Triethylene glycol monoethyl ether; CASRN 112-50-5

Human health assessment information on a chemical substance is included in the IRIS database only after a comprehensive review of toxicity data, as outlined in the <u>IRIS assessment</u> <u>development process</u>. Sections I (Health Hazard Assessments for Noncarcinogenic Effects) and II (Carcinogenicity Assessment for Lifetime Exposure) present the conclusions that were reached during the assessment development process. Supporting information and explanations of the methods used to derive the values given in IRIS are provided in the <u>guidance documents located</u> on the IRIS website.

STATUS OF DATA FOR Triethylene glycol monoethyl ether

Category (section)	Assessment Available?	Last Revised
Oral RfD (I.A.)	not evaluated	
Inhalation RfC (I.B.)	qualitative discussion	09/01/1994*
Carcinogenicity Assessment (II.)	not evaluated	

File First On-Line 09/01/1994

*A comprehensive review of toxicological studies was completed 01/07/05 - please see section I.B for more information.

I. Chronic Health Hazard Assessments for Noncarcinogenic Effects

I.A. Reference Dose for Chronic Oral Exposure (RfD)

Substance Name — Triethylene glycol monoethyl ether CASRN — 112-50-5

Not available at this time.

I.B. Reference Concentration for Chronic Inhalation Exposure (RfC)

Substance Name — Triethylene glycol monoethyl ether CASRN — 112-50-5

The health effects data for triethylene glycol monoethyl ether (TGEE) were reviewed by the U.S. EPA RfD/RfC Work Group and determined to be inadequate for derivation of an inhalation RfC. The verification status of this chemical is currently NOT VERIFIABLE. For additional information on the health effects of this chemical, interested parties are referred to the U.S. EPA documentation listed below.

NOT VERIFIABLE status indicates that the U.S. EPA RfD/RfC Work Group deemed the database at the time of review to be insufficient to derive an inhalation RfC according to the Interim Methods for Development of Inhalation Reference Concentrations (U.S. EPA, 1990). This status does not preclude the use of information in cited references for assessment by others.

Derivation of an inhalation RfC for TGEE is not recommended at this time due to a complete lack of subchronic/chronic studies by any route of exposure in humans and laboratory animals. The lack of developmental toxicity data is a specific data gap because members of this class of compounds are known to be reproductive and developmental toxicants. A concentration-response assessment based on structure/activity relationships is not recommended at this time because of the lack of inhalation data for TGEE and the lack of evidence for toxicologic and pharmacokinetic similarities between TGEE and any other glycol ether, including ethylene glycol ethyl ether. Further, route-to-route extrapolation is not possible given the lack of TGEE pharmacokinetic data and the indication of potential for respiratory tract (portal-of-entry) effects via inhalation.

TGEE is a water soluble, clear crystalline compound with low volatility, less than 0.01 mmHg, at 20 C (Rowe and Wolf, 1982). There is no oral RfD assessment or drinking water health advisory for TGEE. It is used as a component of hydraulic brake fluid, as a solvent in paint stripping formulations, and as a dye carrier for textile dye processes. Commercial trade names for TGEE include Polysolv TE (Olin Corporation) and Ethoxytriglycol (Union Carbide Corporation). No acute inhalation toxicity data are available for TGEE. The oral and dermal LD50s in rats were determined to be 10.6 g/kg and 8.2 g/kg, respectively (Smyth and Carpenter, 1948; Rowe and Wolf, 1982).

In a comparative skin irritation bioassay sponsored by Olin Corporation, approximately 0.03 mL undiluted TGEE or triethylene glycol monomethyl ether (TGME) was applied to human skin with a semioccluded patch for 24 hours on 3 consecutive days (IBT, 1969). The skin reactions ranged from very slight to mild, with TGME causing more skin irritation than TGEE. Mild

erythema was the only effect reported. The data from this study are considered to be of questionable accuracy because they were reported by Industrial Bio-Test Laboratories, a company that developed a reputation for misrepresenting studies.

Leber et al. (1990) performed several tests of TGME, TGEE, and triethylene glycol monobutyl ether (TGBE) to determine the ability of these compounds to penetrate human skin and to cause systemic toxicity from repeated dermal exposure. In the first part of the experiment, human abdominal whole skin (dermis plus epidermis) samples were assessed in vitro. Skin samples were mounted in a glass diffusion apparatus that exposed 2.54 sq.cm of epidermal area for chemical absorption determinations. Samples were tested for integrity (tritiated water diffusion through the skin prior to exposure), diffusion of the glycol ethers through the skin, and epidermal damage after chemical exposures (increase in tritiated water diffusion following exposure). The three compounds crossed human epidermis at molar rates 170-330 times slower than the corresponding monoethylene glycol ethers. The skin damage ratio for TGME, however, was comparable to that of ethylene glycol monomethyl ether, indicating that the diffusion barrier function of the skin was slightly diminished after 12 hours of exposure. In the second part of the experiment, a 21-day dermal study, 20 male and 20 female New Zealand White rabbits were divided into four groups (three chemicals and the controls). A 15-cm-wide shaved strip on the back of each test animal (5/sex/group) was exposed to 1.0 g/kg/day of neat TGME, TGEE, or TGBE and occluded with gauze bandaging. Each rabbit was dosed 6 hours/day, 5 days/week for 3 weeks. Evaluation of the rabbits included an assessment of dermal irritation (Draize method); hematology and clinical chemistry prior to study initiation; and, on day 21, pathologic examination of nearly 40 tissues (including testes) per animal. Slight local irritation (mild erythema/edema, fissuring, and desquamation) was the only effect observed, indicating the potential for direct (portal-of- entry) irritating effects. No systemic effects were observed.

IBT (Industrial Bio-Test Laboratories). 1969. Comparative human skin irritation study on five test materials. Report to Olin Research Center, June 25.

Leber, A.P., R.C. Scott, M.C.E. Hodge, D. Johnson, and W.J. Krasavage. 1990. Triethylene glycol ethers: Evaluation of in vitro absorption through human epidermis, 21-day dermal toxicity in rabbits, and a developmental toxicity screen in rats. J. Am. Coll. Toxicol. 9: 507-515.

Rowe, V.K. and M.A. Wolf. 1982. In: Patty's Industrial Hygiene and Toxicology, 3rd rev. ed. Vol. 2C, p. 3914, 3969.

Smyth, H.F. and C.P. Carpenter. 1948. Further experience with the range finding test in the industrial toxicology laboratory. J. Ind. Hyg. Toxicol. 30: 63-68.

U.S. EPA. 1990. Interim Methods for Development of Inhalation Reference Concentrations (Review Draft), Office of Research and Development, Washington, DC. EPA/600-8-90-066A.

Agency Work Group Review — 03/26/1992

A comprehensive review of toxicological studies published through 2004 indicated that there is insufficient health effects data to derive an RfC for Triethylene glycol monoethyl ether at this time. For more information, IRIS users may contact the IRIS Hotline at <u>hotline.iris@epa.gov</u> or (202)566-1676.

EPA Contacts:

Please contact the IRIS Hotline for all questions concerning this assessment or IRIS, in general, at (202)566-1676 (phone), (202)566-1749 (FAX) or hotline.iris@epa.gov (internet address).

II. Carcinogenicity Assessment for Lifetime Exposure

Substance Name — Triethylene glycol monoethyl ether CASRN — 112-50-5

This substance/agent has not undergone a complete evaluation and determination under US EPA's IRIS program for evidence of human carcinogenic potential.

III. [reserved]
IV. [reserved]
V. [reserved]

VI. Bibliography

Substance Name — Triethylene glycol monoethyl ether CASRN — 112-50-5

VI.A. Oral RfD References

None

VI.B. Inhalation RfC References

IBT (Industrial Bio-Test Laboratories). 1969. Comparative human skin irritation study on five test materials. Report to Olin Research Center, June 25.

Leber, A.P., R.C. Scott, M.C.E. Hodge, D. Johnson, and W.J. Krasavage. 1990. Triethylene glycol ethers: Evaluation of in vitro absorption through human epidermis, 21-day dermal toxicity in rabbits, and a developmental toxicity screen in rats. J. Am. Coll. Toxicol. 9: 507-515.

Rowe, V.K. and M.A. Wolf. 1982. In: Patty's Industrial Hygiene and Toxicology, 3rd rev. ed. Vol. 2C, p. 3914, 3969.

Smyth, H.F. and C.P. Carpenter. 1948. Further experience with the range finding test in the industrial toxicology laboratory. J. Ind. Hyg. Toxicol. 30: 63-68.

U.S. EPA. 1990. Interim Methods for Development of Inhalation Reference Concentrations (Review Draft), Office of Research and Development, Washington, DC. EPA/600-8-90-066A.

VI.C. Carcinogenicity Assessment References

None

VII. Revision History

Substance Name — Triethylene glycol monoethyl ether CASRN — 112-50-5

Date	Section	Description
09/01/1994	I.B.	Inhalation RfC discussion on-line
12/03/2002	I.B.	Screening-Level Literature Review Findings message has been added.
03/03/2005	I.B.	Screening-Level Literature Review Findings message has been removed and replaced by comprehensive literature review conclusions.

VIII. Synonyms

Substance Name — Triethylene glycol monoethyl ether CASRN — 112-50-5 Last Revised — 06/01/1992

- 112-50-5
- Ethanol, 2-(2-(2-ethoxyethoxy)-
- AI3-14498
- Dowanol TE
- ETHOXYTRIETHYLENE GLYCOL
- Ethoxytriglycol
- Ethyltriglycol
- HSDB 899
- TRIETHYLENE GLYCOL ETHYL ETHER
- TRIETHYLENE GLYCOL MONOETHYL ETHER
- TRIGLYCOL MONOETHYL ETHER
- 2-(2-(2-Ethoxyethoxy)ethoxy)ethanol
- 3,6,9-Trioxaundecan-1-ol