsplatz-Konzentration (MAK) values, where maximale Arbeitsplatz-Konzentration translates to maximum workplace concentration in English.

Background Information

Diglycol amine is also referred to as 2-(2-aminoethoxy)ethanol. It has been used as an emulsifying agent for metal-working fluids, in the production of detergents, and in the removal of hydrogen sulfide and carbon dioxide from natural and refinery gases (MAK Collection, 2014). See Figure 1 for the chemical structure. At room temperature, diglycol amine is a colorless liquid with a fishlike odor (Pubchem). Chemical properties are listed in Table 1.

Figure 1. Chemical structure for diglycol amine

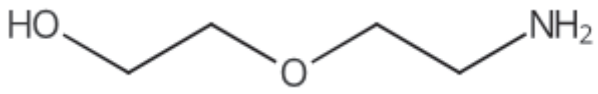


Table 1. Chemical properties of diglycol amine

Molecular weight: 105.14 grams/mole (Pubchem)
Melting point: -12.5 °C (Pubchem)
Boiling point: 222.5-223.8°C at 1013 hPa (ECHA, 2023)
Vapor pressure: 0.5 hPa at 58.5°C (ECHA, 2023)

Few health benchmarks were found for diglycol amine. TCEQ has developed interim health effects screening levels for long-term exposure at 38 µg/m^3 and for short-term exposure at 380 µg/m^3 (TAMIS). There is a German occupational exposure level (OEL) at 0.87 mg/m^3, 8-hour time-weighted average (MAK Collection, 2014).

No inhalation toxicity data was found for human exposure.

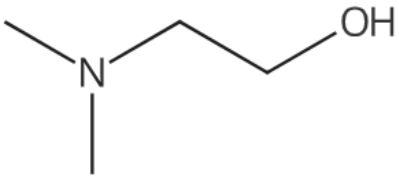
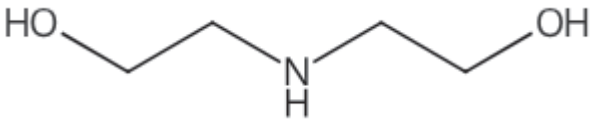
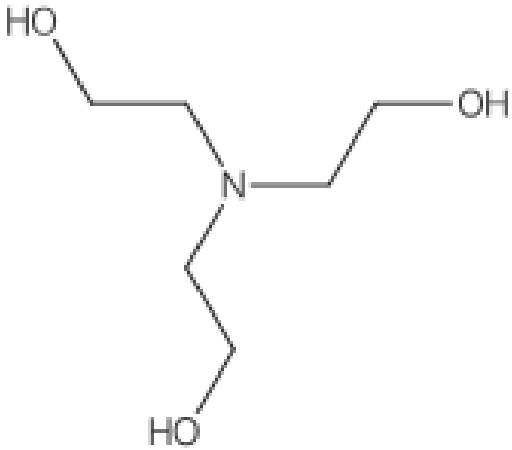
The MAK value documentation summarizes skin sensitization data based on patch tests in both case studies and occupational exposure studies (MAK Collection, 2014). Diglycol amine has been shown to be a skin sensitizer and in one of the worker studies, up to 6.6% of workers tested were positive for reactions to a 1% preparation of diglycol amine in Vaseline.

As compared to the effects observed in humans, the MAK value documentation notes that in guinea pigs, a study on skin sensitization was negative.

Summaries of one inhalation study in rats was found (MAK Collection, 2014; OECD SIDS, 2014; ECHA, 2023). The study was conducted according to OECD Test Guideline 422 (Combined Repeated Dose Toxicity Study with Reproduction/Developmental Toxicity Screening Test), where male and female Wistar rats (N=10 per dose group) were exposed to 0, 4, 16, or 40 mg/m^3 for 6 hours per day, 7 days per week, for 29 days for males and 46-48 days for females. The median mass aerodynamic diameter (MMAD) was not detectable-0.8, 2.6-3.0, or 1.9-2.6 at the low, mid, and high dose, respectively. A no observable adverse effect concentration was observed at 4 mg/m^3. After 14 days of exposure, rats in the F0 generation were mated. As compared to the control group, increased squamous metaplasia was observed in the larynx of male rats at the mid dose. As compared to the control group, increased squamous metaplasia was observed at the highest dose in both genders. Similarly, there was dose-dependent increases in chronic inflammation in the larynx of both genders. There was no noted effect in the nose.

Although the toxicity database on diglycol amine is limited with only one repeat dose inhalation study, similarly structured alkanolamines and primary amines as a group have been shown to be corrosive with eye, lung, and skin irritation as the critical effect (see Table 2). These portal of entry effects are expected to occur because of the alkaline properties of these toxic air contaminants (TACs). Given the potential for portal of entry effects, extrapolation from oral studies is inappropriate.

Table 2. AQD TACs with similar structures and toxicological properties to diglycol amine

Name (CAS#)	Structure	ITSLs
Ethylamine (CAS# 75-04-7)		92 µg/m^3, 8-hour AT (MDEQ, 1998)
Monoethanolamine (CAS# 141-43-5)		80 µg/m^3, 8-hour AT (MDEQ, 2013)
Dimethylethanolamine (CAS# 108-01-0)		5.2 µg/m^3, annual AT; 220 µg/m^3, 8-hour AT (MDEQ, 2013)
Diethanolamine (CAS# 111-42-2)		0.2 µg/m^3, annual AT; 10 µg/m^3, 8-hour AT (MDEQ, 2022)
Triethanolamine (CAS# 102-71-6)		50 µg/m^3, 8-hour AT (MDEQ, 1997)

It is important to note, similar to diglycol amine, most of these TACs have very limited toxicity databases. The TAC with the most toxicity studies, diethanolamine (CAS# 111-42-2), has respiratory irritation as a critical effect, along with liver and kidney effects. Furthermore, diethanolamine has been shown to be a carcinogen via dermal exposure in male and female mice (but not rats) with not enough information to derive an initial risk screening level for

inhalation exposure. Taken together, it will be important to review the basis of the ITSL as more information becomes available for both diglycol amine and structurally similar TACs.

No carcinogenicity studies were identified, so diglycol amine is not classifiable as a carcinogen based on lack of information. However, summaries of *in vivo* and *in vitro* genotoxicity studies are presented in the dossier (ECHA, 2023). All of the studies gave negative results for genotoxicity, indicating that diglycol amine is not likely to be genotoxic.

Derivation of Screening Level

The MAK documentation presented rat inhalation toxicity data as the basis for their occupational exposure limit. Specifically, the basis for the MAK was identified as a rat inhalation study consisting of exposure to diglycol amine at 0, 4, 16, or 40 mg/m^3 for 6 hours/day, 7 days/week for 29 days in male rats and 46-48 days in female rats. The study found no effects at 4 mg/m³. A lowest observable adverse effect level was identified at 16 mg/m^3 based on squamous cell metaplasia and inflammation in the larynx. The MAK of 0.87 mg/m³ for 8-hr exposure period was developed to protect against respiratory effects with acute exposure. Therefore, an acute ITSL will be derived per Rule 336.1232 (1) (c) using the MAK value as shown in Equation 1.

Equation 1.

$$ITSL = \frac{OEL}{100}$$

where

OEL is the occupational exposure level, the MAK value,

$$ITSL = \frac{0.87\ mg/m^3}{100}\ x\ \frac{1000\ \mu g}{mg} = 8.7\frac{\mu g}{m^3} \approx 9\ \frac{\mu g}{m^3}, 8\ hr\ averaging\ time$$

Therefore, the ITSL for diglycol amine (CAS# 929-06-6) is 9 µg/m^3, 8-hour averaging time.

References

Act 451 of 1994, Natural Resources and Environmental Protection Act and Air Pollution Control Rules, Michigan Department of Environmental Quality.

ECHA. 2023. Registration Dossier for 2-(2-aminoethoxy)ethanol (CAS No. 929-06-6). Published in accordance with the Registration, Evaluation, Authorisation and Restriction of Chemicals (i.e., REACH) legislation. Accessed December 12, 2023. Retrieved from https://echa.europa.eu/registration-dossier/-/registered-dossier/13361

MAK Collection. 2014. 2-(2-Aminoethoxy)ethanol (Diglykolamin). In the MAK-Collection for Occupational Health and Safety. https://doi.org/10.1002/3527600418.mb92906kskd0056

MDEQ. 1997. *Memo from Marco Bianchi to File for Triethanolamine (CAS# 102-71-6). Subject: Initial Threshold Screening Level*. August 12, 1997. AQD, MDEQ.

MDEQ. 1998. *Memo from Marco Bianchi to File for Ethylamine (CAS# 75-04-7). Subject: Initial Threshold Screening Level*. July 22, 1998. AQD, MDEQ.

MDEQ. 2013. *Memo from Doreen Lehner to File for Monoethanolamine (CAS# 141-43-5). Subject: Screening Level for Monoethanolamine (CAS# 141-43-5)*. June 4, 2013. AQD, MDEQ.

MDEQ. 2013. *Memo from Doreen Lehner to File for Dimethylethanolamine (CAS# 108-01-0). Subject: Screening Level for Dimethylethanolamine*. January 18, 2013. AQD, MDEQ.

MDEQ. 2022. *Memo from Doreen Lehner to File for Diethanolamine (CAS# 111-42-2). Subject: Screening Level for Diethanolamine (CAS# 111-42-2)*. December 5, 2022. AQD, MDEQ.

OECD SIDS. 2014. 2-[2-(Dimethylamino)ethoxy]ethanol CAS No: 1704-62-7. Accessed on December 12, 2023. Retrieved from https://hpvchemicals.oecd.org/ui/handler.axd?id=fa9b5477-7b93-46d0-b82e-6dcc4a8aea12

PubChem [Internet]. Bethesda (MD): National Library of Medicine (US), National Center for Biotechnology Information; 2004-. PubChem Compound Summary for CID 13578, 2-(2-Amino-ethoxy)ethanol; [cited 2023 Dec. 12]. Available from: https://pubchem.ncbi.nlm.nih.gov/compound/2-_2-Aminoethoxy_ethanol

TAMIS. *Texas Air Monitoring Information System (TAMIS)* [database]. Retrieved from https://www17.tceq.texas.gov/tamis/index.cfm?fuseaction=home.welcome.

KW:lh