Eastman Chemical Company
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EASTMAN

Dr. Scott A. Masten
Director, Office of Nomination and Selection
National Toxicology Program
National Institute of Environmental Health Sciences

P.O. Box 12233, MD EC-31
Research Triangle Park, NC

Dear Dr. Masten:

Eastman Chemical Company wishes to comment on the recent nomination of ethylene glycol 2-ethylhexyl ether (EGEhE)(CAS No.1559-35-9) for toxicological characterization. Eastman Chemical Company is the sole manufacturer of EGEhE in commercial quantities.

The National Toxicology Program has specifically nominated EGEhE for reproductive and developmental toxicity studies. The nomination by the National Institute for Environmental Health Sciences is based on the presumed limited amount of toxicological data for this substance and potential human exposure stemming from high production volume and increasing use. The Chemical Information Profile prepared by the National Toxicology Program also summarizes toxicity information for several studies the NTP has identified.

Eastman Chemical Company recommends that testing of EGEhE by the National Toxicology Program be deferred. This recommendation is based on a current major planned review of EGEhE by government and NGO authorities in the global OECD/SIDS program, and the appropriateness of allowing this review to be completed before beginning a separate toxicological characterization of this substance.

In the following comments, Eastman will further describe the OECD/SIDS review process for EGEhE, and address some of the points made in the NTP Chemical Information Profile.

A. Current OECD/SIDS Review of EGEhE

EGEhE has been sponsored by the U.S. Environmental Protection Agency (EPA) for review as a high production volume chemical in the OECD/SIDS Program. As an integral part of this sponsorship, Eastman Chemical Company has very recently compiled a dossier listing all currently available data for this substance, including production volume, uses, chemical physical properties, environmental fate and environmental and mammalian toxicology. The OECD/SIDS program has over the past eighteen years

reviewed hundreds of high production volume chemicals to determine the adequacy of toxicology screening data. This process includes the following steps:

- Preparation of a dossier of robust summaries of all pertinent studies and data for required endpoints. These endpoints include production volume, use and exposure information, chemical/physical properties, environmental fate, environmental toxicity and mammalian toxicity. In the absence of data on required endpoints, testing must be conducted before the dossier can be considered complete. The mammalian toxicity endpoints must include acute, genetic, subchronic and reproductive/developmental toxicity. Summaries for all other available pertinent studies must also be provided, including eye and dermal irritation, sensitization, chronic toxicity and carcinogenicity. Strict criteria have been developed for robustly summarizing studies with respect to detail and assessing study reliability.
- Preparation of a SIDS Initial Assessment Report (SIAR) and SIDS Initial Assessment Profile (SIAP).
- Review of the dossier, SIAR and SIAP by the U.S. EPA, which recommends appropriate revisions.
- Peer review by government toxicologists and competent authorities and NGOs of all OECD countries. This peer review results in further revisions and improvements to the dossier, SIAR and SIAP. This peer review includes a formal assessment in a SIDS Initial Assessment Meeting (SIAM) and possible recommendations for further work.
- Publication of the final documents under the UNEP program. This step assures that the dossiers and reports on each substance are readily available to the public.

NOTE: We are attaching the following draft SIDS dossier (Attachment 1), SIAR (Attachment 2) and SIAP (Attachment 3) for your review. As mentioned these documents will be submitted to the Environmental Protection Agency within the next month.

B. Upcoming REACh registration of EGEhE in Europe

EGEhE is also being sold into the European Community. As an export to Europe, EGEhE will be subject to registration requirements under the Registration, Evaluation, Authorisation, and Restriction of Chemicals (REACh) program, starting in December 2008. This program will also require extensive information regarding exposure, use, and toxicology, including developmental and reproductive toxicity. The REACh dossier for EGEhE will be reviewed by European competent authorities for adequacy of data before registration is deemed complete. The competent authorities can require additional testing to clarify hazards for particular endpoints, and can restrict exposures and uses of the chemical if necessary to avoid risk to health or environment.

C. Initial Comments on the Assessment of Toxicity Data in the Chemical Information Profile

Availibility of Data on EGEhE

The Chemical Information Profile prepared by the NTP indicates limited available toxicological data for EGEhE. We believe there to be much more data available pertinent to this substance, covering all major toxicological and environmental endpoints. Robust summaries of these studies have been compiled and will be peer reviewed in the OECD/SIDS program. Where needed data are not available on EGEhE itself, data and toxicological studies available for the closely related homolog (ethylene glycol hexyl ether)(EGHE CAS No. 112-25-4) have been used as a surrogate for EGEhE. Both EGEhE and EGHE are glycol ethers with identical functionality. The only difference in the two substances is in the ether alkyl side chain. In the case of EGHE, the side chain is n-hexyl, whereas with EGEhE the side chain is 2-ethylhexyl, which possesses two additional carbons.

Reproductive and Developmental Toxicity

The results of specific toxicological studies for reproductive and developmental effects for EGEhE are lacking. Minimal effects on reproductive organs and tissues were observed at doses that caused toxicity and mortality. Specifically, increased relative testes weights were reported in a subacute (43-day) study in rats at the highest dose, a dose also associated with significant toxicity, manifested as reduced body weights and food consumption and mortality. In subchronic (6-week) studies in rats, degeneration of spermatozoa (2/10 animals) was observed at the highest dose level, a dose also associated with significant toxicity and 100% mortality. In the case of both studies described above, significant toxicity was also observed at lower doses that did not result in effects on reproductive organs. It is most likely that the minimal effects observed on testis weights and spermatozoa were secondary to the overall general toxicity of EGEhE.

In 13-week vapor inhalation studies with the structurally similar ethylene glycol hexyl ether, exposure concentrations up to 71 ppm caused no effects on the reproductive organs of experimental animals. Also, inhalation developmental toxicity studies conducted in rats and rabbits with ethylene glycol hexyl ether at exposure concentrations up to 79.2 ppm, a concentration causing significant maternal toxicity in both rats and rabbits, caused no embryotoxic or teratogenic effects.

D. Conclusion

Eastman again recommends that the National Toxicology Program and National Environmental Health Sciences defer testing of EGEhE for the time being. This recommendation is based on the fact that EGEhE will be reviewed under the auspices of two regulatory intitiatives, the OECD/SIDS program and REACh. Eastman will be submitting the SIDS dossier and SIDS Initial Assessment Report to the EPA within the next month with the expectation that EGEhE will be peer reviewed in a SIDS Initial Assessment Meeting

(SIAM) in 2009. The pre-registration phase of the REACh process described in Section B above will be completed by the end of 2008, and the review process will continue based on overall production volumes. Based on the outcome of those reviews and the final recommendations, the NTP can then determine what further studies it should recommend.

Yours truly,

Signature redacted

Gary Shrum
Director, Product Safety and Health
Eastman Chemical Company

Attachments:

OECD/SIDS dossier for EGEhE
OECD/SIDS SIAR and SIAP for EGEhE

ATTACHMENT 1

OECD/SIDS Dossier

***OECD/SIDS Dossier sent as separate electronic attachment (Filename: OECD – SIDS Dossier.htm). File is in HTML format and is relatively large.**

ATTACHMENT 2

OECD/SIDS SIAP

SIDS INITIAL ASSESSMENT PROFILE

CAS No.	1559-35-9
Chemical Name	Ethanol, 2- (2-ethylhexyl)oxy– (or ethylene glycol 2-ethylhexyl ether)
Structural Formula	$CH_3CH_2CH_2CH_2CH(CH_2CH_3)CH_2OCH_2CH_2OH$

SUMMARY CONCLUSIONS OF THE SIAR

Analogue Rationale

Toxicokinetics

No toxicokinetic data are available for EGEhE. EGHE is a substrate for alcohol dehydrogenase isozyme ADH-3, which catalyzed the conversion of their terminal alcohols to aldehydes (which are transient metabolites). Further, rapid conversion of the aldehydes by aldehyde dehydrogenase produces alkoxyacetic acids, which are the predominant urinary metabolites of mono substituted glycol ethers.

Human Health

Oral LD_{50} values in rats and mice for EGEhE and a commercial mixture containing 84% EGEhE range from 3070- 7832 mg/kg. Clinical signs of toxicity in rats and mice administered EGEhE or the commercial mixture containing 84% EGEhE orally were inactivity, labored breathing, rapid respiration, anorexia, slight to moderate weakness, tremors, prostration, hematuria and death. The dermal LD_{50} value in rabbits is 2584 mg/kg. Inhalation of a saturated vapour of EGEhE for 8 hours does not cause lethality to rats. Oral and dermal LD_{50} values for EGHE (739 and 721 mg/kg) are lower than EGEhE, demonstrating that EGHE is more acutely toxic. EGEhE and the related material EGHE are moderately irritating to rabbit and guinea pig skin and highly irritating to rabbit eyes.

Histopathological changes in the liver, spleen and kidney of rats were reported after six weeks of exposure to oral doses of EGEhE $\geq$ 957 mg/kg/day. Effects on red blood cells were not observed in rats orally exposed with up to 2360 mg/kg/day of a commercial material containing 84% EGEhE for six weeks. Increased liver and kidney weights (but no histopathological changes or red blood cell changes) were seen in rats exposed for 14 weeks with 71 ppm (425 mg/m^3) EGHE.

EGEhE and the related material EGHE show a low potential for reproductive and developmental toxicity. Results of the repeated dose toxicity studies indicate that oral exposure of up to 2360 mg/kg EGEhE over 6 weeks is associated with increased relative testicular weight, but no changes in histopathology. In a 13-week inhalation study, there was no significant effect of exposure to up to 71 ppm EGHE on any reproductive organ examined. Results of a developmental toxicity study conducted with EGHE indicate that this material is not teratogenic. In rats and rabbits exposed to EGHE by inhalation, no effects on the fetus were noted (even at concentrations that produced maternal toxicity). The NOAELs for developmental toxicity in both species are greater than 79.2 ppm (or 474 mg/m^3).

EGEhE has not been tested for genetic toxicity. Results of all available genetic toxicity tests conducted with the related material EGHE [an Ames test in *S. typhimurium* strains TA98, TA100, TA1535, TA1537 and TA1538 (with and without metabolic activation), a mammalian cell mutagenesis test in Chinese Hamster Ovary (CHO) cells, and *in vitro* cytogenicity and sister chromatid exchange assays (SCE) in CHO cells with and without metabolic activation] were negative, suggesting that EGEhE is not genotoxic.

Environment

Adequate aquatic toxicity tests EGEhE (and supplemental studies with EGHE) indicate that these materials are moderately toxic to fish, Daphnia and algae (LC/EC_{50} values are approximately 10-300 mg/l). Based on physical and chemical properties, if released into the aquatic environment, these materials would tend to remain in the water column. Releases to land would tend to move to surface water or groundwater and not accumulate in soil, and releases into the air would be photoxidized or washed out via rainfall. Based on low log Pow and estimated bioconcentration factor values, EGEhE does not have a significant potential to bioconcentrate within aquatic organisms or be adsorbed onto sediments. Although EGEhE is not likely to undergo appreciable hydrolysis, it (and the related material EGHE) is biodegraded in the aqueous environment. Therefore, it is not expected to be a significant hazard to aquatic species. Based on the tendency of EGEhE to move to water, it is not expected to be a hazard to terrestrial species.

Exposure

Human exposure can occur during manufacture, formulation into product, application of products such as water based coatings using EGEhE as coalescent, and from exposures to environmental concentrations caused by environmental release. Exposures during manufacture and formulation are limited by the use of continuous, closed equipment and engineering controls. The primary opportunity for exposure is during its use application. Exposure during use can be via either inhalation or dermal absorption. Environmental exposure would most likely occur via inhalation of possible low concentrations of vapour in the air around the single manufacturing plant or in the vicinity of applications of coatings containing EGEhE. Exposure may also occur to possible very low concentrations of EGEhE in the general environment, however EGEhE has low potential to persist in the environment. No public data have been found on environmental concentrations or presence of EGEhE.

RECOMMENDATION

EGEhE is currently of low priority for further work.

RATIONALE FOR THE RECOMMENDATION AND NATURE OF FURTHER WORK RECOMMENDED

EGEhE is currently of low priority for further work. EGEhE possesses properties indicating hazards to human health (skin and eye irritation). Although these hazards do not warrant further work (as they are related to non-adverse, reversible, transient effects), they should nevertheless be noted by chemical safety professionals and users.

ATTACHMENT 3

OECD/SIDS SIAR

SIDS Initial Assessment Report

For

SIAM X

[City, Country, Date]

1.	**Chemical Name:**	Ethanol, 2- (2-ethylhexyl)oxy – (also called ethylene glycol 2-ethylhexyl ether)
2.	**CAS Number:**	1559-35-9
3.	**Sponsor Country:**	USA U.S. Environmental Protection Agency Mr. Oscar Hernandez, Director Risk Assessment Division (7403M) 1200 Pennsylvania Ave., NW Washington, DC 20460 Phone: 202-564-7641 e-mail: Hernandez.oscar@epa.gov
4.	**Shared Partnership with:**	No partner, single sponsor
5.	**Roles/Responsibilities of the Partners:**	Not Applicable
•	Name of industry sponsor /consortium	American Chemistry Council Glycol Ethers Panel
•	Process used	The industry sponsor conducted a comprehensive literature search, including all generally accepted databases, reference books, unpublished studies and data in company files. This information formed the basis for compilation of the IUCLID dossier
6.	**Sponsorship History**	
•	How was the chemical or category brought into the SIDS Program?	
7.	**Review Process Prior to the SIAM:**	The SIDS Dossier and draft SIAR for Ethanol, 2- (2-ethylhexyl)oxy– (or ethylene glycol 2-ethylhexyl ether) will be reviewed by the U.S. EPA. These documents will be revised to reflect changes recommended by the EPA.
8.	**Quality check process:**	On completing the literature search and data collection, important and significant studies were identified for all endpoints. These studies were reviewed and summarized following current guidelines for robust summaries. Reliability ratings were assigned following the Klimisch rating system. Studies assigned ratings of 1 or 2 were considered to be acceptable. The key studies were identified based on

completeness, protocol and GLP use and other quality factors. These were flagged as critical studies. The summaries were compiled using the IUCLID program.

9. Date of Submission:

10. Date of last Update:

11. Comments:

Ethylene glycol hexyl ether (EGHE)(CAS No. 112-25-4) is used as a closely related analog chemical to provide data for some required endpoints for ethylene glycol 2-ethylhexyl ether. Both of these substances have closely similar molecular structures and functionality, and demonstrate similar physico-chemical, environmental fate and toxicological properties when comparisons are available.

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SIDS Initial Assessment Report

1 IDENTITY

1.1 Identification of the Substance

CAS Number: 1559-35-9
IUPAC Name: Ethanol, 2- (2-ethylhexyl)oxy -

Molecular Formula: $C_{10}H_{22}O_2$
Structural Formula: $CH_3CH_2CH_2CH_2CH(CH_2CH_3)CH_2OCH_2CH_2OH$
Molecular Weight: 174.29
Synonyms: Eastman(TM) EEH Solvent, EGEhE, Ethylene glycol 2-ethylhexyl ether

Ethylene glycol hexyl ether (EGHE) (CAS No. 112-25-4) is used as a closely related analog chemical to provide data for some required endpoints for Ethanol, 2- (2-ethylhexyl)oxy- (also called ethylene glycol 2-ethylhexyl ether). Both of these glycol ethers have closely similar molecular structures and functionality, and demonstrate similar physico-chemical, environmental fate and toxicological properties when comparisons are available (See Sect.1.4 for justification of use of analog data).

EGHE was previously reviewed at SIAM 19, and is included in the category only to fill data gaps and provide supporting data. Therefore, a separate dossier on EGHE is not included. Data for EGHE have been added to the dossier and SIAR for ethylene glycol ethylhexyl ether (EGEhE). The reader should refer to the existing SIDS dossier (at http://www.inchem.org/documents/sids/sids/_Monoethylene GlycolEthers.pdf for additional information on EGHE.

1.2 Purity/Impurities/Additives

The commercial product contains no additives. The composition of this product is as follows:

Ethylene glycol mono-2-ethylhexyl ether, CAS No. 1559-35-9	= 84%
Diethylene glycol mono-2-ethylhexyl ether, CAS No. 1559-36-0	= 15%
Triethylene glycol mono-2-ethylhexyl ether, CAS No. 1559-37-1	< 1%

1.3 Physico-Chemical properties

The data in Table 2 (below) indicate that EGEhE and EGHE have similar physical properties, as might be expected for two glycol ethers, with closely similar molecular structure and identical functionality. The somewhat higher boiling point, lower vapour pressure and water solubility and more positive partition coefficient of EGEhE are consistent with its having a somewhat larger alkyl group (C8 versus C6) compared to EGHE.

1.4 Justification of Use of Analog Data

Ethylene glycol hexyl ether (EGHE) (CAS No. 112-25-4) is used as a closely related analog chemical to provide data for some required endpoints for ethylene glycol 2-ethylhexyl ether. Both of these glycol ethers have closely similar molecular structures and functionality, and demonstrate

Table 1 Summary of physico-chemical properties

Chemical	Physical State at 25°C	Melting Point (°C)	Boiling Point[a] (°C)	Relative Density @20 °C	Vapour Pressure[b] (hPa)	Water Solubil.[b] (mg/l)	Log Pow	Henry's Law Constant[a,c] (atm-m^3/mole)
EGEhE 1559-35-9	liquid	No data	229[d]	0.88[e]	0.028[f]	1510[d]	2.46[c,d]	3.04E-007[c]
EGHE[g] 112-25-4	liquid	-50.1[h]	208.1[h]	0.89[h]	0.067[h]	9900[h]	1.55[c]	1.73E-007[c]

[a]at 1013 hPa; [b]at 20-25 ° C; [c]Estimated using EPIWIN [The EPI (Estimation Programs Interface) Suite™ developed by the Environmental Protection Agency Office of Pollution Prevention Toxics and Syracuse Research Corporation (SRC)(2000)]; [d]SRC (2008);[e]Eastman Chemical Company (2006); [f] Steele and Nguyen, 1993; [g] Data for EGHE were obtained from the OECD submission for the monoethylene glycol ethers category, SIAR for SIAM 19, available at http://www.inchem.org/documents/sids/sids/ MonoethyleneGlycolEthers.pdf, pages 204-216; [h]Verschueren (1996).

similar physico-chemical, environmental fate and toxicological properties when comparisons are available.

Ethylene glycol hexyl ether has the following molecular structure, molecular formula and molecular weight:

$CH_3CH_2CH_2CH_2CH_2CH_2OCH_2CH_2OH$

Molecular formula: $C_8\ H_{18}\ O_2$
Molecular weight: 146.23

Both ethylene glycol hexyl ether and ethylene glycol 2-ethylhexyl ether have the following generic formula:

$ROCH_2CH_2OH$, where R = hexyl or 2-ethylhexyl.

The sole difference in molecular structure is that ethylene glycol 2-ethylhexyl has two more carbons in the alkyl group, with an ethyl group being substituted at the 2- position of the hexyl group for a hydrogen atom. Both substances possess moderately long alkyl chains attached to one ethylene glycol unit.

2 GENERAL INFORMATION ON EXPOSURE

2.1 Production Volumes and Use Pattern

EGEhE is manufactured by a single company; therefore manufacture volume is considered confidential. The current manufacturing volume range is 100-1,000 tonnes.

No use pattern information has been found in public databases. For example, there is no entry in the U.S. NIH Household Products Database online at http://householdproducts.nlm.nih.gov./cgi-bin/household/search. There also is no entry in TOXLINE Hazardous Substances Data Bank on line at http://toxnet.nlm.nih.gov/. Likewise, no entries are found in the Substances in Preparations in Nordic Countries (SPIN) database online at http://195.215.251.229/DotNetNuke/default.aspx.

According to the technical data sheet of the manufacturer, Eastman Chemical Company, EGEhE is used in performance specialty coatings applications, such as a coalescent in water borne architectural and industrial maintenance coatings, or as a retarder solvent in factory-applied original equipment manufacturer (OEM) coatings. It is typically present in such coatings at 1-5% concentration. Its use should therefore be regarded as dispersive.

2.2 Environmental Exposure and Fate

Table 2 Environmental fate parameters for EGEhE and EGHE

Chemical	Photodeg. OH radical rate constant[a] (cm^3/molecule-sec) $T_{1/2}$	Bioconcen-tration Factor (log BCF)[a]	Predicted Environmental Distribution (Level III fugacity model)[a]			
			Air (%)	Water (%)	Soil (%)	Sed. (%)
EGEhE 1559-35-9	3.39 E-11 0.32 days	1.192	1.74	43.3	54.7	0.17
EGHE[b] **112-25-4**	2.63 E-11 0.406 days	0.732	8.83	86.4	4.54	0.195

[a] estimated using EPIWIN AOP (v1.91) for photodegradation, BCF (v2.17) for bioconcentration factor, and Level III fugacity model; [b] Data for EGHE were obtained from the OECD submission for the monoethylene glycol ethers category, SIAR for SIAM 19, available at http://www.inchem.org/documents/sids/sids/ MonoethyleneGlycolEthers.pdf, pages 215-220.

A comparison of the environmental distribution data in Table 2 for EGEhE and EGHE, suggests that EGEhE is less likely to partition to the atmosphere and hydrosphere, and more likely to partition to soil, compared to EGHE. This comparison is consistent with the heavier molecular weight, larger carbon chain (C8 versus C6) and lower water solubility of EGEhE, compared to EGHE.

2.2.1 Sources of Environmental Exposure

No data were located on environmental presence or concentrations of EGEhE.

2.2.2 Photodegradation

EGEhE undergoes hydroxyl radical induced photodegradation on entry to the atmosphere. The OH radical rate constant is estimated by EPIWIN to be 3.39 E-11 cm^3/molecule-sec. The atmospheric half-life is estimated to be 0.32 days (12-hr day at 1.5E6 OH/cm^3 concentration).

2.2.3 Stability in Water

No hydrolysis study data are available for EGEhE. However, it is known practically to be stable in water. Its major use is in water-based coatings as a coalescent. Ether groups are generally stable to water under neutral conditions and ambient temperatures. The ether function is hydrolyzed by heating in the presence of halogen acids, particularly hydrogen iodide (Fieser and Fieser, 1960)

2.2.4 Transport between Environmental Compartments

The data for Level III fugacity modeling for EGEhE are shown in Table 2 above. In addition, the model estimates the following half-lives for EGEhE: Air: 7.57 hours, Water: 208.1 hours, Soil: 208.1 hours and Sediment: 832.3 hours. EGEhE released to the atmosphere will undergo hydroxyl radical induced photodegradation, but can also reenter the hydrosphere via precipitation- induced

wash down. EGEhE released to water will tend to remain in the hydrosphere or migrate primarily to soil. Based on a Henry's Law constant of 3.04E-007 atm-m^3/mole, volatilization from water will be low. The bioconcentration factor (BCF) has been estimated by EPIWIN BCF to be 15.57 (log BCF 1.192). The Koc (soil/sediment partition constant) has been estimated by EPIWIN PCKOC to be 10. Therefore, EGEhE exhibits some degree of soil mobility.

2.2.5 Biodegradation

As shown in Table 3 below, EGEhE was biodegradable in a non-standard test performed with a strain of *Pseudomonas* capable of utilizing ethylene glycol monobutyl ether. As shown by Waggy (1987), 100% biodegradation of EGHE was observed in a modified BOD study conducted according to APHA standards.

Table 3 Biodegradation rates for EGEhE and EGHE

Category Member	Biodegradation Rate
EGEhE 1559-35-9	47.7% biodegradation by glycol ether-utilizing bacteria [a]
EGHE 112-25-4	100% after 20 days (APHA)[b]

Data for EGHE were obtained from the OECD submission for the monoethylene glycol ethers category, SIAR for SIAM 19, available at http://www.inchem.org/documents/sids/sids/ MonoethyleneGlycolEthers.pdf and are included in the EGEhE dossier.
[a] Kawai, 1995; [b] Waggy, 1987

2.2.6 Bioaccumulation

No data were located. EPIWIN-generated log BCF values for EGEhE and EGHE are 1.192 and 0.732, respectively, indicating little potential for these chemicals to bioaccumulate.

2.3 Human Exposure

Human exposure can occur during manufacture, formulation into product, application of products such as water based coatings using EGEhE as coalescent, and from exposures to environmental concentrations caused by environmental release. Exposure during use can be via either inhalation or dermal absorption. Environmental exposure would most likely occur via inhalation of possible low concentrations of vapour in the air around the single manufacturing plant or in the vicinity of applications of coatings containing EGEhE. Exposure may also occur to possible very low concentrations of EGEhE in the general environment, however EGEhE has low potential to persist in the environment (See Sections 2.2.4 and 2.2.5). No public data have been found on environmental concentrations or presence of EGEhE.

2.3.1 Occupational Exposure

Occupational exposure can occur during manufacture when sampling the process equipment for quality control purposes. Although production takes place several times per year, manufacture is carried out in closed continuous equipment equipped with conservation vents. Manufacture is controlled and monitored in control rooms removed from the equipment. Therefore opportunities for significant exposure during normal operating conditions are limited. Similarly, equipment used for formulating EGEhE into water-based coatings is also closed and operating steps that could result in exposure (e.g., quality control sampling) are limited. Exposure (dermal or inhalation) is most

likely to occur during application of architectural and industrial maintenance coatings containing EGEhE as a coalescent.

2.3.2 Consumer Exposure

Consumer exposure is most likely to occur during application of architectural and industrial maintenance coatings containing EGEhE as a coalescent. As in commercial use, the routes of exposure are most likely to be dermal or inhalation.

3 HUMAN HEALTH HAZARDS

3.1 Effects on Human Health

3.1.1 Toxicokinetics, Metabolism and Distribution

No toxicokinetic data are available for EGEhE. However, data are available for the related material EGHE.

The toxicokinetics of ethylene glycol monohexyl ether (EGHE) were investigated in Fisher 344 rats and New Zealand white rabbits (Ballantyne et al., 2003). Given i.v. to 4 male rats (2.5 – 25 mg/kg bw), [^{14}C]EGHE demonstrated first order kinetics. Carbon-14 was eliminated mainly in urine (68-74%) as metabolites, with no free EGHE. The plasma free EGHE concentration declined rapidly after dosing and was not detectable by 8 hours. Similar results were obtained for [^{14}C] EGHE given i.v. to 4 male rabbits at 1-10 mg/kg bw, except that the metabolism of EGHE was more rapid, with no free EGHE being detected in plasma 1 hour after dosing.

After cutaneous dosing of four male and four female rats with 25 mg/kg bw, there was rapid percutaneous absorption, with > 95% of the radiolabel being recovered. Percutaneous bioavailability was > 75%. Carbon-14 was excreted in urine (21-33%) to a lesser extent than by the i.v. route, and $^{14}CO_2$ and volatiles accounted for 15-18%. Carbon-14 recovery was low from tissues and organs (0.39-0.46%), with no preferential accumulation. Extensive metabolism was indicated by the rapid decline in plasma free EGHE, with none being detected at 48 hours. Free EGHE was not present in urine. Urinary radioactivity was associated with up to seven unidentified metabolites. After cutaneous dosing of four male and four female rabbits (10 mg/kg bw), approximately 75% of the dose was recovered, with most ^{14}C in urine (58-60%). Urine radioactivity was associated with up to 9 unidentified metabolites, but no free EGHE.

Mono-substituted glycol ethers (i.e. EGHE) are substrates for alcohol dehydrogenase (ADH), which catalyzes the conversion of their terminal alcohols to aldehydes (Asamoe et al, 1998; Ghanayem et al., 1987a). Using liver homogenate from Wistar rats, Aasmoe and coworkers (1998) demonstrated that a single isozyme of alcohol dehydrogenase (ADH-3) was responsible for oxidizing EGHE. The respective V_{max} and K_m values for EGHE were 1.66 nmol NADH/min/mg protein and 0.15 mM, respectively.

Further conversion of the aldehydes by aldehyde dehydrogenase produces alkoxyacetic acids, which are the predominant urinary metabolites of mono substituted glycol ethers (Boatman *et al*., 1998; Ghanayem et al., 1987b). The conversion of the terminal alcohols to the alkoxyacetic acids occurs rapidly. Sulfate and glucuronide conjugation of the parent glycol ethers may occur and glycine (rodents) and glutamine (humans) conjugates of the alkoxyacetic acid metabolites may also be produced (Boatman *et al*., 1998; Ghanayem *et al*., 1987b; Rettenmeier *et al*., 1993), and their formation contributes to detoxification (Ghanayem *et al*., 1987a).

3.1.2 Acute Toxicity

The acute toxicity of EGEhE is summarized Table 4. Data are available for oral, inhalation and dermal exposure. Data for EGHE are included for comparative purposes.

Table 4 Acute mammalian toxicity for category members

Category member	Acute Oral LD_{50} (mg/kg bw)	Acute Rat Inhalation LC_{50} (ppm)	Acute Rabbit Dermal LD_{50} (mg/kg bw)
EGEhE 1559-35-9	3080[a], 5149[b] (fed rat) 7832[b] (fasted rat) 3898[b] (fed mouse) 7308[b] (fasted mouse)	LC_0 > 8 hr exposure to saturated vapour [a]	2.12 ml/kg [a] 2.9 ml/kg (2584 mg/kg)[b, e]
EGHE 112-25-4	739[c] (rat)	LC_0 > 6 hr exposure to saturated vapour [c] > 85[d] (4 hr LC_{Lo})	721[c]

Data for EGHE were obtained from the OECD submission for the monoethylene glycol ethers category, SIAR for SIAM 19 (available at http://www.inchem.org/documents/sids/sids/ MonoethyleneGlycolEthers.pdf) and are included in the attached EGEhE dossier.
LD_{50} = lethal dose in 50% of animals; LC_{50} = lethal conc. in 50% of animals; LC_{Lo} = lowest lethal conc.
[a]Smyth et al., 1954; [b]Krasavage and Terhaar, 1981; [c] Ballantyne and Myers, 1989; [d]Klonne et al. 1987;
[e] Burdock et al., 1980

Studies in Animals

Inhalation

Available data in rats indicate that all six rats exposed to a saturated vapour of EGEhE for 8 hour survived the 14 day observation period (Smyth et al., 1954). Similar results were obtained with EGHE (Klonne et al., 1987; Ballantyne and Myers, 1989).

Dermal

The dermal LD_{50} value in rabbits from the key study for EGEhE is 2.9 ml/kg (2584 mg/kg) (Burdock et al., 1980; Krasavage and Terhaar, 1981). Signs of toxicity in animals administered EGEhE included skin irritation, depression, prostration, ataxia, anorexia and/or nasal discharge.

Oral

The oral LD_{50} values for EGEhE in male rats range from 3080 – 7832 mg/kg (Smyth et al., 1954; Krasavage and Terhaar, 1981), with lower values obtained in fed than fasted animals. The oral LD_{50} value for EGEhE in fed male mice (3898 mg/kg) is also lower than fasted male mice (7308 mg/kg) (Krasavage and Terhaar, 1981). Conversely, the oral LD_{50} values of a commercial mixture containing ethylene glycol mono-2-ethylhexyl ether (84%), diethylene glycol mono-2-ethylhexyl ether (15%), and triethylene glycol mono-2-ethylhexyl ether (1%) are lower in fasted (3070 mg/kg) than fed mice (5778 mg/kg) (Krasavage, 1981). Clinical signs of toxicity in rats and mice administered EGEhE or the commercial mixture containing 84% EGEhE were inactivity, labored breathing, rapid respiration, anorexia, slight to moderate weakness, tremors, prostration and death. Hematuria was noted in fed rats administered “intermediate levels” of EGEhE.

Conclusion

EGEhE has a very low potential for acute toxicity. Oral LD_{50} values in rats for EGEhE range from 3080 – 7832 mg/kg, and the dermal LD_{50} value from the key study is 2584 mg/kg. Hematuria was noted in fed rats administered "intermediate" oral doses EGEhE. Inhalation of a saturated vapour of EGEhE for 8 hours does not cause lethality to rats. Oral and dermal LD_{50} values for EGHE are lower than EGEhE, demonstrating that EGHE is more acutely toxic.

3.1.3 Irritation

Skin Irritation

Studies in Animals

Adequate studies performed with EGEhE indicate that this material is moderately irritating to rabbit and guinea pig skin (Smyth et al., 1954; Burdock et al., 1980; Krasavage and Terhaar, 1981). Necrosis was noted in rats exposed to 4.13 ml/kg. Similar results were obtained with EGHE (Ballantyne and Myers, 1987).

Eye Irritation

Studies in Animals

A study performed by Smyth et al. (1954) with EGEhE of unknown purity indicated that the material was highly irritating to rabbit eyes. Additional, poorly documented studies performed with EGEhE of > 99.5% and 84% purity (Krasavage, 1981; Krasavage and Terhaar, 1981) support this result. Similar results have been obtained with EGHE (Ballantyne and Myers, 1987).

3.1.4 Sensitisation

The only sensitization studies that have been performed with EGEhE are not considered adequate for purposes of this program. EGHE has not been tested for sensitization.

3.1.5 Repeated Dose Toxicity

Oral repeated dose toxicity testing has performed with EGEhE, and inhalation and dermal with EGHE (Table 5).

Oral

A repeated dose oral (gavage) study with EGEhE was conducted in male SD rats (Krasavage and Vlaovic, 1982). Animals were given 957, 1914 and 3828 mg/kg/day, 5 days/week for 6 weeks. Nine out of 10 animals given 3828 mg/kg/day (nearly four times the current recommended limit dose) died within 4 days of treatment, and the remaining animal died by day 33. Blood was noted in the urinary bladders of 3/10 animals that died. Histopathologic changes observed in the decedents included degenerated spermatozoa in the epididymides (2/10), diffuse hemorrhage in the thymus (5/10), hyperkeratosis of the stomach (3/10), acanthosis of the stomach (2/10), aniosokaryosis of the liver (3/10), splenic congestion (3/10), and vacuolation of bone marrow (4/10) The significance of these changes is uncertain, as they were observed in animals found dead, and could therefore be artefacts of post-mortem changes. It should be noted that none of these changes were observed at the next highest dose (1914 mg/kg/day), which is approximately twice the level of the limit dose (1000 mg/kg/day) of current guidelines. Changes observed at 1914 mg/kg/day included reduced body weights and food consumption, decreased plasma hemoglobin and glucose, decreased absolute brain weights, and increased absolute and relative liver weights, and relative heart, testes and kidney

weights. However, these latter relative effects occurred in the face of decreased body weights. The decrease in hemoglobin is very slight and not of biological or toxicological significance and is

Table 5 Repeated dose toxicity for category members

Category Member	Species/ Exposure	Dose in ppm (mg/m^3) or mg/kg	Gross Changes	Histopathological Changes	Clin. Chem/Hemat. Changes
EGEhE (Krasavage and Vlaovic, 1982)	SD male rat, 5 d.wk, 6 wk (oral)	957 [b] (10/10) 1914 3828	↑ kidney, liver, heart, testes wt ↓ bw, food, ↑ kidney, liver, heart, testes wt. All animals died within 4 days of treatment	stomach, liver stomach, liver, spleen thymus, stomach, liver, spleen, bone marrow, epididymis	↓hb, ↑ WBC ↓ hb, glucose not determined
(Krasavage, 1981)*	male rat, 31 doses over 43 days (oral)	590 1180 2360	↑ liver wt depression, brown staining of fur, ↓ heart wt, food, ↑ liver wt changes observed at 1180 mg/kg, plus prostration, ↓ bw, food, ↑relative ~~relative~~ kidney, adrenal, testes, brain wt	kidney kidney, liver stomach, liver, kidney	none none ↓SGOT, glucose, ↑ ALP
EGHE 112-25-4 (Klonne et al., 1987)	F344 rat, 6 hr/d, 5 d/wk, 13 wk (inhalation)	20 (120) 41[a] (245) 71 (425)	urogenital wetness, ↑ kidney wt urogenital wetness , ↓ bw, ↑ kidney, liver wt ↓ bw, ↑ kidney, liver wt	none none none	none none ↓ AST, ALT, SDH, ↑ ALP
(Ballantyne et al., 2003)	NZW rabbit, 6 hr/day for 11 days (dermal)	44 222 [a] 444 (2/10)	None none ↓ bw, food	none none none	none none ↓ rbc, hb, hc, MCH

Data for EGHE were obtained from the OECD submission for the monoethylene glycol ethers category, SIAR for SIAM 19 (available at http://www.inchem.org/documents/sids/sids/ MonoethyleneGlycolEthers.pdf) and are included in the EGEhE dossier.

[a] No observable adverse effect level (systemic effects). Dose is in mg/kg bw/day (for oral experiments) and ppm (for inhalation experiments) unless listed otherwise. The number of deaths is listed (if significant); [b] No observable effect level (NOAEL) less than lowest dose; *material contained EGEhE (84%), diethylene glycol mono-2-ethylhexyl ether (15%), triethylene glycol mono-2-ethylhexyl ether (1%)

NZW = New Zealand White, WBC = white blood cells, hb = hemoglobin, hc = hematocrit, MCH = mean corpuscular hemoglobin, AST = aspartate aminotransferase, ALT = alanine aminotransferase, SDH = sorbitol dehydrogenase, ALP = alkaline phosphatase, SGOT = glutamic oxaloacetic transaminase

probably related to a slight but non-significant decrease in hematocrit and total red blood cells. Since the mean cell volume and mean cell hemoglobin and mean cell hemoglobin concentration are normal, the animals do not appear to be anemic.

Enlarged livers and kidneys were noted in 3/10 and 1/10 animals, respectively. Histopathologic changes observed included hyperkeratosis of the stomach, acanthosis of the stomach, aniosokaryosis of the liver, hepatocytomegally of the liver, lack of cytoplasmic basophilia in the liver and splenic congestion. Similar changes in hemoglobin, organ weights and histopathology (with the exception of splenic congestion and decreased brain weight) were noted in animals administered 957 mg/kg/day.

In a repeated dose study in male rats treated orally (31 days of dosing over 43 days) with a commercial mixture containing ethylene glycol mono-2-ethylhexyl ether (84%), diethylene glycol mono-2-ethylhexyl ether (15%), and triethylene glycol mono-2-ethylhexyl ether (1%) (Krasavage,

1981), effects on the liver (increased absolute and relative weight) were also noted at the lowest dose administered (590 mg/kg). Additional changes observed at 1180 mg/kg bw were reduced feed intake, depression, a brownish colored deposit around the prepuce and on the hair of the abdomen, decreased absolute heart weight, enlarged livers and hyaline degeneration of proximate convoluted tubules of kidneys. Animals administered the highest dose (2360 mg/kg) also exhibited reduced weight gain, prostration, ~~and~~ increased relative ~~relative~~ kidney, adrenal, testes, and brain weights, decreased serum glutamic oxaloacetic transaminase and glucose, increased serum alkaline phosphatase, erosion of mucosa of the stomach, stomach ulcer, and minor to moderate hyperkeratois and acanthosis of the stomach.

Inhalation

In a repeated exposure (6h/day, 5d/wk for 13 weeks) inhalation study performed at exposure levels of 20, 41, or 71 ppm (120, 245, or 425 mg/m^3) EGHE in F344 rats (Klonne et al., 1987), the reported NOAEL by the investigators was 41 ppm (245 mg/m^3). Decreases in body weight and increases in male kidney and female liver weights occurring at this concentration were considered to be adaptive (and not adverse) since there were no correlative changes in histopathology or serum chemistry. The changes in liver enzymes in animals exposed to 71 ppm (425 mg/m^3) are difficult to interpret since levels of 3 out of 4 enzymes were decreased and only 1 out of 4 was increased. Whereas the effects on the kidney were not dose-dependent, liver weights increased in a dose-dependent manner and were not reversed after 4 weeks of recovery in animals exposed to 71 ppm. No effects on red blood cells or histologic changes in the liver or kidney were noted at concentrations up to and including the highest concentration tested (71 ppm or 425 mg/m^3).

Dermal

EGHE (0, 44, 222 or 444 mg/kg bw) was applied topically to New Zealand White rabbits for a period of 6 hours/day for five consecutive days, and for an additional four consecutive days after a 2 day rest period (for a total of 9 days over an 11 day period) (Ballantyne et al., 2003). The NOAEL for systemic toxicity was 222 mg/kg/day. Two females in the high dose group died (one on day 9 and the other on day 12). The cause of death could not be determined. In 9/12 males and 10/12 females exposed to 44 mg/kg bw, mild erythema was noted from Days 3 to 4 to study termination. Mild edema was found in 8 low dose females after Day 5. Moderate erythema and edema were noted by Days 4-5 in 10-11 mid and high dose males and females. A few high dose animals (numbers were not stated) had ecchymoses or ulceration.

Body weights of high dose females were significantly less than control ($p < 0.01$) at Days 8 and 12. Body weight gains and food consumption of high dose males and females were significantly lower than control (at least $p < 0.05$) from Days 1-8. Red blood cell counts ($p < 0.01$), hemoglobin ($p < 0.01$), hematocrit ($p < 0.01$) and mean corpuscular hemoglobin ($p < 0.05$) were lower than control in high dose males. Red blood cell counts and hemoglobin were lower than control in high dose females ($p < 0.01$).

There were no effects of treatment on absolute or relative organ weights. No gross pathology was seen at necropsy. Histological changes were limited to the skin (acanthosis, hyperkeratosis and dermatitis).

Conclusion

Decreased plasma hemoglobin (of questionable significance) and histopathological changes in the liver, spleen and kidney of rats were reported after six weeks of exposure to oral doses of EGEhE ≥

957 mg/kg. Decreases in several red blood cell indices were noted in rabbits dermally exposed to 444 mg/kg/day EGHE for 11 days. Effects on red blood cells were not observed in rats orally exposed with up to 2360 mg/kg/day of a commercial material containing 84% EGEhE for six weeks. Increased liver and kidney weights (but no histopathological changes or red blood cell changes) were seen in rats exposed for 14 weeks with 71 ppm (425 mg/m^3) EGHE.

3.1.6 Mutagenicity

Genetic toxicity tests have not been performed with EGEhE; however, data exist for the related material EGHE (Table 6).

Table 6 Genotoxicity of EGEhE and EGHE

Category Member	Ames Test (w/wout activation)	Mammalian Cell Mutagenesis[a]	Cytogenicity[a]	SCE assay[a]	Mouse Micronucleus
EGEhE 1559-35-9	No data	No data	No data	No data	No data
EGHE 112-25-4	Negative (1)	Negative (2)	Negative (3)	Negative (2)	No data

Data for EGHE were obtained from the OECD submission for the monoethylene glycol ethers category, SIAR for SIAM 19 (available at http://www.inchem.org/documents/sids/sids/ MonoethyleneGlycolEthers.pdf) and are included in the EGEhE dossier. [a]Chinese Hamster Ovary Cell.
(1) Marples, 1985; (2) Slesinski et al., 1988. Given a reliability rating of 4 because the primary reference was not available for review; (3) Guzzie, 1985

Studies in Animals

In vitro Studies

An Ames test (in the absence and presence of metabolic activation) has been performed with up to 15,000 micrograms/plate EGHE, in S. typhimurium strains TA98, TA100, TA1535, TA1537 and TA1538 (Marples, 1985). Results of this study were negative. EGHE also tested negative in a mammalian cell mutagenesis test in Chinese Hamster Ovary (CHO) cells that was not available for review (Slesinski et al., 1988).

In vitro cytogenicity and sister chromatid exchange assays (SCE) with EGHE (up to 400 micrograms/ml) in CHO cells with and without metabolic activation were negative (Guzzie, 1985; Slesinski et al., 1988).

Conclusion

All genetic toxicity studies performed with EGHE were negative, suggesting that EGEhE is not genotoxic.

3.1.7 Carcinogenicity

No carcinogenicity or long term repeated dose studies have been performed with EGEhE or EGHE.

3.1.8 Toxicity for Reproduction

Reproductive organ toxicity has been examined in animals given EGEhE or EGHE repeatedly for 6 or 13 weeks (respectively), and a developmental toxicity test has been performed with EGHE (Tables 7 and 8).

Results of the repeated dose toxicity studies indicate that although oral exposure of up to 2360 mg/kg EGEhE over 6 weeks is associated with increased relative testicular weight, changes in absolute testicular weight and histology of the testes are not observed. In a 13-week inhalation study, there was no significant effect of exposure to up to 71 ppm EGHE on any reproductive organ examined (Table 7).

Table 7 Reproductive toxicity of EGEhE and EGHE

Category Member	Animal	Treatment	Effects
EGEhE 1559-35-9 (Krasavage and Vlaovic, 1982)	SD male rat, exam of reproductive organs	Oral, 957, 1914, 3828 mg/kg, 5 d/wk, 6 wk	Increased relative testes weights at 957 and 1914 mg/kg. No histological changes in testes at 957 and 1914 mg/kg.
(Krasavage, 1981)*	Male rat, exam of reproductive organs	Oral, 590, 1180, 2360 mg/kg, 31 doses over 43 days	Increased relative testes weights at 2360 mg/kg. No histological changes in testes.
EGHE 112-25-4 (Klonne et al., 1987)	F344 rat, exam of reproductive organs	Inhalation, 20, 41, 71 ppm, (120, 245, 425 mg/m^3) 6 hr/d, 5 d/wk for 13 wk	There was no effect of treatment on weight of testes or histology of reproductive organs (types not stated).

Data for EGHE were obtained from the OECD submission for the monoethylene glycol ethers category, SIAR for SIAM 19 (available at http://www.inchem.org/documents/sids/sids/ MonoethyleneGlycolEthers.pdf) and are included in the EGEhE dossier.
NOAEL = No observable adverse effect level; SD = Sprague Dawley; F344 = Fischer 344
*material contained EGEhE (84%), diethylene glycol mono-2-ethylhexyl ether (15%), triethylene glycol mono-2-ethylhexyl ether (1%)

Developmental Toxicity

Results of the developmental toxicity study conducted with EGHE (Table 8) indicate that this material is not teratogenic. In rats and rabbits exposed to EGHE by inhalation, no effects on the fetus were noted (even at concentrations that produced maternal toxicity). The NOAELs for developmental toxicity in both species are greater than 79.2 ppm (or 474 mg/m^3).

Conclusion

Repeated dose toxicity studies indicate no effect of oral administration of up to 2360 mg/kg EGEhE for 6 weeks, or inhalation of up to 71 ppm (425 mg/m^3) EGHE for 13 weeks on the histology of reproductive organs of rats. The NOAELs for developmental toxicity of EGHE in the rat and rabbit are ≥ 79.2 ppm (474 mg/m^3). In rats and rabbits exposed to EGHE by inhalation, no developmental effects were noted (even at concentrations that produced maternal toxicity). Based on the structural similarities between EGEhE and EGHE, developmental toxicity data for EGHE is expected to be predictive of data for EGEhE.

3.2 Initial Assessment for Human Health

EGEhE and the related material EGHE are of low-moderate acute toxicity. Signs of acute toxicity in rats, rabbits and mice are consistent with non-specific CNS depression (which is typical of many solvents). EGEhE and EGHE are irritating to skin and eyes. The results of some repeated dose

Table 8 Developmental Toxicity of category members

Category Member	Animal	Treatment ppm (mg/m^3)	Effects
EGEhE 1559-35-9	No data		
EGHE 112-25-4 (Tyl et al. 1989)	F344 rat	Inhalation, 20.8, 41.4, 79.2 ppm (124, 248, 474 mg/m^3) 6 hr/d, day 6-15 of gestation	NOAEL (maternal) = 20.8 ppm NOAEL (fetal) ≥ 79.2 ppm 41.4 ppm (maternal) - ↓ bw gain 79.2 ppm (maternal) - ↓ bw, bw gain, food consumption, ↑ water consumption, lacrimation
(Tyl et al., 1989)	NZ White Rabbit	Inhalation, 20.8, 41.1, 79.2 ppm (124, 248, 474 mg/m^3) 6 hr/day, day 6-18 of gestation	NOAEL (maternal) = 41.1 ppm NOAEL (fetal) ≥ 79.2 ppm 79.2 ppm (maternal) - ↓ bw gain

Data for EGHE were obtained from the OECD submission for the monoethylene glycol ethers category, SIAR for SIAM 19 (available at http://www.inchem.org/documents/sids/sids/ MonoethyleneGlycolEthers.pdf) and are included in the EGEhE dossier.
NOAEL = No observable adverse effect level; F344 = Fischer 344; NZ = New Zealand

toxicity tests with the EGEhE show effects on the liver, spleen and kidney at very high doses. Effects on red blood cells noted in rabbits exposed dermally to EGHE are not noted in rats exposed orally to higher concentrations of EGEhE (with the exception of a decrease in hemoglobin). This is of questionable significance, since other indices of red blood cell toxicity were not affected significantly. The related material EGHE is not mutagenic, clastogenic, or selectively toxic to the reproductive system or developing fetus.

4 HAZARDS TO THE ENVIRONMENT

4.1 Aquatic Effects

As shown in Table 9, reliable aquatic toxicity data in fish, invertebrates and algae exist for the related material EGHE. Studies also have been conducted with EGEhE; however, since reliability was not assignable, they are only considered to be supportive of the use of EGHE data for EGEhE.

Table 9 Aquatic toxicity of EGEhE and EGHE

Chemical	Fish Acute Toxicity 96-h LC_{50} (mg/l)	Invertebrate Acute Toxicity 48-h LC/EC_{50} (mg/l)	Algae Acute Toxicity 72-h EC_{50} (mg/l)
EGEhE 1559-35-9	10 – 100 (RR4) (1)	10 – 100 (RR4) (1)	no data available
EGHE 112-25-4	> 94 and <215 (2) 140[b] (3)	145 (4) 305 (3)	98[c] (5) 198[d] (5)

Data for EGHE were obtained from the OECD submission for the monoethylene glycol ethers category, SIAR for SIAM 19 (available at http://www.inchem.org/documents/sids/sids/ Monoethylene GlycolEthers.pdf) and are included in the EGEhE dossier. RR 4 = Reliability Rating of 4

[a]estimated using EPIWIN; [b]Given a reliability score of 4; [c]biomass; [d]growth rate
(1) Boatman, 1982 (2) BASF AG, 1994; (3) Waggy, 1987; (4) BASF AG, 1990; (5) BASF AG, 1989c

Toxicity to Fish, Invertebrates and Algae

For EGHE, the 96-hour LC_{50} for *Brachydanio rerio* (zebra fish) was 94-215 mg/l, and the no effect concentration (NOEC) was 41 mg/l. The 48-hour EC_{50} and EC_{100} values for EGHE in *Daphnia magna* were 145 mg/l and 320 mg/l (respectively), and the 72-hour EC_{50} values for biomass and growth rate of algae (*Scenedesmus subspicatus*) were 98 and 198 mg/l, respectively. Available studies for EGEhE in *Pimephales promelas* and several different aquatic invertebrates indicate LC0 and LC100 values of 10 mg/l and 100 mg/l, respectively.

Toxicity to Microorganisms

Toxicity data for bacteria are available for the related material EGHE. Results of studies conducted with 16 or 17 hour incubation times show IC_{50} values ranging from 770 – 2100 mg/l (BASF AG, 1989c; Waggy, 1987).

4.2 Terrestrial Effects

Available terrestrial toxicity data for EGEhE is not considered to be reliable for purposes of this assessment. No terrestrial toxicity data are available for EGHE.

4.3 Other Environmental Effects

No other data were located.

4.4 Initial Assessment for the Environment

In conclusion, aquatic toxicity tests with EGEhE and EGHE indicate that these materials are moderately toxic to fish, Daphnia and algae (LC/EC_{50} values are approximately 10-300 mg/l). Based on physical and chemical properties, if released into the aquatic environment, these materials would tend to remain in the water column. Releases to land would tend to move to surface water or groundwater and not accumulate in soil, and releases into the air would be photoxidized or washed out via rainfall. Based on low log Pow and estimated bioconcentration factor values, EGEhE does not have a significant potential to bioconcentrate within aquatic organisms or be adsorbed onto sediments. Although EGEhE is not likely undergo appreciable hydrolysis, it (and the related material EGHE) is biodegraded in the aqueous environment. Therefore, it is not expected to be a significant hazard to aquatic species. Based on the tendency of EGEhE to move to water, it is not expected to be a hazard to terrestrial species.

5 RECOMMENDATIONS

Human Health: EGEhE possess properties indicating a hazard for human health (reversible eye and skin irritation, reversible CNS depression). These hazards do not warrant further work. However, they should nevertheless be noted by chemical safety professionals and users. Countries may desire to investigate any exposure scenarios that were not presented by the Sponsor country.

Environment: EGEhE is of low priority for further work because of its low hazard profile. Any hazards do not warrant further work as they are related to acute toxicity which may become evident

only at very high exposure levels and the substance is biodegradable. However, they should be noted by chemical safety professionals and users.

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