# TRIETHYLENE GLYCOL

## (CAS #112-27-6)

## GREENSCREEN® FOR SAFER CHEMICALS (GREENSCREEN®) ASSESSMENT

**Prepared by:**

**ToxServices LLC**

**Assessment Date: September 15, 2019[a]**

**Expiration Date: September 15, 2024**

TOXSERVICES
TOXICOLOGY RISK ASSESSMENT CONSULTING
1367 Connecticut Ave., N.W., Suite 300
Washington, D.C. 20036

[a] ToxServices incorporated January 2020 comments submitted by the Washington State Department of Ecology into this document.

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# GreenScreen® Executive Summary for Triethylene Glycol (CAS #112-27-6)

Triethylene glycol is an ethylene glycol ether containing three ethylene oxide subunits. It is a colorless, hygroscopic liquid with low volatility and flammability. Triethylene glycol is manufactured by the reaction of ethylene oxide and ethylene glycol in the presence of sulfuric acid, or by the reaction of hydroxyacetic acid with glycol followed by hydrogenation. Its uses are predominantly industrial, including natural gas dehydration (28% of consumption in the United States) and as a solvent (6%), a plasticizer (6%), a chemical intermediate (6%), and a humectant (2%). Triethylene glycol is also used as a pesticide, bacteriostat, fungicide, virucide, miticide, and insecticide, and is approved by the U.S. FDA as a preservative for food packaging adhesives. Additionally, it is used as a fragrance ingredient and viscosity controlling agent and the reported maximum use level is 0.2% in personal care products. About 74,000 metric tons are produced in the United States and Japan every year

Triethylene glycol was assigned a **GreenScreen Benchmark™ Score of 2** ("Use but Search for Safer Substitutes"). This score is based on the following hazard score combinations:

- Benchmark 2e
    - Moderate Group I Human Toxicity (developmental toxicity-D and endocrine activity-E)

A data gap (DG) exists for neurotoxicity (repeated exposure) Nr*. As outlined in GreenScreen® Guidance Section 11.6.2.1 and Annex 5 (Conduct a Data Gap Analysis), triethylene glycol meets requirements for a GreenScreen Benchmark™ Score of 2 despite the hazard data gap. In a worst-case scenario, if triethylene glycol were assigned a High score for the data gap Nr*, it would remain a Benchmark 2 Chemical.

## GreenScreen® Hazard Summary Table for Triethylene Glycol

| Group I Human | | | | | Group II and II* Human | | | | | | | | | Ecotox | | Fate | | Physical | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| C | M | R | D | E | AT | ST | | N | | SnS* | SnR* | IrS | IrE | AA | CA | P | B | Rx | F |
| | | | | | | single | repeat* | single | repeat* | | | | | | | | | | |
| **L** | *L* | **L** | **M** | *M* | **L** | **M** | **L** | **M** | DG | *L* | *L* | **L** | **L** | **L** | **L** | **L** | **vL** | *L* | **L** |

Note: Hazard levels (Very High (vH), High (H), Moderate (M), Low (L), Very Low (vL)) in *italics* reflect lower confidence in the hazard classification while hazard levels in **BOLD** font reflect higher confidence in the hazard classification. Group II Human Health endpoints differ from Group II* Human Health endpoints in that they have four hazard scores (i.e., vH, H, M, and L) instead of three (i.e., H, M, and L), and are based on single exposures instead of repeated exposures. Group II* Human Health endpoints are indicated by an * after the name of the hazard endpoint or after "repeat" for repeated exposure sub-endpoints. Please see Appendix A for a glossary of hazard acronyms.

# GreenScreen® Chemical Assessment for Triethylene Glycol (CAS #112-27-6)

**Method Version: GreenScreen® Version 1.4**
**Assessment Type[1]: Certified**
**Assessor Type: Licensed GreenScreen® Profiler**

**GreenScreen® Assessment Prepared By:**
Name: Mouna Zachary, Ph.D

Title: Toxicologist
Organization: ToxServices LLC
Date: October 23, 2013

**Quality Control Performed By:**
Name: Dr. Margaret H. Whittaker, Ph.D., M.P.H., CBiol., F.S.B., E.R.T., D.A.B.T.
Title: Managing Director and Chief Toxicologist
Organization: ToxServices LLC
Date: December 5, 2013

**GreenScreen® Assessment Updated By:**
Name: Rachel Galante, M.P.H.
Title: Associate Toxicologist
Organization: ToxServices LLC
Date: July 12, 2018

**Quality Control Performed By:**
Name: Bingxuan Wang, Ph.D., D.A.B.T.
Title: Senior Toxicologist
Organization: ToxServices LLC
Date: July 13, 2018

**GreenScreen® Assessment Prepared By:**
Name: Grace Kuan, M.P.H.
Title: Associate Toxicologist
Organization: ToxServices LLC
Date: August 26, 2019

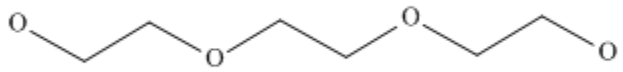
**Quality Control Performed By:**
Name: Bingxuan Wang, Ph.D., D.A.B.T.
Title: Senior Toxicologist
Organization: ToxServices LLC
Date: September 15, 2019

Expiration Date: September 15, 2024[2]

**Chemical Name:** Triethylene Glycol

**CAS Number:** 112-27-6

**Chemical Structure(s):**



**Also called:**
2,2'-(1,2-Ethanediylbis(oxy))bisethanol; 1,2-Bis(2-hydroxyethoxy)ethane; 2,2'-Ethylenedioxybis(ethanol); 2,2'-Ethylenedioxydiethanol; 2,2'-Ethylenedioxyethanol; 3,6-Dioxaoctane-1,8-diol; Bis(2-hydroxyethoxyethane); Di-beta-hydroxyethoxyethane; Ethanol, 2,2-;(1,2-ethanediylbis(oxy))bis-; Ethanol, 2,2'-(ethylenedioxy)di-; Ethylene glycol dihydroxydiethyl ether; Ethylene glycol-bis-(2-hydroxyethyl ether); Glycol bis(hydroxyethyl) ether; TEG; Triethyleneglycol; Trigen; Triglycol; 2,2'-(Ethylenedioxy)diethanol (ChemIDplus 2019)

[1] GreenScreen® reports are either "UNACCREDITED" (by unaccredited person), "AUTHORIZED" (by Authorized GreenScreen® Practitioner), or "CERTIFIED" (by Licensed GreenScreen® Profiler or equivalent)
[2] Assessments expire five years from the date of completion starting from January 1, 2019. An assessment expires three years from the date of completion if completed before January 1, 2019 (CPA 2018a).

**Suitable surrogates or moieties of chemicals used in this assessment (CAS #'s):**
A relatively complete dataset was identifed for triethylene glycol. Data gaps were identified for single and repeated dose neurotoxicity. However, no surrogates with adequate data were identified for these endpoints. Therefore, no surrogates were used in this evaluation.

**Identify Applications/Functional Uses:** (HSDB 2007, OECD 2004)
1. Drying agent for natural gas (28% of total consumption in the U.S.).
2. Solvent in applications such as cleaning polyethylene terephthalate production equipment and for nitrocellulose and other gums and resins, textile dyeing, printing inks, pharmaceuticals and cosmetics (6% of total consumption in the U.S.).
3. Plasticizer for materials such as composition cork (6% of total consumption in the U.S.).
4. Chemical intermediate for the synthesis of unsaturated polyester resin (2% of total consumption in the U.S), alkyd resins used as laminating agents in adhesives, esterification products in plasticizer intermediates for nitrocellulose lacquers and vinyl resins, and polyester polyols for polyurethane (4% of total consumption in the U.S.).
5. Humectant for tobacco and printing inks (2% of total consumption in the U.S.).
6. Pesticide, bacteriostat in air sanitation and deodorization, fungicide, virucide, miticide, insecticide, United States Food and Drug Administration (U.S. FDA)-approved preservative for food packaging adhesives (minor use).
7. Fragrance ingredient at up to 0.03% in personal care products (minor use).

**Known Impurities[3]:**
Commercial grade triethylene glycol has been found to contain <1 ppm dioxane. Twenty-six samples of 99.9% pure triethylene glycol were found to contain 0.02 to 0.13% diethylene glycol (HSDB 2007).

**GreenScreen® Summary Rating for Triethylene Glycol[4,5,6,7]:** Triethylene glycol was assigned a **GreenScreen Benchmark™ Score of 2** ("Use but Search for Safer Substitutes") (CPA 2018b). This score is based on the following hazard score combinations:

- Benchmark 2e
    - Moderate Group I Human Toxicity (developmental toxicity-D and endocrine activity-E).

A data gap (DG) exists for neurotoxicity (repeated exposure) Nr*. As outlined in GreenScreen® Guidance Section 11.6.2.1 and Annex 5 (Conduct a Data Gap Analysis), triethylene glycol meets requirements for a GreenScreen® Benchmark Score of 2 despite the hazard data gap. In a worst-case scenario, if triethylene glycol were assigned a High score for the data gap Nr*, it would remain a Benchmark 2 Chemical.

[3] Impurities of the chemical will be assessed at the product level instead of in this GreenScreen®.
[4] For inorganic chemicals with low human and ecotoxicity across all hazard endpoints and low bioaccumulation potential, persistence alone will not be deemed problematic. Inorganic chemicals that are only persistent will be evaluated under the criteria for Benchmark 4.
[5] See Appendix A for a glossary of hazard endpoint acronyms.
[6] For inorganic chemicals only, see GreenScreen® Guidance v1.4 Section 12 (Inorganic Chemical Assessment Procedure).
[7] For Systemic Toxicity and Neurotoxicity, repeated exposure data are preferred. Lack of single exposure data is not a Data Gap when repeated exposure data are available. In that case, lack of single exposure data may be represented as NA instead of DG. See GreenScreen® Guidance v1.4 Annex 2.

**Figure 1: GreenScreen® Hazard Summary Table for Triethylene Glycol**

| Group I Human | | | | | Group II and II* Human | | | | | | | | | Ecotox | | Fate | | Physical | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| C | M | R | D | E | AT | ST | | N | | SnS* | SnR* | IrS | IrE | AA | CA | P | B | Rx | F |
| | | | | | | single | repeat* | single | repeat* | | | | | | | | | | |
| **L** | *L* | **L** | **M** | *M* | **L** | **M** | **L** | **M** | DG | *L* | *L* | **L** | **L** | **L** | **L** | **L** | **vL** | *L* | **L** |

Note: Hazard levels (Very High (vH), High (H), Moderate (M), Low (L), Very Low (vL)) in *italics* reflect lower confidence in the hazard classification while hazard levels in **BOLD** font reflect higher confidence in the hazard classification. Group II Human Health endpoints differ from Group II* Human Health endpoints in that they have four hazard scores (i.e., vH, H, M, and L) instead of three (i.e., H, M, and L), and are based on single exposures instead of repeated exposures. Group II* Human Health endpoints are indicated by an * after the name of the hazard endpoint or after "repeat" for repeated exposure sub-endpoints. Please see Appendix A for a glossary of hazard acronyms.

## Environmental Transformation Products:

No environmental transformation products were identified from the literature for triethylene glycol. It is not expected to undergo hydrolysis or direct photolysis as it lacks functional groups susceptible to these reactions (HSDB 2007). It is expected to have high mobility in soil and its volatilization is considered low based on its Henry's Law constant. Due to its rapid degradability (see Persistence section below), it is not expected to form toxic degradation products persistent enough to be of concern. Based on its molecular formula, possible combustion products of triethylene glycol are CO and $CO_2$, which are naturally occurring, ambient substances and not relevant with respect to the GreenScreen Benchmark™ Score for triethylene glycol. Therefore, the benchmark score of triethylene glycol is not affected by the hazards of its environmental transformation products.

## Introduction

Triethylene glycol is an ethylene glycol ether containing three ethylene oxide subunits. It is a colorless, hygroscopic liquid with low volatility and flammability. Triethylene glycol is manufactured by the reaction of ethylene oxide and ethylene glycol in the presence of sulfuric acid, or by the reaction of hydroxyacetic acid with glycol followed by hydrogenation (HSDB 2007). Its uses are predominantly industrial, including natural gas dehydration (28% of consumption in the United States) and as a solvent (6%), a plasticizer (6%), a chemical intermediate (6%), and a humectant (2%). Triethylene glycol is also used as a pesticide, bacteriostat, fungicide, virucide, miticide, and insecticide, and is approved by the U.S. FDA as a preservative for food packaging adhesives. Additionally, it is used as a fragrance ingredient and viscosity controlling agent and the reported maximum use level is 0.2% in personal care products. About 74,000 metric tons are produced in the United States and Japan every year (OECD 2004, 2007).

ToxServices assessed triethylene glycol against GreenScreen® Version 1.4 (CPA 2018b) following procedures outlined in ToxServices' SOPs (GreenScreen® Hazard Assessment) (ToxServices 2016).

## U.S. EPA Safer Choice Program's Safer Chemical Ingredients List

The SCIL is a list of chemicals that meet the Safer Choice standard (U.S. EPA 2018). It can be accessed at: http://www2.epa.gov/saferchoice/safer-ingredients. Chemicals on the SCIL have been assessed for compliance with the Safer Choice Standard and Criteria for Safer Chemical Ingredients (U.S. EPA 2015).

Triethylene glycol is not listed on the U.S. EPA SCIL.

## GreenScreen® List Translator Screening Results

The GreenScreen® List Translator identifies specific authoritative or screening lists that should be searched to identify GreenScreen Benchmark™ 1 chemicals (CPA 2018b). Pharos (Pharos 2019) is an online list-searching tool that is used to screen chemicals against all of the lists in the List Translator electronically. ToxServices also checks the U.S. Department of Transportation (U.S. DOT) lists (U.S. DOT 2008a,b),[8] which are not considered GreenScreen® specified lists but are additional information sources, in conjunction with the Pharos query. The output indicates benchmark or possible benchmark scores for each human health and environmental endpoint. The output for triethylene glycol can be found in Appendix C.

- Triethylene glycol is an LT-P1 chemical when screened using Pharos, and therefore a full GreenScreen® is required.
- Triethylene glycol is on the following GreenScreen® specified lists that each covers multiple endpoints
    - EC – CEPA DSL – Inherently Toxic to Humans (iTH).
    - German FEA – Substances Hazardous to Waters – Class 1 – Low Hazard to Waters.
- GreenScreen® specified lists that corresponds to single endpoints are listed in their respective hazard assessment sections below.
- Triethylene glycol is not listed on the U.S. DOT lists.

## Hazard Statement and Occupational Control

No harmonized H statements were identified for triethylene glycol. Neither its REACH registration dossier nor the majority of the self-notifiers to the ECHA C&L Inventory (1,477/1,529 (96.6%)) classified triethylene glycol with any H statements. Recommended personal protective equipment and occupational exposure limits are presented in Table 1 below.

**Table 1: Occupational Exposure Limits and Recommended Personal Protective Equipment for Triethylene Glycol (CAS #112-27-6)**

| Personal Protective Equipment (PPE) | Reference | Occupational Exposure Limits (OEL) | Reference |
|---|---|---|---|
| Eye/face protection (safety glasses with side-shields), hand protection (chemical-resistant gloves), body protection (apron, protective boots, chemical-protection suit, depending on exposure scenarios), respiratory protection (with organic gases filters, if ventilation is inadequate) | ECHA 2019b | MAK: 1,000 mg/m$^3$ | NIOSH 1996 |

## Physicochemical Properties of Triethylene Glycol

Triethylene glycol is a colorless liquid with high water solubility and a relatively low vapor pressure. Based on its measured and estimated log $K_{ow}$ of -1.98 – -1.75, it is hydrophilic and not expected to bioaccumulate.

**Table 2: Physical and Chemical Properties of Triethylene Glycol (CAS #112-27-6)**

| Property | Value | Reference |
|---|---|---|
| Molecular formula | $C_6H_{14}O_4$ | ChemIDplus 2019 |
| SMILES Notation | C(COCCO)OCCO | ChemIDplus 2019 |

[8] DOT lists are not required lists for GreenScreen® List Translator v1.4. They are reference lists only.

| Table 2: Physical and Chemical Properties of Triethylene Glycol (CAS #112-27-6) | | |
|---|---|---|
| **Property** | **Value** | **Reference** |
| Molecular weight | 150.173 | ChemIDplus 2019 |
| Physical state | Liquid | ECHA 2019b |
| Appearance | Colorless | ECHA 2019b |
| Melting point | -7°C | ECHA 2019b, ChemIDplus 2019 |
| Boiling point | 286.5˚C at 1,013 hPa | ECHA 2019b |
| Vapor pressure | 0.001 hPa at 24.7°C;<br>0.00132 mm Hg at 25°C | ECHA 2019b;<br>ChemIDplus 2019 |
| Water solubility | 1,000 g/L at 20°C | ECHA 2019b, ChemIDplus 2019 |
| Dissociation constant | Not identified | |
| Density/specific gravity | 1.13 g/cm$^3$ at 15°C | ECHA 2019b |
| Partition coefficient | -1.75 – -1.98 (estimated)<br><br>-1.75 | ECHA 2019b, ChemIDplus 2019;<br>U.S. EPA 2017 |

**Toxicokinetics**

- ECHA 2019b
  - Female New Zealand White rabbits (2/dose) were orally administered doses of 0, 200, or 2,000 mg/kg of triethylene glycol (purity and vehicle unreported) via gavage for 3 consecutive days in a non-GLP-compliant study (no guideline). Urine was collected from low- and high-dose animals for 24 hours as well as during treatment and for 3 days post-exposure, respectively. In low-dose animals, 34.4% of the administered dose was recovered in excreted urine. In high-dose animals, 28.3% was recovered in urine, and 35.2% was recovered as a hydroxyacid form of triethylene glycol. The REACH dossier authors assigned a Klimisch score of 2 (reliable with restrictions) due to the study being well-documented, meeting generally accepted scientific principles, and being acceptable for assessment.
  - In a non-GLP-compliant toxicokinetic study (no guideline), male albino rats (4/dose for low dose, and 2/dose for all other dose levels) were orally administered doses of 0, 22.5, 125, 140, 550, or 600 mg/kg/day triethylene glycol (purity and vehicle unreported) via gavage. Urine, feces, and expired air were collected for 5 days. Of the 90.6-98.3% recovered from the administered dose, 0.8-1.2, 2-6.3, and 86.1-94% was recovered from expired air, feces, and urine, respectively. The REACH dossier authors assigned a Klimisch score of 2 (reliable with restrictions) due to the study being well-documented, meeting generally accepted scientific principles, and being acceptable for assessment.
- OECD 2004
  - *Absorption:* Based on data on shorter chain ethylene glycol ethers and on its high water solubility, triethylene glycol is expected to be completely absorbed by the oral route, and extensively (if not completely) absorbed by the inhalation route. Its dermal absorption is expected to be lower than that for the smaller glycol ether diethylene ethylene glycol, which was tested to be 1 – 51% absorbed dermally in rats.
  - *Distribution:* Due to its high water solubility, triethylene glycol is expected to be distributed uniformly to all aqueous tissues of the body.
  - *Metabolism:* Triethylene glycol is mainly metabolized by oxidation of the hydroxyl groups through the action of alcohol dehydrogenases (ADH) and aldehyde dehydrogenases (ALD), instead of ether cleavage. Metabolites reported include carbon dioxide (1% of the

administered dose), ethylene dioxyacetic acid (major metabolite) and oxalic acid (minor metabolite detected at no more than 0.00001% of the administered dose). The metabolic pathway leading to the generation of carbon dioxide is saturable. The acid metabolites can be further metabolized to carbon dioxide.
    - *Elimination:* Triethylene and its metabolites are mainly eliminated through the urine. A much smaller fraction is eliminated in the feces and as carbon dioxide in the expired air.

In summary, triethylene glycol is expected to be substantially absorbed via the oral and inhalation routes and to have lower absorption rates via the dermal route. It is anticipated to distribute to aqueous tissues throughout the body, and is metabolized via oxidation by alcohol and aldehyde dehydrogenases to aldehydes and acids, respectively. The acids may be further metabolized to carbon dioxide. Triethylene glycol and its metabolites are primarily eliminated in the urine.

## Hazard Classification Summary

### Group I Human Health Effects (Group I Human)

**Carcinogenicity (C) Score (H, M, or L): L**
Triethylene glycol was assigned a score of Low for carcinogenicity based on no evidence of carcinogenic effects in 2-year and 13-month carcinogenicity studies. GreenScreen® criteria classify chemicals as a Low hazard for carcinogenicity when adequate data are available and negative and they are not GHS classified (CPA 2018b). Confidence in the score is high as it is based on reliable experimental data.

- Authoritative and Screening Lists
    - *Authoritative:* Not present on any authoritative lists.
    - *Screening:* Not present on any screening lists.
- HSDB 2007 (no Klimisch scores assigned)
    - *Oral:* Groups of Osborne-Mendel rats (12/group) received triethylene glycol in diet at 0, 1, 2, or 4% (purity and vehicle unreported) for 2 years in a non-GLP-compliant study (no guideline followed). Body weights and food consumption were measured weekly. No toxic effects or lesions were observed in the triethylene glycol group.
    - *Inhalation:* Rats (n=24 male and 12 female) exposed to supersaturated triethylene glycol (dose, purity, and vehicle unreported) from 6 months to 13 months showed no adverse reactions or histopathological changes suggestive of toxicity from prolonged exposure to triethylene glycol. No further details were provided for this study (GLP status and guideline adherence unreported).
    - *Inhalation:* In another carcinogenicity study, no evidence of tumorigenicity or carcinogenicity was found in monkeys exposed by inhalation to approximately 1 ppm (approximately 0.5 to 1 ppm) vapor triethylene glycol (purity and vehicle unreported) from two weeks to 13 months (GLP status and guideline adherence unreported).

**Mutagenicity/Genotoxicity (M) Score (H, M, or L):** *L*
Triethylene glycol was assigned a score of Low for mutagenicity/genotoxicity based on negative results in several bacterial mutagenicity assays and *in vitro* clastogenicity assays. While positive results were obtained in one Ames assay, the tested concentrations exceeded the maximum concentration recommended by OECD guideline, and cytotoxicity information was not provided. High quality bacterial reverse mutation assays were all negative. Weakly positive results were obtained in a sister chromatid exchange assay. However, high quality chromosomal aberration assays were negative. The

overall weight of evidence suggests that triethylene glycol is not genotoxic. GreenScreen® criteria classify chemicals as a Low hazard for mutagenicity/genotoxicity when negative data are available for both gene mutations and chromosome aberrations, and they are not GHS classified (CPA 2018b). The confidence in the score is reduced as mixed data were identified.

- Authoritative and Screening Lists
  - *Authoritative:* Not present on any authoritative lists.
  - *Screening:* Not present on any screening lists.
- NTP 2018 (no Klimisch scores assigned)
  - *In vitro*: Triethylene glycol was positive for mutagenicity in a bacterial reverse mutation assay (no information on guidelines and GLP compliance status provided) conducted with *Salmonella typhimurium tester* strains TA100 and TA98 at concentrations of 0, 100, 333, 1,000, 3,333, 6,667, and 10,000 µg/plate (water vehicle, purity unreported) with and without metabolic activation. The tested substance was positive when tested without metabolic activation and negative with metabolic activation (rat and hamster liver S9). No information was provided on other test conditions, cytotoxicity or statistical significance. ToxServices noted that the concentrations tested exceeded the maximum recommended test concentration of 5 mg/plate by OECD guideline 471.
- NTP 1991a (no Klimisch scores assigned)
  - *In vitro*: Triethylene glycol had negative results in a chromosome aberration test (no information on guidelines and GLP and GLP compliance status provided) conducted with Chinese hamster ovary (CHO) cells at concentrations of 0, 1,081, 2,325, and 5,000 µg/mL (water vehicle, purity unreported) with and without metabolic activation (rat liver S9 mix).
- NTP 1991b (no Klimisch scores assigned)
  - *In vitro*: Triethylene glycol achieved mixed results in a sister chromatid exchange (SCE) test (no information on guidelines and GLP compliance status provided) conducted with CHO cells at concentrations of 0, 500, 1,667, and 5,000 µg/mL (water vehicle, purity unreported) with and without metabolic activation. Triethylene glycol was weakly positive when tested without metabolic activation and negative when tested with metabolic activation (rat liver S9 mix).
- ECHA 2019b
  - *In vitro:* Triethylene glycol was negative for mutagenicity in a GLP-compliant OECD Guideline 471 bacterial reverse mutation assay. *S. typhimurium* strains TA98, TA100, TA1535 and TA1537 and *Escherichia coli* strain WP2 uvr A were exposed to the test substance (99.8% purity; water vehicle) at concentrations of 0, 33, 100, 333, 1,000, 2,500 and 5,000 µg/plate with and without metabolic activation (beta-naphthoflavone and phenobarbital induced Wistar rat liver S9). A slight increase in the number of revertants was observed in *E. coli* $WP_2$ *uvr* A at 5,000 µg/plate with metabolic activation; however, this effect was not reproducible, and the authors did not consider the finding as relevant. No other increases in the number of revertants was observed in any strain at any concentration with or without metabolic activation. The REACH dossier authors assigned a Klimisch score of 1 (reliable without restriction).
  - *In vitro:* Triethylene glycol was negative for clastogenicity in a GLP-compliant chromosome aberration test similar to OECD Guideline 473. CHO cells were exposed to the test substance (purity not reported; water vehicle) at concentrations of 0, 35, 42 and 50 mg/mL with and without metabolic activation (rat liver S9 mix). There were no significant increases in the proportion of cells with chromosome aberrations observed at any concentration with or without metabolic activation. The REACH dossier authors assigned a Klimisch score of 2 (reliable with restrictions), due to the study being well-documented, meeting generally

accepted scientific principles, and being acceptable for assessment.
    - *In vitro:* Triethylene glycol was negative in a SCE assay similar to OECD Guideline 479 (GLP status not reported). CHO cells were exposed to the test substance (water vehicle, purity unreported) at concentrations of up to 50 mg/mL with and without metabolic activation (rat liver S9 mix). There was no increase in the incidence of SCEs observed at any concentration with or without metabolic activation. The REACH dossier authors assigned a Klimisch score of 2 (reliable with restrictions), due to the study being well-documented, meeting generally accepted scientific principles, and being acceptable for assessment.
- CCRIS 2003 (no Klimisch scores assigned)
    - *In vitro:* Triethylene glycol was negative for mutagenicity in a bacterial reverse mutation assay (GLP-status and guideline adherence unreported). *S. typhimurium* strains TA98, TA100, TA1535, TA1537 and TA1538 and *E. coli* strain $WP_2$ *uvr* A were exposed to the test substance (water vehicle, purity unreported) at concentrations of 100-10,000 µg/plate with and without metabolic activation (beta-naphthoflavone and phenobarbital induced rat liver S9). No increase in the number of revertants was observed in any strain at any concentration with or without metabolic activation.
- ESIS 2000 (no Klimisch scores assigned)
    - *In vitro:* A GLP-compliant Ames bacterial mutation assay (OECD 471) was conducted utilizing *S. typhimurium* tester strains TA98, TA 100, TA 1535, TA 1537 and TA 1538 at concentrations of up to 112,600 µg/plate (purity and vehicle unreported), in the presence and absence of metabolic activation. No increase in revertants was observed and triethylene glycol was reported as negative for mutagenicity under the tested conditions.
- HSDB 2007 (no Klimisch scores assigned)
    - *In vitro:* Triethylene glycol produced negative results in a DNA damage and repair assay (GLP status and guideline adherence unreported) conducted with *E. coli* $WP_2$ *uvr*A- strain at concentrations up to 10,000 µg/plate (purity and vehicle unreported), with and without metabolic activation.

**Reproductive Toxicity (R) Score (H, M, or L): L**

Triethylene glycol was assigned a score of Low for reproductive toxicity based on no evidence of reproductive toxicity in a two-generation study in mice at oral doses of up to 68,000 mg/kg/day. GreenScreen® criteria classify chemicals as a Low hazard for reproductive toxicity when adequate data are available and negative and they are not GHS classified (CPA 2018b). Confidence in the score is high as it is based on high-quality, reliable experimental data.

- Authoritative and Screening Lists
    - *Authoritative:* Not present on any authoritative lists.
    - *Screening:* Not present on any screening lists.
- ECHA 2019b, NTP 1984, MAK 2007
    - The reproductive toxicity of triethylene glycol was evaluated in Swiss CD-1 mice using the continuous breeding protocol (RACB) in a non-GLP-compliant study (no guideline followed). CD-1 mice (20/sex/dose) were administered 0%, 0.3%, 1.5%, or 3.0% of triethylene glycol (97% purity) in the drinking water. The authors of the study calculated these doses to be equivalent to roughly 0, 0.59, 3.3, or 6.78 g/kg/day. The $F_1$ mice were killed and necropsied after the $F_2$ pups were delivered and evaluated. Relative liver weight was increased by 5% and 6% in males and females, respectively, but there were no changes in body weight or other organ weights at necropsy. Epididymal sperm concentration, motility, and morphology were unaffected by triethylene glycol exposure at 3%. Triethylene

glycol was not a reproductive toxicant at doses up to 3%. The study authors reported a reproductive NOAEL of 3%, or 6.78 g/kg/day based on no effects at the highest dose. The REACH dossier authors assigned a Klimisch score of 2, due to the study being well-documented, meeting generally accepted scientific principles, and being acceptable for assessment.

**Developmental Toxicity incl. Developmental Neurotoxicity (D) Score (H, M, or L): M**

Triethylene glycol was assigned a score of Moderate for developmental toxicity based on developmental toxicity, including reduced fetal body weights and skeletal variations, observed at high oral doses in studies with rats and mice. GreenScreen® criteria classify chemicals as a Moderate hazard for developmental toxicity when data indicate a GHS Category 2 classification is warranted (CPA 2018b). Confidence in the score is high as it is based on high-quality, reliable experimental data.

- Authoritative and Screening Lists
  - *Authoritative:* MAK - Pregnancy Risk Group B.
  - *Screening:* Not present on any screening lists.
- ECHA 2019b, HSDB 2007
  - In a GLP-compliant developmental toxicity study according to TSCA Testing Guidelines, Sprague-Dawley rats (n=176) were administered triethylene glycol (water vehicle, 99.9% purity) at 0, 1, 5, or 10 mL/kg/day (equivalent to 0, 1,130, 5,650 and 11,300 mg/kg/day[9]) via oral gavage on gestation days 6-15. The ovary and uterine content of dams was examined after termination. Fetuses were weighed and sexed, and examined for external malformations, thoracic and abdominal visceral abnormalities, and skeletal malformations and variations. Pregnancy rate was comparable for all treated groups. Maternal body weights were reduced at 5 and 10 mL/kg/day, but there were no treatment related findings reported at necropsy. Corrected terminal body weight and corrected body weight change were significantly reduced in high dose dams. There were no adverse effects on the number of ovarian corpora lutea, total, viable or non-viable implantations per litter or sex ratio. Percent preimplantation and postimplantation loss was comparable across groups. Fetal body weights per litter were significantly reduced at 10 mL/kg/day. The incidence of individual and total malformations and external or visceral variations was not significantly increased, however, the incidence of unilateral rudimentary rib #13 was 4.6 times higher than in control fetuses at 10 mL/kg/day, and the total number of fetuses with skeletal malformations appeared slightly increased in the highest dose. Bilobed thoracic centrum exhibited a significantly increased incidence at 10 mL/kg/day. While not statistically significant, there were apparent increases in the incidences of several other individual skeletal variations involving reduced ossification in bones of the thoracic region at 10 ml/kg/day. The authors identified a maternal toxicity NOAEL of 1 mL/kg/day (1,130 mg/kg/day) and a developmental toxicity NOAEL of 5 mL/kg/day (5,650 mg/kg/day) for this study. The REACH dossier authors assigned a Klimisch score of 2, due to the study being well-documented, meeting generally accepted scientific principles, and being acceptable for assessment.
  - In a GLP-compliant developmental toxicity study conducted according to TSCA Testing Guidelines, CD-1 mice (n=206) were administered triethylene glycol (water vehicle, 99.9% purity) at 0, 0.5, 5, or 10 mL/kg/day (equivalent to 0, 565, 5,650 and 11,300 mg/kg/day[10])

[9] Using a density of 1.13 g/cm$^3$ (ECHA 2019): 1.13 g/cm$^3$ * (1,000 mg/g) * (1 cm$^3$/mL) = 1,130 mg/mL * 1 mL/kg/day = 1,130 mg/kg/day.
[10] Using a density of 1.13 g/cm$^3$ (ECHA 2019): 1.13 g/cm$^3$ * (1,000 mg/g) * (1 cm$^3$/mL) = 1,130 mg/mL * 0.5 mL/kg/day = 565 mg/kg/day.

via oral gavage on gestation days 6-15. Maternal animals were examined for body weight, food and water consumption, and clinical signs of toxicity. Gravid uterus, ovaries (including corpora lutea), cervix, vagina and abdominal and thoracic cavities were examined grossly. Ovarian corpora lutea of pregnancy were counted and maternal uterine weights were determined. Fetuses were weighed and sexed and examined for external variations and malformations, thoracic and abdominal abnormalities, and head and skeletal malformations and variations. There were no maternal mortalities, no effects on maternal body weight, no effects on food and water consumption, and no significant clinical signs of toxicity observed. Pregnancy rate was comparable for all dose groups; however, one female each at 0, 0.5 and 10 mL/kg/day and 2 females at 5 mL/kg/day contained only non-viable implants (early or late resorptions or dead fetuses) at scheduled sacrifice. There were no treatment-related necropsy findings of the dams at scheduled sacrifice; however, dams exposed to 0.5 mL/kg/day had an increased incidence of cystic ovaries. While not statistically significant, gravid uterine weight was reduced at 5 and 10 mL/kg/day. Relative kidney weight was significantly increased in the high dose group, however, there were no treatment-related histological changes. There was no effect of treatment on the number of ovarian corpora lutea, total, viable or non-viable (early and late resorptions and dead fetuses) implantations, sex ratio, or percent preimplantation and postimplantation losses. Fetal body weights were significantly reduced at 5 and 10 mL/kg/day. Significantly increased incidences of skeletal variations were observed in fetuses of the high dose group and a statistically significant increase in the incidence of poorly ossified supraoccipital and frontal bones was observed at 5 mL/kg/day. Based on these results, the authors established a maternal toxicity NOEL of 5 mL/kg/day (5,650 mg/kg/day) and a developmental toxicity NOAEL of 0.5 mL/kg/day (565 mg/kg/day). The REACH dossier authors assigned a Klimisch score of 2, due to the study being well-documented, meeting generally accepted scientific principles, and being acceptable for assessment.

- NTP 1984 (no Klimisch scores assigned)
    - In the NTP 2-generation reproduction toxicity study (no information on guidelines and GLP compliance status provided) described in the reproductive toxicity section above, CD-1 mice were administered 0%, 0.3%, 1.5%, or 3.0% of triethylene glycol in the drinking water. No effect on the number of litters/pair delivered, nor the number of live pups/litter were observed. However, the mean live pup weight adjusted for litter size was reduced in the 1.5% and the 3.0% groups by 4% & 4.5%, respectively. Based on this, the study authors reported the developmental LOAEL of 1.5%, or 3.3 g/kg/day, and the developmental NOAEL of 0.3%, or 0.6 g/kg/day.
- Based on the weight of evidence, triethylene glycol is associated with developmental toxicity in animal studies. Developmental toxicity effects were seen at high oral doses and included reduced fetal body weights and skeletal variations in the presence and absence of maternal toxicity. Triethylene glycol is listed by MAK as Pregnancy Risk Group B, which corresponds to a Moderate to High score. According to GHS classification criteria, triethylene glycol is at most classified to category GHS category 2 and a Moderate score is appropriate.

**Endocrine Activity (E) Score (H, M, or L):** *M*

Triethylene glycol was assigned a score of Moderate for endocrine activity based on its presence on the TEDX list as a potential endocrine disruptor. GreenScreen® criteria classify chemicals as a Moderate hazard for endocrine activity when they are included on the TEDX list as a potential endocrine disruptor and there is limited evidence of endocrine activity (CPA 2018b). Confidence in the score is reduced as it is based on screening lists and limited evidence of endocrine changes in animals without a plausibly

related effect. Additionally, there is a lack of concordance between the Kassotis et al. (2015) results and the U.S. EPA Tox21 assay results.

- Authoritative and Screening Lists
  - *Authoritative:* Not present on any authoritative lists.
  - *Screening:* TEDX - Potential Endocrine Disruptors - Potential Endocrine Disruptor.
- TEDX 2017
  - Triethylene glycol was placed on the TEDX list of potential endocrine disruptors in 2017. This listing appears to be based on developmental toxicity. The study abstract was reviewed and is summarized below:
    - Kassotis et al (2015) measured the endocrine-disrupting activities of 24 chemicals used and/or produced by oil and gas operations for five nuclear receptors using a reporter gene assay in human endometrial cancer cells. Triethylene glycol displayed potent activity for the estrogen and androgen receptors, with little activity exhibited for other receptor systems. Additionally, Kassotis et al (2015) assessed reproductive and developmental outcomes in male C57BL/6J mice after the prenatal exposure to a mixture of these chemicals. Prenatal exposure to a mixture of 23 oil and gas operation chemicals at 3, 30, and 300 μg/kg/day (purity and vehicle unreported) caused decreased sperm counts and increased testes, body, heart, and thymus weights and increased serum testosterone in male mice. A Klimisch score was not assigned (GLP status and guideline adherence unreported).
- U.S. EPA 2019
  - Triethylene glycol was inactive in 16/16 high throughput screening assays for estrogen receptor agonism and antagonism, 8/8 assays for androgen receptor agonism and antagonism, and 4/4 assays for thyroid receptor binding activity (Appendix D).
- Based on the weight of evidence, a score of Moderate was assigned. Triethylene glycol is included on the TEDX list as a potential endocrine disruptor based on positive binding activities to the estrogen and androgen receptors *in vitro* and *in vivo* data suggesting reproductive effects and hormone level changes with a mixture containing triethylene glycol. However, no receptor binding activity was detected in the Tox21 high throughput screening assays conducted by U.S. EPA, and the use of a mixture in the *in vivo* study could not establish a causal link between triethylene glycol and endocrine effects. GreenScreen® criteria classify chemicals as a Moderate to High hazard for endocrine activity when listed on the TEDX list as a potential endocrine disruptor. A preliminary score of Moderate is assigned, and can be raised when there are plausibly related effects that led to High score(s) for carcinogenicity, reproductive toxicity, developmental toxicity, and/or repeated dose systemic toxicity (CPA 2018b). A high confidence Moderate score was assigned for developmental toxicity based on reduced fetal weights and skeletal variations following high oral doses, however, this may not be plausibly related to endocrine effects and cannot be used to increase the confidence level of a Moderate score for endocrine activity. Additionally, there is a lack of concordance between the Kassotis et al. (2015) results and the U.S. EPA Tox21 assay results. Therefore, the final score of Moderate was assigned with low confidence.

**Group II and II* Human Health Effects (Group II and II* Human)**

***Note: Group II and Group II* endpoints are distinguished in the v 1.4 Benchmark system (the asterisk indicates repeated exposure). For Systemic Toxicity and Neurotoxicity, Group II and II* are considered sub-endpoints. See GreenScreen® Guidance v1.4, Annex 2 for more details.***

**Acute Mammalian Toxicity (AT) Score (vH, H, M, or L): L**

Triethylene glycol was assigned a score of Low for acute toxicity based on oral and dermal $LD_{50}$ values of greater than 2,000 mg/kg. Additionally, inhalation $LC_{50}$ values were > 5 mg/L in two of three tests, with the third test identifying an $LC_{50}$ > 3.9 mg/L. GreenScreen® criteria classify chemicals as a Low hazard for acute toxicity when oral and dermal $LD_{50}$ values are >2,000 mg/kg and inhalation $LC_{50}$ values are > 5 mg/L for dusts, mists, and fumes (CPA 2018b). Confidence in the score is high as it is based on multiple reliable experimental studies.

- Authoritative and Screening Lists
  - *Authoritative:* Not present on any authoritative lists.
  - *Screening:* Not present on any screening lists.
- ECHA 2019b
  - *Oral:* $LD_{50}$ (male and female Sprague-Dawley rats) > 16 mL/kg (reported as equivalent to >2,000 mg/kg) (GLP-compliant, no guideline)
    - The REACH dossier authors assigned a Klimisch score of 2 (reliable with restrictions) due to the study being well documented, meeting generally accepted scientific principles, and being acceptable for assessment.
  - *Dermal:* $LD_{50}$ (male and female New Zealand white rabbits) >16 mL/kg (equivalent to >18,080 mg/kg[11]) (GLP-compliant, no guideline)
    - The REACH dossier authors assigned a Klimisch score of 2 (reliable with restrictions) due to the study being well documented, meeting generally accepted scientific principles, and being acceptable for assessment.
  - *Inhalation (aerosol):* 4 hr $LC_{50}$ (male and female Sprague-Dawley rats) >5.2 mg/L (GLP-compliant, no guideline)
    - The REACH dossier authors assigned a Klimisch score of 2 (reliable with restrictions) due to the study being well documented, meeting generally accepted scientific principles, and being acceptable for assessment.
- ESIS 2000 (no information on guideline and GLP compliance status provided; Klimisch scores not assigned)
  - *Oral:* $LD_{50} \geq$ 17,000 mg/kg (rats).
  - *Oral:* $LD_{50} \geq$ 18,500 mg/kg (mice).
  - *Oral:* $LD_{50} \geq$ 8,400 mg/kg (rabbits).
  - *Oral:* $LD_{50} \geq$ 7,900 mg/kg (guinea pig).
  - *Dermal:* $LD_{50}$ > 5,000 mg/kg (rabbits).
- MAK 2007 (no information on guideline and GLP compliance status provided; Klimisch scores not assigned)
  - *Oral:* The lethal dose for humans is 5,000-15,000 mg/kg.
  - *Oral:* $LD_{50}$ = 31,800 mg/kg (rats).
  - *Oral:* $LD_{50}$ =27,800 mg/kg (female rats).
  - *Oral:* $LD_{50}$ =22,100 mg/kg (rats).
  - *Oral:* $LD_{50}$ =18,900 mg/kg (rats).
  - *Oral:* $LD_{50}$ >18,000 mg/kg (rats).

[11] Using a density of 1.13 g/cm$^3$ (ECHA 2018): 1.13 g/cm$^3$ * (1,000 mg/g) * (1 cm$^3$/mL) = 1,130 mg/mL * 16 mL/kg = 18,080 mg/kg.

- *Oral:* $LD_{50}$ =15,000 - 18,000 mg/kg (rats).
- *Oral:* $LD_{50}$ = 27,000 mg/kg (mice).
- *Oral:* $LD_{50}$ = 21,000 mg/kg (mice).
- *Oral:* $LD_{50}$ = 20,800 mg/kg (mice).
- *Oral:* $LD_{50}$ = 18,500 mg/kg (mice).
- *Oral:* $LD_{50}$ >15,800 mg/kg (mice).
- *Oral:* $LD_{50}$ = 9,500 mg/kg (rabbits).
- *Oral:* $LD_{50}$ = 14,700 mg/kg (guinea pigs).
- *Oral:* $LD_{50}$ = 8,900 mg/kg (guinea pigs).
- *Oral:* $LD_{50}$ = 7,900 mg/kg (guinea pigs).
- *Dermal:* $LD_{50}$ >18,000 - 22,500 mg/kg (rabbits) .
- *Dermal:* $LD_{50}$ >5,000 mg/kg (rats).
- *Inhalation:* $LC_{50}$ (rat, sex and strain not reported) > 5,000 mg/$m^3$ (> 5 mg/L).

- HSDB 2007 (no information on guideline and GLP compliance status provided; Klimisch scores not assigned)
  - *Oral:* $LD_{50}$ = 18,500 mg/kg (mice).
  - *Oral:* $LD_{50}$ = 17,000 - 31,669 mg/kg (rat).
  - *Oral:* $LD_{50}$ = 9,500 mg/kg (rabbit).
  - *Oral:* $LD_{50}$ = 7,900 - 14,660 (guinea pig).
  - *Dermal:* $LD_{50}$ = 22,460 - 22,600 mg/kg (rabbit).
  - *Inhalation:* 4-hr $LC_{50}$ >3.9 mg/L (Sprague-Dawley rat).

**Systemic Toxicity/Organ Effects incl. Immunotoxicity (ST-single) Score (vH, H, M, or L): M**
Triethylene glycol was assigned a score of Moderate for systemic toxicity (single dose) based on evidence of respiratory irritation in animals. GreenScreen® criteria classify chemicals as a Moderate hazard for systemic toxicity (single dose) when a GHS Category 3 classification is warranted (CPA 2018b). Confidence in the score is high as it is based on high quality data.

- Authoritative and Screening Lists
  - *Authoritative:* Not present on any authoritative lists.
  - *Screening:* Not present on any screening lists.
- ECHA 2019b
  - *Oral:* In a GLP-compliant oral acute toxicity assay (no guideline followed), male and female Sprague-Dawley rats (5/sex/dose) were administered 16 mL/kg (reported in ECHA as 2,000 mg/kg/day) (no vehicle, 99.82% purity) triethylene glycol via gavage and observed for 14 days. There were no mortalities and no remarkable gross lesions at necropsy. Clinical signs included sluggishness and unsteady gait. Recovery occurred within 3 hours to 1 day. The REACH dossier authors assigned a Klimisch score of 2 (reliable with restrictions), due to the study being well-documented, meeting generally accepted scientific principles, and being acceptable for assessment.
  - *Dermal:* In a GLP-compliant dermal acute toxicity assay (no guideline followed), male and female New Zealand White rabbits (5/sex/dose) were administered 16 mL/kg triethylene glycol (no vehicle, 99.82% purity) to intact skin for 24 hours and observed for 14 days. One female died on day 6, and necropsy revealed gas-filled intestines. No other mortalities were reported. Necropsy of surviving animals revealed tan lungs (one female), liquid filled stomach and intestines (one female) and slight vascularization of the treated skin (one male). Clinical signs included emaciation (one female) and abdominal distention (two females). The REACH dossier authors assigned a Klimisch score of 2 (reliable with restrictions), due to the study being well-documented, meeting generally accepted scientific principles, and

being acceptable for assessment.
    - *Inhalation (aerosol):* In a GLP-compliant inhalation acute toxicity assay (no guideline followed), male and female Sprague-Dawley rats (5/sex/dose) were exposed to 5.2 mg/L triethylene glycol (air vehicle, ≥99.7% purity) via whole body inhalation for 4 hours and observed for 14 days. There were no mortalities and no remarkable gross lesions at necropsy. Clinical signs included periocular wetness, oily fur, absence of toe and nail pinch reflexes and unkempt fur. Recovery occurred within 3 hours to 1 day. The REACH dossier authors assigned a Klimisch score of 2 (reliable with restrictions), due to the study being well-documented, meeting generally accepted scientific principles, and being acceptable for assessment.
- HSDB 2007 (no Klimisch scores assigned)
    - *Inhalation:* In a non-GLP-compliant sensory irritation study (no guideline followed) in male Swiss-Webster mice (4/dose), animals were exposed head only to respirable aerosols of triethylene glycol for 30 minutes at concentrations of 3.601, 4.545, 4.744 and 5.099 mg/L (purity and vehicle unreported) showed an exposure concentration-related depression of breathing rate that allowed the calculation of an $RD_{50}$ of 5.14 mg/L. The study indicated that triethylene glycol has properties of a peripheral chemosensory irritant.
- Based on the weight of evidence, triethylene glycol has properties of a peripheral chemosensory irritant upon single exposure and according to GHS classification criteria, triethylene glycol is, at most, classified to GHS Category 3.

**Systemic Toxicity/Organ Effects incl. Immunotoxicity (ST-repeat) (Group II*) Score (H, M, or L): L**

Triethylene glycol was assigned a score of Low for systemic toxicity (repeated dose) based on the lack of systemic effects below the guidance value of 100 mg/kg/day for 90-day oral studies. GreenScreen® criteria classify chemicals as a Low hazard for systemic toxicity (repeated dose) when animal studies identify oral LOAEL values greater than 100 mg/kg/day for 90-day studies (CPA 2018b). Confidence in the score is high as it is based on reliable experimental data.

- Authoritative and Screening Lists
    - *Authoritative:* Not present on any authoritative lists.
    - *Screening:* Not present on any screening lists.
- ECHA 2019b, HSDB 2007
    - *Oral:* In a GLP-compliant 90-day oral feeding study similar to OECD Guideline 408, male and female Fischer 344 rats (30/sex/dose in control and high dose groups, 20/sex/dose in low and mid dose groups) were fed 0, 10,000, 20,000 or 50,000 ppm of triethylene glycol (vehicle unreported, 99.74-99.9% purity) in their diet daily for 13 weeks. According to the authors, these doses were equivalent to 0, 748, 1,522 or 3,849 mg/kg for males, and 0, 848, 1,699 or 4,360 mg/kg for females. The authors reported no mortality or signs of toxicity, and no dosage-related effects with serum chemistry, or gross and microscopic pathology. High-dose males and females showed a reduction in body weights, while body weight gains were decreased in all dose groups for both sexes. Females showed no hematological effects. Mid- and high-dose males showed a slight reduction in erythrocyte count and hematocrit, and high-dose males had decreased hemoglobin concentration with increased mean corpuscular volume. The authors of the study considered these effects to reflect mild hemodilution related to the absorption of large triethylene glycol doses. Urinalysis resulted in a dosage-related decreased pH, and increased urine volume mainly observed at the high dose. High-dose females had increased kidney weights, and increased relative kidney weights were noted for males and females from the mid- and high-dose groups. The overall

findings from these two studies indicate that continuous subchronic exposure to triethylene glycol does not result in local or systemic specific organ or tissue toxicity in rats. The LOAEL was established at 1,522 mg/k/day for males and 1,699 mg/kg/day for females, based on increased relative kidney weights, and the NOAELs were 748 and 848 mg/kg/day for males and females, respectively. The REACH dossier authors assigned a Klimisch score of 2 (reliable with restrictions), due to the study being well-documented, meeting generally accepted scientific principles, and being acceptable for assessment.

- MAK 2007 (no Klimisch scores assigned)
    - *Oral:* In a 13-month study (GLP status and guideline adherence unreported), male and female rats (7-24/group) were administered triethylene glycol in drinking water at 0, 0.14, 0.32, and 2.8 mL/kg/day (reported as equivalent to 160, 360, and 3,150 mg/kg/day) (vehicle and purity unreported). No significant adverse effects were reported at any dose level.
- HSDB 2007 (no Klimisch scores assigned)
    - *Oral:* In a subacute study (GLP status and guideline adherence unreported), albino rats (5 rats/dose) were administered triethylene glycol via stomach tube for 30 consecutive days. The daily doses were 0.1 ml/kg of a 5% aqueous solution, 3.0 ml/kg of a 30% solution, 10 mL/kg of undiluted triethylene glycol, and 20.0 mL/kg of undiluted triethylene glycol (vehicle and purity unreported). The two lower dose groups showed no signs of toxicity and normal weight gain. Slowed weight gain, hair loss, and diarrhea were observed in animals in the 10 mL/kg dose group. The 20 mL/kg dose group had high mortality rates, with three deaths within the first 24 hours after the first dose, and the remaining two dying before the third day of the study.
    - *Oral:* In a subacute drinking water study (GLP status and guideline adherence unreported), albino rats (5 rats/dose) received drinking water containing 5% or 10% of triethylene glycol (purity and vehicle unreported) for 30 days. Signs of toxicity were noted in both the 5% and 10% dose groups. For animals in the 5% dose group, one died each on day 8, 21, and 28. The remaining two animals survived the study duration and recovered after exposure ended. All animals in the 10% dose group died by Day 12.
    - *Oral:* In a similar study (GLP status and guideline adherence unreported) with drinking water, young (3-week old) rats (5 rats/dose, species not specified) received 3% or 5% by volume of triethylene glycol (purity and vehicle unreported) in their drinking water for 30 days. No signs of toxicity were observed in animals in the 3% dose group, and all animals survived to study completion. Toxicity (weight loss, alopecia, and poor grooming) was noted in animals in the 5% dose group in the first 2 weeks of exposure, after which the severity reduced. A reduction in body weight gain was observed in the 5% dose group, with weights returning to normal after the exposure period. One animal in the 5% dose group died on Day 25.
    - *Oral:* In a two-year feeding study (GLP status and guideline adherence unreported), no toxic effects were reported in Osborne-Mendel rats (12 rats/dose) fed a daily diet containing 0, 1%, 2%, or 4% triethylene glycol (purity and vehicle unreported).
- MAK 2007 (no Klimisch scores assigned)
    - *Inhalation (aerosol):* In an 11-day repeated dose study (GLP status and guideline adherence unreported), male and female Sprague-Dawley rats (10/sex/dose) were exposed nose only to triethylene glycol at 0, 100, 500, and 1,000 mg/m$^3$ 6 hours/day 5 days/week for 9 total exposures. Additional 5 rats/sex from the control and 1,000 mg/m$^3$ groups were exposed to a 4-week recovery period. At 500 mg/m$^3$ and above body weight gain was decreased, but not significantly. No other effects were observed and the authors established a NOEC of 100 mg/m$^3$ and a NOAEC of 1,000 mg/m$^3$ (vehicle and purity unreported).

- HSDB 2007 (no Klimisch scores assigned)
    - *Inhalation:* For a 9-day repeated exposure study (GLP status and guideline adherence unreported) conducted in Sprague Dawley rats (number of animals not provided), animals were exposed nose-only to triethylene glycol aerosol concentrations of 0, 102, 517 and 1,036 mg/m$^3$ (vehicle and purity unreported) for 6 hr/day. No clinical signs, no effects on food and water consumption, and no biochemical or histological evidence of hepatorenal dysfunction were noted. The threshold for toxicity by nose-only exposure to triethylene glycol aerosols was established at 1,036 mg/m$^3$.

**Neurotoxicity (single dose, N-single) Score (vH, H, M, or L): M**
Triethylene glycol was assigned a score of Moderate for neurotoxicity (single dose) based on clinical signs indicative of reversible narcotic effects that warrants GHS Category 3 classification. GreenScreen® criteria classify chemicals as a Moderate hazard for neurotoxicity (single dose) when they are classified to GHS category 3 for transient narcotic effects (CPA 2018b). Confidence in the score was high as it was based on reliable animal studies.

- Authoritative and Screening Lists
    - *Authoritative:* Not present on any authoritative lists.
    - *Screening:* Not present on any screening lists.
- Not classified as a developmental neurotoxicant (Grandjean and Landrigan 2006, 2014).
- ECHA 2019b
    - *Oral:* In the previously described GLP-compliant oral acute toxicity assay (no guideline followed), male and female Sprague-Dawley rats (5/sex/dose) were administered 16 mL/kg (reported in ECHA as 2,000 mg/kg/day) (no vehicle, 99.82% purity) triethylene glycol via gavage and observed for 14 days. There were no remarkable gross lesions at necropsy. Clinical signs included sluggishness and unsteady gait. Recovery occurred within 3 hours to 1 day. The REACH dossier authors assigned a Klimisch score of 2 (reliable with restrictions), due to the study being well-documented, meeting generally accepted scientific principles, and being acceptable for assessment.
    - *Inhalation (aerosol):* In the previously described GLP-compliant inhalation acute toxicity assay (no guideline followed), male and female Sprague-Dawley rats (5/sex/dose) were exposed to 5.2 mg/L triethylene glycol (air vehicle, ≥99.7% purity) via whole body inhalation for 4 hours and observed for 14 days. There were no remarkable gross lesions at necropsy. Clinical signs included absence of toe and nail pinch reflexes. Recovery occurred within 3 hours to 1 day. The REACH dossier authors assigned a Klimisch score of 2 (reliable with restrictions), due to the study being well-documented, meeting generally accepted scientific principles, and being acceptable for assessment.

**Neurotoxicity (repeated dose, N-repeated) (Group II*) Score (H, M, or L):** DG
Triethylene glycol was assigned a score of Data Gap for neurotoxicity (repeated dose) based on the lack of data identified for this endpoint.

- Authoritative and Screening Lists
    - *Authoritative:* Not present on any authoritative lists.
    - *Screening:* Not present on any screening lists.
- Not classified as a developmental neurotoxicant (Grandjean and Landrigan 2006, 2014).
- No data were identified.

**Skin Sensitization (SnS) (Group II*) Score (H, M, or L):** *L*

Triethylene glycol was assigned a score of Low for skin sensitization based on negative data in human and animal studies. GreenScreen® criteria classify chemicals as a Low hazard for skin sensitization when adequate data are available and negative and they are not GHS classified (CPA 2018b). Confidence in the score is reduced as limited details were available on studies identified.

- Authoritative and Screening Lists
  - *Authoritative:* Not present on any authoritative lists.
  - *Screening:* Not present on any screening lists.
- ECHA 2019b
  - Triethylene glycol was non-sensitizing in a non-GLP-compliant repeated insult patch test (no guideline followed) in human volunteers (37 males, 360 females). Subjects were induced and challenged with 0.2 mL triethylene glycol (vehicle and purity unreported) under occlusive or semi-occlusive conditions. There were no positive reactions reported. The REACH dossier authors assigned a Klimisch score of 4 (reliability not assignable), due to the study being from a secondary source.
  - Triethylene glycol was non-sensitizing in a non-GLP-compliant guinea pig maximization test similar to OECD Guideline 406. Guinea pigs (number sex and strain not specified) were intradermally and epicutaneously induced and epicutaneously challenged with undiluted test material (vehicle and purity unreported). No positive skin sensitization reactions were reported. The REACH dossier authors assigned a Klimisch score of 4 (reliability not assignable), due to the study being from a secondary source.
- HSDB 2007 (no Klimisch scores assigned)
  - Negative in human volunteer repeated insult patch test (no further details about the study were reported, GLP status and guideline adherence unreported).
  - Negative in animal maximization test (no further details about the study were reported).
- MAK 2007 (no Klimisch scores assigned)
  - Triethylene glycol (20% in petrolatum, purity unreported) was not sensitizing to the skin of 25 human volunteers in a maximization test (GLP status and guideline adherence unreported).

**Respiratory Sensitization (SnR) (Group II*) Score (H, M, or L):** *L*

Triethylene glycol was assigned a score of Low for respiratory sensitization based on the lack of dermal sensitization potential and the ECHA (2017) guidance. GreenScreen® criteria classify chemicals as a Low hazard for respiratory sensitization when adequate data are available and negative and they are not GHS classified (CPA 2018b). Confidence in the score is reduced as this evaluation does not include non-immunologic mechanisms of respiratory sensitization, and no specific data are available for respiratory sensitization.

- Authoritative and Screening Lists
  - *Authoritative:* Not present on any authoritative lists.
  - *Screening:* Not present on any screening lists.
- OECD 2019
  - Triethylene glycol does not contain any structural alerts for respiratory sensitization (Appendix E).
- Based on the weight of evidence and guidance from ECHA regarding assessment of respiratory sensitization potential, a score of Low was assigned. The guidance from ECHA states that the mechanisms leading to respiratory sensitization are essentially similar to those leading to skin sensitization (ECHA 2017). ECHA recommended that if a chemical is not a dermal sensitizer based on high quality data, it is unlikely to be a respiratory sensitizer. ECHA also noted that this rationale does not cover respiratory hypersensitivity caused by non-immunological mechanisms, for which

human experience is the main evidence of activity (ECHA 2017). As triethylene glycol was not sensitizing to the skin (see skin sensitization section above), and a literature search did not find any human evidence of respiratory sensitization by triethylene glycol, and as triethylene glycol does not contain any structural alerts for respiratory sensitization (OECD 2019), triethylene glycol is not expected to be a respiratory sensitizer.

**Skin Irritation/Corrosivity (IrS) Group II Score (vH, H, M, or L): L**

Triethylene glycol was assigned a score of Low for skin irritation/corrosivity based on negative data in standard animal tests supported by human data. GreenScreen® criteria classify chemicals as a Low hazard for skin irritation/corrosivity when adequate data are available and negative and they are not GHS classified (CPA 2018b). Confidence in the score is high as it is based on reliable experimental data.

- Authoritative and Screening Lists
  - *Authoritative:* Not present on any authoritative lists.
  - *Screening:* Not present on any screening lists.
- ECHA 2019b
  - Triethylene glycol was not irritating in a GLP-compliant Draize test (no guideline followed) in New Zealand white rabbits (n=6). Animals were administered 0.5 mL undiluted test substance (no vehicle, 99.82% purity) to clipped intact skin under occlusive conditions for 4 hours. No erythema or edema reactions were reported. Authors of the REACH dossier assigned a Klimisch score of 2 (reliable with restrictions) based on the study being well-documented, meeting generally accepted scientific principles, and being acceptable for assessment.
- ESIS 2000 (no Klimisch scores assigned)
  - Triethylene glycol was slightly irritating to the skin when 500 mg (purity and vehicle unreported) was applied to rabbits for 24 hours during a Draize test (no further details about the study design provided, GLP status and guideline adherence unreported).
- HSDB 2007 (no Klimisch scores assigned)
  - In an occluded patch test (GLP status and guideline adherence unreported), rabbits (n=6) were exposed to 0.5 mL triethylene glycol (purity and vehicle unreported) for 4 hours. Triethylene glycol did not produce any erythema, edema or other dermal reaction.
- MAK 2007 (no Klimisch scores assigned)
  - Triethylene glycol produced minimal skin irritation when 41 human volunteers were administered 0.2 mL (purity and vehicle unreported) to the skin (GLP status and guideline adherence unreported). 14 subjects produced no reaction, 23 subjects produced very weak skin irritation and 4 subjects had clear irritation. An irritation index of 35.9 (max 300) was reported.
  - Triethylene glycol (20% in petrolatum, purity unreported) was not irritating to the skin of humans in a 48-hour occlusive patch test (GLP status and guideline adherence unreported) according to Kligman.
  - Triethylene glycol (purity and vehicle unreported) was not irritating to the skin when applied for 24 hours under occlusive conditions in a patch test (GLP status and guideline adherence unreported) in rabbits. No further details were available.
  - Triethylene glycol (purity and vehicle unreported) was slightly irritating to intact or scarified rabbit skin following 24 hours of exposure under occlusive conditions (GLP status and guideline adherence unreported). No further details were available.
  - Maximum mean irritation scores of 0.73 and 0.0 were reported following application of 2 mL undiluted triethylene glycol or 10% aqueous triethylene glycol (purity unreported),

respectively, once a day for six weeks to the skin of rabbits (3/group) (GLP status and guideline adherence unreported).

**Eye Irritation/Corrosivity (IrE) Group II Score (vH, H, M, or L): L**

Triethylene glycol was assigned a score of Low for eye irritation/corrosivity based on negative findings in standard animal tests supported by limited evidence from non-standard tests. GreenScreen® criteria classify chemicals as a Low hazard for eye irritation/corrosivity when adequate data are available and negative and they are mildly irritating to the eye (CPA 2018b). Confidence in the score is high as it is based on measured *in vivo* data.

- Authoritative and Screening Lists
  - *Authoritative:* Not present on any authoritative lists.
  - *Screening:* Not present on any screening lists.
- ECHA 2019b
  - Triethylene glycol was not irritating in a GLP-compliant Draize test (no guideline followed) in New Zealand white rabbits (n=6). One eye of each animal was instilled with 0.1 mL undiluted test substance (no vehicle, 99.82% purity)and animals were observed for 7 days. No corneal injury was observed; however, iritis and transient conjunctival irritation was observed in all treated eyes at 1 hour. Effects were fully reversible by 24 hours. Moderate to substantial discharge was observed in 5 of the treated eyes. An overall irritation score of 0 was reported by the authors. The REACH dossier authors assigned a Klimisch score of 2 (reliable with restrictions), due to the study being well-documented, meeting generally accepted scientific principles, and being acceptable for assessment.
- ESIS 2000 (no Klimisch scores assigned)
  - Triethylene glycol was slightly irritating to the eyes when 500 mg was applied to rabbits during a Draize test (no further details about the study design were provided, GLP status and guideline adherence unreported).
  - Ocular exposure to 0.5 mL triethylene glycol in rabbits produced slight eye irritation (no further details about the study were reported).
- HSDB 2007 (no Klimisch scores assigned)
  - Triethylene glycol (undiluted) did not produce eye irritation in rabbits. 0.5 mL triethylene glycol (purity unreported) was instilled into one eye of each of five albino rabbits for 1 minute (GLP status and guideline adherence unreported). The eyes were evaluated for hyperemia, edema and corneal opacity at hourly intervals during the first 4 hours, the end of 24 hours and daily for a week. Triethylene glycol produced zero to minimal eye injury (no further details about the study were reported).
  - In an acute ocular irritation study (GLP status and guideline adherence unreported) in rabbits, exposure to 0.1 mL triethylene glycol (vehicle and purity unreported) in six rabbits produced no corneal injury; however, all rabbits displayed acute iritis and minor transient conjunctival irritation; the affected tissues had healed and were back to normal within 24 hour of exposure.
- MAK 2007 (no Klimisch scores assigned)
  - Triethylene glycol was not irritating when 0.5 mL undiluted test substance (purity unreported) was instilled into the conjunctival sac of rabbits (n=5) (GLP status and guideline adherence unreported). No further details were available.
  - Triethylene glycol was slightly irritating when undiluted test substance (purity unreported) was instilled into the conjunctival sac of rabbits (GLP status and guideline adherence unreported). An acute irritation index of 11.3 (max 110) was reported. No further details were available.

- Slight erythema and congestion were observed following instillation of 0.5 mL undiluted test substance (purity unreported) into the conjunctival sac of rabbits (n=5) (GLP status and guideline adherence unreported). No further details were available.

**Ecotoxicity (Ecotox)**

**Acute Aquatic Toxicity (AA) Score (vH, H, M, or L): L**

Triethylene glycol was assigned a score of Low for acute aquatic toxicity based on L/$EC_{50}$ values >100 mg/L in all three trophic levels. GreenScreen® criteria classify chemicals as a Low hazard for acute aquatic toxicity when acute aquatic toxicity values are greater than 100 mg/L (CPA 2018b). Confidence in the score is high as it is based on reliable experimental data.

- Authoritative and Screening Lists
  - *Authoritative:* Not present on any authoritative lists.
  - *Screening:* Not present on any screening lists.
- ECHA 2019b
  - An $LC_{50}$ value of > 10,000 mg/L was identified for *Lepomis macrochirus* (fish, 96-hr) (non-GLP-compliant, no guideline)
    - The REACH dossier authors assigned a Klimisch score of 2 (reliable with restrictions), due to the study being well-documented, meeting generally accepted scientific principles, and being acceptable for assessment.
  - An $LC_{50}$ value of 69,800 mg/L was identified for *Pimephalas promelas* (fish, 96-hr) (non-GLP-compliant, no guideline)
    - The REACH dossier authors assigned a Klimisch score of 2 (reliable with restrictions), due to the study being well-documented, meeting generally accepted scientific principles, and being acceptable for assessment.
  - An $LC_{50}$ value of 54,800 mg/L was identified for *Danio rerio* (fish, 96-hr) (non-GLP-compliant, OECD Guideline 236)
    - The REACH dossier authors assigned a Klimisch score of 2 (reliable with restrictions), due to the study being well-documented, meeting generally accepted scientific principles, and being acceptable for assessment.
  - An $LC_{50}$ value of 48,000 mg/L was identified for *Cyprinodon variegatus* (fish, 96-hr) (non-GLP-compliant, no guideline)
    - The REACH dossier authors assigned a Klimisch score of 3 (not reliable), due to the sparse information on methods and results provided.
  - An $LC_{50}$ value of 70,200 mg/L was identified for *P. promelas* (fish, 96-hr) (non-GLP-compliant, no guideline)
    - The REACH dossier authors assigned a Klimisch score of 2 (reliable with restrictions), due to the study being scientifically acceptable and the methods and results are provided in detail.
  - An $EC_{50}$ value of > 10,000 mg/L was identified for *Daphnia magna* (invertebrate, 24-hr) (non-GLP-compliant, DIN 38412/11 Guideline)
    - The REACH dossier authors assigned a Klimisch score of 2 (reliable with restrictions), due to the study being conducted according to a test procedure compliant with national standards methods and acceptable restrictions.
  - An $EC_{50}$ value of 52,400 mg/L was identified for *D. magna* (invertebrate, 48-hr) (non-GLP-compliant, ASTM Guideline)
    - The REACH dossier authors assigned a Klimisch score of 2 (reliable with restrictions), due to the study being well-documented, meeting generally accepted

scientific principles, and being acceptable for assessment.
    - An $LC_{50}$ value of 35,000 mg/L was identified for *D. magna* (invertebrate, 48-hr) (non-GLP-compliant, no guideline)
        - The REACH dossier authors assigned a Klimisch score of 2 (reliable with restrictions), due to the study being well-documented, meeting generally accepted scientific principles, and being acceptable for assessment.
    - An $LC_{50}$ value of 11,000,000 mg/L was identified for *Americamysis bahia* (invertebrate, 96-hr) (non-GLP-compliant, no guideline)
        - The REACH dossier authors assigned a Klimisch score of 3 (not reliable), due to the sparse information on methods and results provided.
    - An $LC_{50}$ value of 43,500 mg/L was identified for *Hyalella azteca* (invertebrate, 96-hr) (non-GLP-compliant, no guideline)
        - The REACH dossier authors assigned a Klimisch score of 2 (reliable with restrictions), due to the study being conducted according to a test procedure compliant with national standards methods and acceptable restrictions.
    - An $EC_{50}$ value of >10,000 mg/L was identified for *Scenedesmus quadricauda* (algae, growth rate, 8-day) (non-GLP-compliant, no guideline)
        - The REACH dossier authors assigned a Klimisch score of 2 (reliable with restrictions), due to the study being well-documented, meeting generally accepted scientific principles, and being acceptable for assessment.
- ESIS 2000 (Klimisch scores were not assigned)
    - An $LC_{50}$ value of 59,900 to 77,400 mg/L was identified for *P. promelas* (fish, 96-hr) (non-GLP-compliant, no guideline).
    - An $LC_{50}$ value of 73,500 mg/L was identified for *Salvelinus fontinalis* (fish, 96-hr) (non-GLP-compliant, no guideline).
    - An $EC_{50}$ value of > 3,600 mg/L was identified for *Anacystis aeruginosa* (algae, growth rate, 7-day) (non-GLP-compliant, no guideline).
    - An $EC_{50}$ value of > 1,000 mg/L was identified for *Scenedesmus subspicatus* (algae, growth rate, 7-day) (non-GLP-compliant, no guideline).

**Chronic Aquatic Toxicity (CA) Score (vH, H, M, or L): L**

Triethylene glycol was assigned a score of Low for chronic aquatic toxicity based on chronic toxicity values >10 mg/L in all three trophic levels. GreenScreen® criteria classify chemicals as a Low hazard for chronic aquatic toxicity when chronic aquatic toxicity values are greater than 10 mg/L (CPA 2018b). Confidence in the score is high as it is based on reliable experimental data.

- Authoritative and Screening Lists
    - *Authoritative:* Not present on any authoritative lists.
    - *Screening:* Not present on any screening lists.
- ECHA 2019b
    - A NOEC of 40 mg/L was identified for *Menidia peninsulae* (fish, 28-day) (non-GLP-compliant, ASTM E-47.01 Guideline)
        - The REACH dossier authors assigned a Klimisch score of 2 (reliable with restrictions), due to the study being conducted according to a test procedure compliant with national standards methods and acceptable restrictions.
    - A NOEC value (growth) of 7,500 - 15,000 mg/L was identified for *D. magna* (invertebrate, 21-day) (non-GLP-compliant, ASTM E-47.01 Guideline)

        - The REACH dossier authors assigned a Klimisch score of 2 (reliable with restrictions), due to the study being conducted according to a test procedure compliant with national standards methods and acceptable restrictions.
    - A NOEC value (reproduction and survival) of >15,000 mg/L was identified for *D. magna* (invertebrate, 21-day) (non-GLP-compliant, ASTM E-47.01 Guideline)
        - The REACH dossier authors assigned a Klimisch score of 2 (reliable with restrictions), due to the study being conducted according to a test procedure compliant with national standards methods and acceptable restrictions.
    - A NOEC value (reproduction) of >5,500 mg/L was identified for *D. magna* (invertebrate, 28-day) (non-GLP-compliant, no guideline)
        - The REACH dossier authors assigned a Klimisch score of 2 (reliable with restrictions), due to the study being well-documented, meeting generally accepted scientific principles, and being acceptable for assessment.
    - A NOEC value (reproduction rate) > 1,000 mg/L was identified for *Mysidopsis bahia* (invertebrate, 23-day) (non-GLP-compliant, ASTM E-47.01 Guideline)
        - The REACH dossier authors assigned a Klimisch score of 2 (reliable with restrictions), due to the study being conducted according to a test procedure compliant with national standards methods and acceptable restrictions.
    - A TTC value of >10,000 mg/L was identified for *S. quadricauda* (algae, growth rate, 8-day) (non-GLP-compliant, no guideline)
        - The REACH dossier authors assigned a Klimisch score of 2 (reliable with restrictions), due to the study being well-documented, meeting generally accepted scientific principles, and being acceptable for assessment.

**Environmental Fate (Fate)**

**Persistence (P) Score (vH, H, M, L, or vL): L**

Triethylene glycol was assigned a score of Low for persistence based on it meeting the GHS criteria for rapid degradability. GreenScreen® criteria classify chemicals as a Low hazard for persistence when they meet the GHS rapid degradability criteria (CPA 2018b). Confidence in the score is high as it is based on reliable experimental data.

- Authoritative and Screening Lists
    - *Authoritative:* Not present on any authoritative lists.
    - *Screening:* Not present on any screening lists.
- ECHA 2019b, HSDB 2007
    - Triethylene glycol was readily biodegradable in a non-GLP-compliant OECD Guideline 301C Modified MITI Test. In this study, 100 mg/L of the test substance was exposed to aerobic, activated sludge (adaption not specified) for 28 days. The test substance degraded 25-92% in 28 days. The REACH dossier authors assigned a Klimisch score of 2 (reliable with restrictions) due to the study being conducted according to guideline with acceptable restrictions.
- ESIS 2000 (no Klimisch scores assigned)
    - A non-GLP-compliant Ready biodegradability: modified OECD Screening test (OECD 301E) was conducted under aerobic conditions in domestic activated sludge. Triethylene glycol was reported as reaching 80% biodegradation after 44 days.
    - A non-GLP-compliant Inherent biodegradability: Modified Zahn-Wellens tests (OECD 302B) was conducted under aerobic conditions using industrial activated sludge. Triethylene glycol was reported as 95% biodegradable after 14 days.

- HSDB 2007 (no Klimisch scores assigned)
    - Aerobic river die-away tests (no information regarding GLP compliance and guideline provided), utilizing several different sources of freshwater, have demonstrated that triethylene glycol should biodegrade rapidly in the environment.
- U.S. EPA 2017
    - The BIOWIN modeling Ready Biodegradable Predictor indicates that triethylene glycol is expected to be readily biodegradable (Appendix F). The Level III Fugacity Model (MCI Method) predicts 69.4% will partition to soil with a half-life of 30 days, 30.6% will partition to water with a half-life of 15 days, and 0.0688% will partition to sediment with a half-life of 135 days.
- Based on the weight of evidence, a score of Low was assigned. As no data on the 10-day window were available in experimental biodegradation studies, triethylene glycol meets the criteria for "rapid degradability." ToxServices considered these results in conjunction with modeled data, but placed more weight on the measured values. Modeling predicts that triethylene glycol is readily biodegradable, with a half-life of 30 days in soil, its major compartment. It is ToxServices internal policy to assign the hazard score for persistence based on the dominant environmental compartment(s) identified via fugacity modeling (ToxServices 2016). Collectively, these data suggest that triethylene glycol at least meets the criteria for rapid degradability, and therefore a score of Low was assigned.

**Bioaccumulation (B) Score (vH, H, M, L, or vL): vL**
Triethylene glycol was assigned a score of Very Low for bioaccumulation based on estimated BCF values of 0.8933 - 3 and an experimental partition coefficient of -1.75. GreenScreen® criteria classify chemicals as a Very Low hazard for bioaccumulation when BCF values are ≤100 and log $K_{ow}$ values are ≤ 4 (CPA 2018b). Confidence in the score is high as it is based on an experimental partition coefficient.

- Authoritative and Screening Lists
    - *Authoritative:* Not present on any authoritative lists.
    - *Screening:* Not present on any screening lists.
- HSDB 2007
    - An estimated BCF of 3 was calculated in fish for triethylene glycol.
- U.S. EPA 2017
    - Triethylene glycol has an experimental log $K_{ow}$ of -1.75 in the EPISuite database.
    - BCFBAF predicts a BCF of 0.8933 based on a log $K_{ow}$ of -1.75, indicating this chemical is not likely to bioaccumulate (Appendix F).

## Physical Hazards (Physical)

**Reactivity (Rx) Score (vH, H, M, or L):** *L*
Triethylene glycol was assigned a score of Low for reactivity based on it not being oxidizing or explosive. GreenScreen® criteria classify chemicals as a Low hazard for reactivity when they are not GHS classified (CPA 2018b). Confidence in the score is reduced due to the lack of measured data.

- Authoritative and Screening Lists
    - *Authoritative:* Not present on any authoritative lists.
    - *Screening:* Not present on any screening lists.
- HSDB 2007
    - Triethylene glycol would not be classified as an oxidizing chemical as it does not contain structural groups that would cause concern for explosion.

**Flammability (F) Score (vH, H, M, or L): L**

Triethylene glycol was assigned a score of Low for flammability based on a flash point of 176 - 177°C. GreenScreen® criteria classify chemicals as a Low hazard for flammability when they are not GHS classified (CPA 2018b). Confidence in the score is high as it is based on reliable experimental data.

- Authoritative and Screening Lists
  - *Authoritative:* Not present on any authoritative lists.
  - *Screening:* Not present on any screening lists.
- HSDB 2007, ECHA 2019b
  - Flashpoint of triethylene glycol is reported to be 176 - 177°C in a non-GLP-compliant open cup study (no guideline). The REACH dossier authors assigned a Klimisch score of 2 (reliable with restrictions) due to the study being from a handbook or collection of data.
- Based on the weight of evidence, a score of Low was assigned. The flashpoint of triethylene glycol is 176 - 177°C, which is higher than the cut-off of 93ºC to classify chemicals (liquid) into GHS Category 4. Therefore, it is not considered flammable.

## References

Chemical Carcinogenesis Research Information System (CCRIS). 2003. Entry for triethylene glycol (CAS #112-27-6). United States National Library of Medicine. Available at: https://toxnet.nlm.nih.gov/cgi-bin/sis/search2/r?dbs+ccris:@term+@rn+112-27-6.

ChemIDplus. 2019. Entry for Triethylene Glycol (CAS #112-27-6). United States National Library of Medicine. Available at: http://chem.sis.nlm.nih.gov/chemidplus/chemidheavy.jsp.

Clean Production Action (CPA). 2018a. GreenScreen® Assessment Expiration Policy. October 2, 2018.

Clean Production Action (CPA). 2018b. The GreenScreen® for Safer Chemicals Guidance. Version 1.4 Guidance. January 2018. Available at: https://www.greenscreenchemicals.org/static/ee_images/uploads/resources/GreenScreen_Guidance_v1_4_2018_01_Final.pdf.

European Chemicals Agency (ECHA). 2017. Guidance on information requirements and Chemical Safety Assessment. Chapter R.7a: Endpoint specific guidance. Version 6.0. July 2017. Available at: https://echa.europa.eu/documents/10162/13632/information_requirements_r7a_en.pdf.

European Chemicals Agency (ECHA). 2019a. C&L Inventory. Available at: https://echa.europa.eu/information-on-chemicals/cl-inventory-database.

European Chemicals Agency (ECHA). 2019b. 2,2'-(Ethylenedioxy)diethanol (CAS #112-27-6). Available at: https://echa.europa.eu/information-on-chemicals.

European Chemical Substances Information System (ESIS). 2000. Triethylene glycol IUCLID Dataset. European Commission Joint Research Center. Available at: https://www.toxplanet.com/.

Grandjean, P., and P.J. Landrigan. 2006. Developmental Neurotoxicity of Industrial Chemicals. Lancet 368: 2167-2178.

Grandjean, P., and P.J. Landrigan. 2014. Neurobehavioral Effects of Developmental Toxicity. The Lancet 13: 330-338.

Hazardous Substances Data Bank (HSDB). 2007. Triethylene glycol online record. United States National Library of Medicine. Available at: https://pubchem.ncbi.nlm.nih.gov/source/hsdb/898.

Kassotis, C.D., K.C. Klemp, D.C. Vu, C.H. Lin, C.X. Meng, C.L. Besch-Williford, L. Pinatti, R. T. Zoeller, E.Z. Drobnis, V.D. Balise, C.J. Isiguzo, M.A. Williams, D.E. Tillitt, and S.C. Nagel. 2015. Endocrine-disrupting activity of hydraulic fracturing chemicals and adverse health outcomes after prenatal exposure in male mice. *Endocrinology*. 156(12): 4458-4473.

MAK. 2007. Triethylene Glycol. Available at: https://onlinelibrary.wiley.com/doi/pdf/10.1002/3527600418.mb11227e4214.

National Institute for Occupational Safety and Health (NIOSH). 1996. International Chemical Safety Card for Triethylene Glycol. Validated March 28, 1996. Available at: https://www.cdc.gov/niosh/ipcs/default.html.

National Toxicology Program (NTP). 1984. Reproductive and Fertility Assessment of Triethylene Glycol (CAS #112-27-6) in CD-1 Mice when Administered in Drinking Water. NTP Report # RACB83115. Available at: http://ntp.niehs.nih.gov/?objectid=071C4F68-9010-14C3-92069F54D6988DCF.

National Toxicology Program (NTP). 1991a. Cytogenic Study of Triethylene Glycol in Chinese Hamster Ovary Cell Chromosome Aberrations Test. Available at: https://manticore.niehs.nih.gov/cebssearch//genetox/002-02955-0002-0000-5/.

National Toxicology Program (NTP). 1991b. Cytogenic Study of Triethylene Glycol in Chinese Hamster Ovary Cell Sister Chromatid Exchange Test. Available at: https://manticore.niehs.nih.gov/cebssearch//genetox/002-02955-0001-0000-4/.

National Toxicology Program (NTP). 2018. Genetic Toxicity Evaluation of Triethylene Glycol in Salmonella/E.coli Mutagenicity Test or Ames Test. Study 261099. Available at: https://manticore.niehs.nih.gov/cebssearch/study/002-02955-0003-0000-6.

Organisation for Economic Co-operation and Development (OECD). 2004. SIDS Initial Assessment Report for Ethylene Glycol Category. Available at: https://hpvchemicals.oecd.org/UI/SIDS_Details.aspx?id=EBC827DF-0FA3-416F-9946-FB5C015BC16D.

Organisation for Economic Co-operation and Development (OECD). 2007. SIDS Dossier for Triethylene Glycol (CAS #112-27-6). OECD HPV Chemical Programme, SIDS Dossier. Available at: https://hpvchemicals.oecd.org/UI/SIDS_Details.aspx?id=EBC827DF-0FA3-416F-9946-FB5C015BC16D.

Organisation for Economic Co-operation and Development (OECD). 2019. OECD QSAR Toolbox for Grouping Chemicals into Categories Version 4.3.1. Available at: http://toolbox.oasis-lmc.org/?section=download&version=latest.

Pharos. 2019. Pharos Chemical and Material Library Entry for Triethylene Glycol (CAS #112-27-6). Available at: http://www.pharosproject.net/material/.

Sigma Aldrich. 2014. Safety data sheet for triethylene glycol (CAS #112-27-6). Version 3.6. Dated June 27, 2014. Available at: https://www.sigmaaldrich.com/catalog/search?interface=CAS+No.&term=112-27-6&N=0+9679402&mode=partialmax&focus=product&lang=en&region=US.

TEDX. 2017. TedX List. Record for triethylene glycol (CAS #112-27-6). Available at: https://endocrinedisruption.org/interactive-tools/tedx-list-of-potential-endocrine-disruptors/search-the-tedx-list.

ToxServices. 2016. SOP 1.37: GreenScreen® Hazard Assessments. August 30, 2016.

United States Department of Transportation (U.S. DOT). 2008a. Chemicals Listed with Classification. 49 CFR § 172.101. Available at: http://www.gpo.gov/fdsys/pkg/CFR-2008-title49-vol2/pdf/CFR-2008-title49-vol2-sec172-101.pdf.

United States Department of Transportation (U.S. DOT). 2008b. Classification Criteria. 49 CFR § 173. Available at: http://www.ecfr.gov/cgi-bin/text-idx?c=ecfr&tpl=/ecfrbrowse/Title49/49cfr173_main_02.tpl.

United States Environmental Protection Agency (U.S. EPA). 2015. Safer Choice Standard. Available at: http://www2.epa.gov/saferchoice/safer-choice-standard.

United States Environmental Protection Agency (U.S. EPA). 2017. Estimation Programs Interface (EPI) Suite™ Web, v4.11, Washington, DC, USA. Available at: http://www.epa.gov/opptintr/exposure/pubs/episuitedl.htm.

United States Environmental Protection Agency (U.S. EPA). 2018. Safer Chemical Ingredients List (SCIL). Available at: http://www2.epa.gov/saferchoice/safer-ingredients.

United States Environmental Protection Agency (U.S. EPA). 2019. Endocrine Disruption Screening Program for the 21st Century. EDSP21 Dashboard. Available at: https://comptox.epa.gov/dashboard/chemical_lists/EDSPUOC.

## APPENDIX A: Hazard Classification Acronyms
**(in alphabetical order)**

**(AA) Acute Aquatic Toxicity**

**(AT) Acute Mammalian Toxicity**

**(B) Bioaccumulation**

**(C) Carcinogenicity**

**(CA) Chronic Aquatic Toxicity**

**(D) Developmental Toxicity**

**(E) Endocrine Activity**

**(F) Flammability**

**(IrE) Eye Irritation/Corrosivity**

**(IrS) Skin Irritation/Corrosivity**

**(M) Mutagenicity and Genotoxicity**

**(N) Neurotoxicity**

**(P) Persistence**

**(R) Reproductive Toxicity**

**(Rx) Reactivity**

**(SnS) Sensitization- Skin**

**(SnR) Sensitization- Respiratory**

**(ST) Systemic/Organ Toxicity**

# APPENDIX B: Results of Automated GreenScreen® Score Calculation for Triethylene Glycol (CAS #112-27-6)

TOXSERVICES
TOXICOLOGY RISK ASSESSMENT CONSULTING

## GreenScreen® Score Inspector

**Table 1: Hazard Table**

| | | | Group I Human | | | | | Group II and II* Human | | | | | | | | Ecotox | | Fate | | Physical | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | Carcinogenicity | Mutagenicity/Genotoxicity | Reproductive Toxicity | Developmental Toxicity | Endocrine Activity | Acute Toxicity | Systemic Toxicity | | Neurotoxicity | | Skin Sensitization* | Respiratory Sensitization* | Skin Irritation | Eye Irritation | Acute Aquatic Toxicity | Chronic Aquatic Toxicity | Persistence | Bioaccumulation | Reactivity | Flammability |
| **Table 2: Chemical Details** | | | | | | | | | S | R * | S | R * | * | * | | | | | | | | |
| Inorganic Chemical? | Chemical Name | CAS# | C | M | R | D | E | AT | STs | STr | Ns | Nr | SNS* | SNR* | IrS | IrE | AA | CA | P | B | Rx | F |
| No | Triethylene glycol | 112-27-6 | L | *L* | L | M | *M* | L | M | L | M | DG | *L* | *L* | L | L | L | L | L | vL | *L* | L |

**Table 3: Hazard Summary Table**

| Benchmark | a | b | c | d | e | f | g |
|---|---|---|---|---|---|---|---|
| 1 | No | No | No | No | No | | |
| 2 | No | No | No | No | Yes | No | No |
| 3 | STOP | | | | | | |
| 4 | STOP | | | | | | |

**Table 4**

| Chemical Name | Preliminary GreenScreen® Benchmark Score |
|---|---|
| Triethylene glycol | 2 |

**Note:** Chemical has not undergone a data gap assessment. Not a Final GreenScreen™ Score

**Table 6**

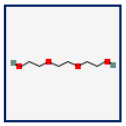
| Chemical Name | Final GreenScreen® Benchmark Score |
|---|---|
| Triethylene glycol | 2 |

After Data gap Assessment
**Note:** No Data gap Assessment Done if Preliminary GS Benchmark Score is 1.

**Table 5: Data Gap Assessment Table**

| Datagap Criteria | a | b | c | d | e | f | g | h | i | j | bm4 | End Result |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 1 | | | | | | | | | | | | |
| 2 | Yes | Yes | Yes | Yes | Yes | | | | | | | 2 |
| 3 | | | | | | | | | | | | |
| 4 | | | | | | | | | | | | |

## APPENDIX C: Pharos Output for Triethylene Glycol (CAS #112-27-6)



112-27-6

TRIETHYLENE GLYCOL

ALSO CALLED [121202-29-7] Triethylene glycol (primary CASRN is 112-27-6), [676-18-6] Triethylene glycol (primary...

View all synonyms (5)

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Pharos Hazards View

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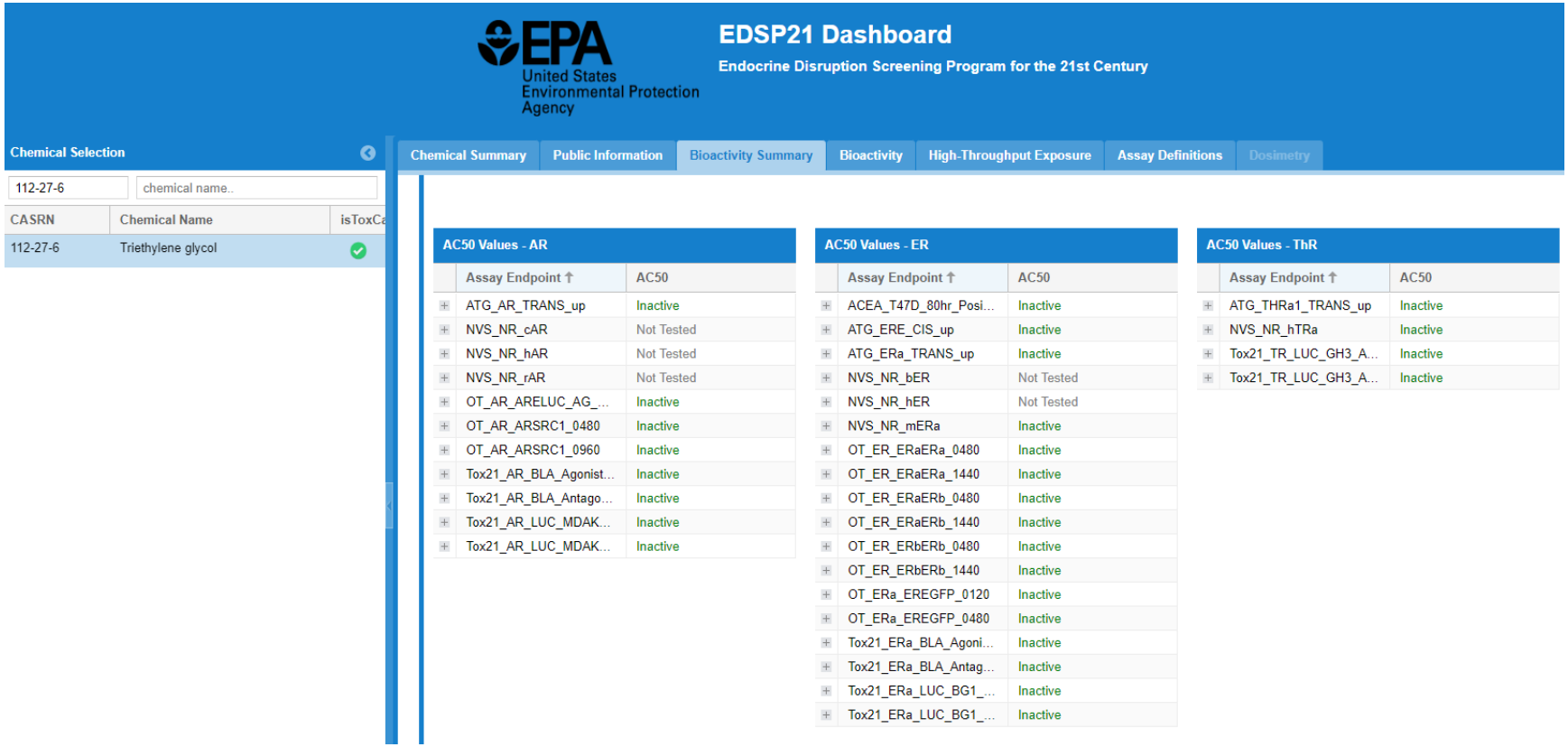
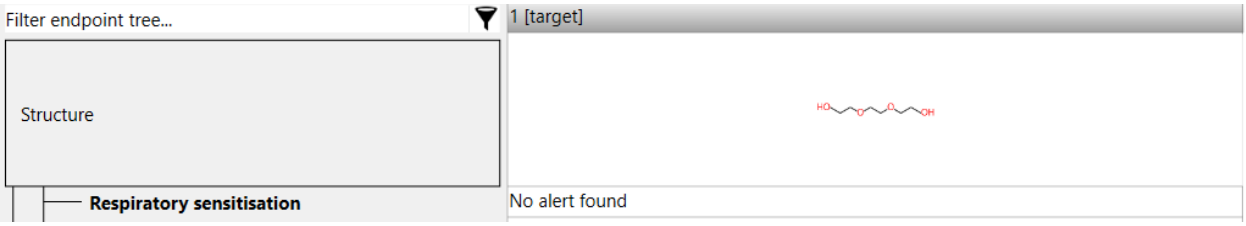
| ENDPOINT | HAZARD LEVEL | HAZARD LIST | HAZARD DESCRIPTION | OTHER LISTS |
|---|---|---|---|---|
| Developmental | High | MAK | Pregnancy Risk Group B | |
| Endocrine | Medium | TEDX - Potential Endocrine Disruptors | Potential Endocrine Disruptor | |
| Mammalian | Potential Concern | US EPA - OPP - Registered Pesticides | FIFRA Registered Pesticide | +1 |
| | Potential Concern | EU - Manufacturer REACH hazard submissions | H332 - Harmful if inhaled (unverified) | |
| Eye irritation | Potential Concern | EU - Manufacturer REACH hazard submissions | H319 - Causes serious eye irritation (unverified) | |
| Skin irritation | Potential Concern | EU - Manufacturer REACH hazard submissions | H315 - Causes skin irritation (unverified) | |
| Organ toxicant | Potential Concern | EU - Manufacturer REACH hazard submissions | H335 - May cause respiratory irritation (unverified) | |
| Multiple | Potential Concern | EC - CEPA DSL | Inherently Toxic to Humans (iTH) | +1 |
| | Potential Concern | German FEA - Substances Hazardous to Waters | Class 1 - Low Hazard to Waters | |

## APPENDIX D: EDSP21 Dashboard for Triethylene Glycol (CAS #112-27-6)



## APPENDIX E: OECD Toolbox Respiratory Sensitization Results for Triethylene Glycol (CAS #112-27-6)



## APPENDIX F: EPISuite Modeling Results for Triethylene Glycol (CAS #112-27-6)

CAS Number: 112-27-6
SMILES : O(CCOCCO)CCO
CHEM : Ethanol, 2,2 -[1,2-ethanediylbis(oxy)]bis-
MOL FOR: C6 H14 O4
MOL WT : 150.18
---------- EPI SUMMARY (v4.11) ----------
Physical Property Inputs:
Log Kow (octanol-water): ------
Boiling Point (deg C) : ------
Melting Point (deg C) : ------
Vapor Pressure (mm Hg) : ------
Water Solubility (mg/L): ------
Henry LC (atm-m3/mole) : ------

Log Octanol-Water Partition Coef (SRC):
Log Kow (KOWWIN v1.69 estimate) = -1.75
Log Kow (Exper. database match) = -1.75
Exper. Ref: MEYLAN,WM & HOWARD,PH (1995)

Boiling Pt, Melting Pt, Vapor Pressure Estimations (MPBPVP v1.43):
Boiling Pt (deg C): 270.06 (Adapted Stein & Brown method)
Melting Pt (deg C): 47.17 (Mean or Weighted MP)
VP(mm Hg,25 deg C): 0.000199 (Modified Grain method)
VP (Pa, 25 deg C) : 0.0265 (Modified Grain method)
MP (exp database): -7 deg C
BP (exp database): 285 deg C
VP (exp database): 1.32E-03 mm Hg (1.76E-001 Pa) at 25 deg C

Water Solubility Estimate from Log Kow (WSKOW v1.42):
Water Solubility at 25 deg C (mg/L): 1e+006
log Kow used: -1.75 (expkow database)
no-melting pt equation used
Water Sol (Exper. database match) = 1e+006 mg/L ( deg C)
Exper. Ref: RIDDICK,JA ET AL. (1986)

Water Sol Estimate from Fragments:
Wat Sol (v1.01 est) = 1e+006 mg/L

ECOSAR Class Program (ECOSAR v1.11):
Class(es) found:
Neutral Organics

Henrys Law Constant (25 deg C) [HENRYWIN v3.20]:
Bond Method : 3.16E-011 atm-m3/mole (3.20E-006 Pa-m3/mole)
Group Method: 2.56E-016 atm-m3/mole (2.60E-011 Pa-m3/mole)
For Henry LC Comparison Purposes:
User-Entered Henry LC: not entered

Henrys LC [via VP/WSol estimate using User-Entered or Estimated values]:
HLC: 3.932E-011 atm-m3/mole (3.984E-006 Pa-m3/mole)
VP: 0.000199 mm Hg (source: MPBPVP)
WS: 1E+006 mg/L (source: WSKOWWIN)

Log Octanol-Air Partition Coefficient (25 deg C) [KOAWIN v1.10]:
Log Kow used: -1.75 (exp database)
Log Kaw used: -8.889 (HenryWin est)
Log Koa (KOAWIN v1.10 estimate): 7.139
Log Koa (experimental database): None

Probability of Rapid Biodegradation (BIOWIN v4.10):
Biowin1 (Linear Model) : 0.2988
Biowin2 (Non-Linear Model) : 0.0230
Expert Survey Biodegradation Results:
Biowin3 (Ultimate Survey Model): 3.1699 (weeks)
Biowin4 (Primary Survey Model) : 3.8705 (days)
MITI Biodegradation Probability:
Biowin5 (MITI Linear Model) : 0.7214
Biowin6 (MITI Non-Linear Model): 0.8170
Anaerobic Biodegradation Probability:
Biowin7 (Anaerobic Linear Model): 0.7430
Ready Biodegradability Prediction: YES

Hydrocarbon Biodegradation (BioHCwin v1.01):
Structure incompatible with current estimation method!

Sorption to aerosols (25 Dec C)[AEROWIN v1.00]:
Vapor pressure (liquid/subcooled): 0.176 Pa (0.00132 mm Hg)
Log Koa (Koawin est ): 7.139
Kp (particle/gas partition coef. (m3/ug)):
Mackay model : 1.7E-005
Octanol/air (Koa) model: 3.38E-006
Fraction sorbed to airborne particulates (phi):
Junge-Pankow model : 0.000615
Mackay model : 0.00136
Octanol/air (Koa) model: 0.00027

Atmospheric Oxidation (25 deg C) [AopWin v1.92]:
Hydroxyl Radicals Reaction:
OVERALL OH Rate Constant = 36.3529 E-12 cm3/molecule-sec
Half-Life = 0.294 Days (12-hr day; 1.5E6 OH/cm3)
Half-Life = 3.531 Hrs
Ozone Reaction:
No Ozone Reaction Estimation
Fraction sorbed to airborne particulates (phi):
0.000989 (Junge-Pankow, Mackay avg)
0.00027 (Koa method)
Note: the sorbed fraction may be resistant to atmospheric oxidation

Soil Adsorption Coefficient (KOCWIN v2.00):
Koc : 10 L/kg (MCI method)
Log Koc: 1.000 (MCI method)
Koc : 0.08975 L/kg (Kow method)
Log Koc: -1.047 (Kow method)

Aqueous Base/Acid-Catalyzed Hydrolysis (25 deg C) [HYDROWIN v2.00]:
Rate constants can NOT be estimated for this structure!

Bioaccumulation Estimates (BCFBAF v3.01):
Log BCF from regression-based method = 0.500 (BCF = 3.162 L/kg wet-wt)
Log Biotransformation Half-life (HL) = -2.4845 days (HL = 0.003277 days)
Log BCF Arnot-Gobas method (upper trophic) = -0.049 (BCF = 0.8933)
Log BAF Arnot-Gobas method (upper trophic) = -0.049 (BAF = 0.8933)
log Kow used: -1.75 (expkow database)

Volatilization from Water:
Henry LC: 3.16E-011 atm-m3/mole (estimated by Bond SAR Method)
Half-Life from Model River: 2.271E+007 hours (9.461E+005 days)
Half-Life from Model Lake : 2.477E+008 hours (1.032E+007 days)

Removal In Wastewater Treatment:
Total removal: 1.85 percent
Total biodegradation: 0.09 percent
Total sludge adsorption: 1.75 percent
Total to Air: 0.00 percent
(using 10000 hr Bio P,A,S)

Level III Fugacity Model: (MCI Method)

| | Mass Amount (percent) | Half-Life (hr) | Emissions (kg/hr) |
|---|---|---|---|
| Air | 0.000675 | 7.06 | 1000 |
| Water | 30.6 | 360 | 1000 |
| Soil | 69.4 | 720 | 1000 |
| Sediment | 0.0688 | 3.24e+003 | 0 |

Persistence Time: 640 hr

Level III Fugacity Model: (MCI Method with Water percents)

| | Mass Amount (percent) | Half-Life (hr) | Emissions (kg/hr) |
|---|---|---|---|
| Air | 0.000675 | 7.06 | 1000 |
| Water | 30.6 | 360 | 1000 |
| water | (30.6) | | |
| biota | (2.72e-008) | | |
| suspended sediment | (0.000458) | | |
| Soil | 69.4 | 720 | 1000 |
| Sediment | 0.0688 | 3.24e+003 | 0 |

Persistence Time: 640 hr

Level III Fugacity Model: (EQC Default)

| | Mass Amount (percent) | Half-Life (hr) | Emissions (kg/hr) |
|---|---|---|---|
| Air | 0.000746 | 7.06 | 1000 |
| Water | 39 | 360 | 1000 |
| water | (39) | | |
| biota | (3.47e-008) | | |
| suspended sediment | (4.27e-007) | | |
| Soil | 60.9 | 720 | 1000 |
| Sediment | 0.0713 | 3.24e+003 | 0 |

Persistence Time: 579 hr

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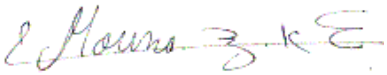
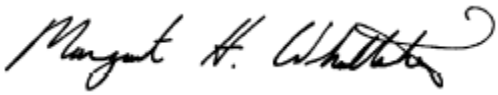
**Triethylene Glycol GreenScreen® Evaluation Prepared By:**



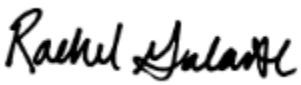
Mouna Zachary, PhD
Toxicologist
ToxServices LLC

**Triethylene Glycol GreenScreen® Evaluation QC'd By:**



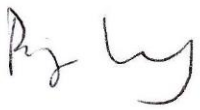
Margaret H. Whittaker, Ph.D., M.P.H., CBiol., F.S.B., E.R.T., D.A.B.T.
Managing Director and Chief Toxicologist
ToxServices LLC

**Triethylene Glycol GreenScreen® Evaluation Updated by:**



Rachel Galante, M.P.H.
Associate Toxicologist
ToxServices LLC

**Triethylene Glycol GreenScreen® Update QC'd by:**



Bingxuan Wang, Ph.D., D.A.B.T.
Senior Toxicologist
ToxServices LLC

**Triethylene Glycol GreenScreen® Evaluation Updated by:**

Grace Kuan, M.P.H.
Associate Toxicologist
ToxServices LLC

**Triethylene Glycol GreenScreen® Update QC'd by:**

Bingxuan Wang, Ph.D., D.A.B.T.
Senior Toxicologist
ToxServices LLC