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SRC TR 81-637

SECOND DRAFT

Information Profiles on Potential Occupational Hazards: Epoxy Compounds (non-cyclic)

Center for Chemical Hazard Assessment
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15. Supplementary Notes

16. Abstract (Limit: 200 words) Information profiles were presented for the following epoxy compounds deemed to be significant due to their commercial importance: n-alkyl-glycidyl-ethers, allyl-glycidyl-ether (106923), 1,2-butylene-oxide (106887), butyl-glycidyl-ether (2426086), 1,2-epoxy-hexadecane (7320378), ethylene-oxide (75218), 2-ethylhexyl-glycidyl-ether (2461156), glycidol (556525), glycidyl-acrylate (106901), glycidyl-methacrylate (106912), and propylene-oxide (75569). The median lethal toxicity value in rats for these compounds ranged from 232mg/kg for glycidyl-acrylate to 17100mg/kg for n-alkyl-glycidyl. Most of the compounds were mild to moderate skin and eye irritants. Ethylene-oxide was shown to be teratogenic in mice when given by intravenous injection, but not in rats exposed by inhalation. Several of these compounds demonstrated positive mutagenic responses. Butylene-oxide and glycidyl-methacrylate caused no increase in tumors after administered dermally and by gavage, respectively. Ethylene-oxide demonstrated a weak positive response in a carcinogenicity bioassay. A positive carcinogenic result was obtained for 1,2-epoxyhexadecane in a skin painting study. Propylene-oxide produced tumors at the site of injection following subcutaneous administration.

17. Document Analysis a. Descriptors

b. Identifiers/Open-Ended Terms NIOSH-Publication, NIOSH-Contract, Contract-210-79-0030, Resins, Surfactants, Adhesives, Fumigants, Mutagens, Carcinogens, Toxic-effects, Occupational-exposure, Teratogens

c. COSATI Field/Group

18. Availability Statement	19. Security Class (This Report)	21. No. of Pages 122
	22. Security Class (This Page)	22. Price

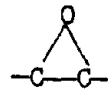
(See ANSI-Z39.18) *See Instructions on Reverse* **OPTIONAL FORM 272(4-77)** (Formerly NTIS-35) Department of Commerce

EPOXY COMPOUNDS (non-cyclic)

I. SCOPE OF DOCUMENT AND SUMMARY OF MAJOR FINDINGS

A. CLASS IDENTIFICATION

An epoxy compound is an organic compound that contains a reactive epoxy group resulting from the union of an oxygen atom and two carbon atoms joined as indicated:



The epoxy compounds addressed in this report are limited to the non-cyclic (aliphatic) hydrocarbons with one or more epoxy groups. Although these epoxy compounds may contain heteroatoms such as chlorine or bromine, those discussed in the profiles are composed solely of carbon, hydrogen, and oxygen.

The Appendix contains a list of all the epoxy compounds identified and considered under the preceding definition.

B. CHEMICALS TO BE ADDRESSED

Individual profiles have been prepared for the following epoxy compounds:

n-Alkyl glycidyl ethers (C_{12} to C_{18})
Allyl glycidyl ether
1,2-Butylene oxide
Butyl glycidyl ether
1,2-Epoxy hexadecane
9,10-Epoxyoctadecanoic acid, 2-ethylhexyl ester
Ethylene oxide
2-Ethylhexyl glycidyl ether
Glycidol
Glycidyl acrylate
Glycidyl methacrylate
Propylene oxide

Individual profiles have been prepared for all compounds identified as having commercial importance. Here, commercial importance is defined as annual produc-

tion in the thousands of pounds and a specific industrial or commercial use as opposed to a reagent or laboratory use.

C. SUMMARY OF BIOLOGICAL EFFECTS

No information was found on the toxicity of 2-ethylhexyl glycidyl ether or 9,10-epoxyoctadecanoic acid, 2-ethylhexyl ester. The acute toxicity of the remaining epoxide compounds discussed here varied widely from an oral LD50 value in rats of 232 mg/kg for glycidyl acrylate to 17100 mg/kg for n-alkyl glycidyl. Ethylene oxide, the highest production volume compound of the group, had an oral LD50 value of 330 mg/kg in rats. Most of the epoxide compounds were moderate to severe skin and eye irritants. The health effects of three of the compounds, butyl glycidyl ether, allyl glycidyl ether, and n-alkyl glycidyl, are detailed in a NIOSH criteria document.

Ethylene oxide, the only compound of the group studied for teratogenicity, was shown to be teratogenic in mice given the compound by intravenous injection, but not in an inhalation study in rats. Ethylene oxide exposure to male rats resulted in adverse effects on the outcome of pregnancy following mating to non-exposed females. Also, glycidol has been shown to cause reversible sterility in male rats.

Of the epoxides tested for mutagenicity, ethylene oxide, propylene oxide, butylene oxide, glycidol, n-alkyl glycidyl, allyl glycidyl ether, and butyl glycidyl ether, demonstrated positive responses. Glycidyl acrylate and glycidyl methacrylate were negative; however, the test systems employed were non-conventional, and positive results may be obtained if the compound is tested in other systems. Also, a number of epoxide compounds have been tested for carcinogenicity in animal bioassays. Butylene oxide and glycidyl methacrylate produced no increase in tumors after administration by skin painting and gavage, respectively. Ethylene oxide gave a weak positive response after exposure by

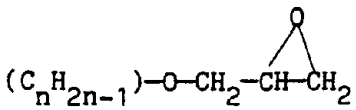
subcutaneous injection and inhalation, while 1,2-epoxyhexadecane was positive in a skin painting study. Propylene oxide produced tumors only at the site of injection following subcutaneous administration. The other epoxy compounds have not been tested for carcinogenicity.

II. INFORMATION PROFILES

A. n-ALKYL GLYCIDYL ETHERS

1. Chemical Name: n-Alkyl Glycidyl Ether

2. Chemical Structure:



$(C_nH_{2n-1})-O-CH_2-CH-CH_2$ n=12 to 18

3. Synonyms: Epoxide No. 8 (for C_{12}, C_{13}, C_{14})
Epoxide No. 45 (for C_{16}, C_{17}, C_{18})
Ether, alkyl 2,3-epoxypropyl-
Propane, 1-alkyloxy-2,3-epoxy-

4. Chemical Abstract Service (CAS) Number: ---

5. Registry of Toxic Effects of Chemical Substances (RTECS) Number:

Not listed

6. Chemical and Physical Properties:

Description:	---
Molecular Weight:	variable
Boiling Point:	---
Melting Point:	---
Vapor Pressure:	---
Solubility:	---
Specific Gravity:	---
Stability:	combustible

7. Production

It is estimated that one to two million pounds of alcohol were consumed in the production of mixed n-alkyl glycidyl ethers in 1970 (Deacetis, 1973). Therefore, production of n-alkyl glycidyl ethers in 1970 was on the order of 1.2 to 2.4 million pounds.

8. Use

n-Alkyl glycidyl ethers are recommended for use as reactive diluents for epoxy resins systems, stabilizers for PVC resins, and stabilizers for chlorinated paraffins and other halogenated products (Deacetis, 1973). They are also used in the synthesis of specialty anionic surfactants (Oosterhof, 1975a).

9. Manufacturers and Distributors

The n-alkyl glycidyl ethers are manufactured by the Proctor and Gamble Co. in Ivorydale, Ohio, and Kansas City, Kansas (SRI International, 1980).

10. Manufacturing Processes

The n-alkyl glycidyl ethers are produced by the condensation of C_{12}-C_{18} alcohols with epichlorohydrin (Deacetis, 1973).

11. Impurities or Additives

There is no evidence in the literature searched to indicate the presence of impurities or deliberate additives in commercially produced n-alkyl glycidyl ethers.

12. Occupational Exposure

The National Occupational Hazard Survey does not provide an estimate of the number of workers who are potentially exposed to n-alkyl glycidyl ethers.

13. Control Technology and Work Practices

Specific factors that may contribute to or prevent employee exposure to n-alkyl glycidyl ethers were not found in the literature searched.

14. Biological Effects

A detailed discussion of the limited toxicological information on n-alkyl glycidyl ethers (C_{12}-C_{14} mixture) will not be presented here, since this information is available in the NIOSH (1978) criteria document on occupational

exposure to glycidyl ethers. There was no information found in the literature searched on C_{12}-C_{18} mixtures of n-alkyl glycidyl ethers. The oral LD50 value for the C_{12}-C_{14} mixture in rats is 17.1 g/kg body weight, and it appears that higher molecular weight species are less toxic than lower molecular weight species. The C_{12}-C_{14} mixture is moderately irritating to the skin and a mild irritant to the eyes. The mixture has also been shown to be mutagenic in the Ames Salmonella assay in the presence of a mammalian metabolic activation system.

15. Ongoing Studies

No current toxicological or environmental studies of n-alkyl glycidyl ethers were found.

16. Exposure Standards

No recommended or promulgated occupational exposure standards for n-alkyl glycidyl ethers were found.

17. Sources of Additional Relevant Information

No sources of additional relevant information were identified.

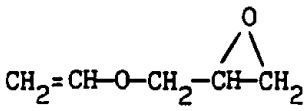
18. Other Pertinent Data

No other information that would aid in the assessment of n-alkyl glycidyl ethers as an occupational hazard was found in the literature searched.

B. ALLYL GLYCIDYL ETHER

1. Chemical Name: Allyl Glycidyl Ether

2. Chemical Structure:



3. Synonyms: AGE
Allyl 2,3-epoxypropyl ether
1-(allyloxy)-2,3-epoxypropane
Ether, allyl 2,3-epoxypropyl
Oxirane,((2-propenyloxy)methyl)-
Propane, 1-(allyloxy)-2,3-epoxy-

4. Chemical Abstract Service (CAS) Number: 106-92-3

5. Registry of Toxic Effects of Chemical Substances (RTECS) Number:

RR0875000

6. Chemical and Physical Properties:

Description:	liquid
Molecular Weight:	114.16
Boiling Point:	75.0°C (50 mm Hg); 154°C (760 mm Hg)
Melting Point:	57°C
Vapor Pressure:	---
Solubility:	---
Specific Gravity:	---
Stability:	combustible

7. Production

An exact production figure for allyl glycidyl ether is not available; however, production in 1973 is estimated to have been less than 5 million pounds (SRC Estimate; Oosterhof, 1975a).

Data available from the U.S. EPA (1980) regarding producers of allyl glycidyl ether and production volumes are presented in Table 1.

Table 1. Producers of Allyl Glycidyl Ether and Production Ranges (U.S. EPA, 1980)

Producer	Type of Production	1977 Production Range
Haven Chemical Co.		
Philadelphia, PA	Manufacturer	confidential
Alcolac Inc.		
Ossining, NY	Manufacturer	confidential
Sedalia, MO	Manufacturer	none
Marubeni America Corp.		
New York, NY	Importer	<1000 lb
Shell Chemical		
Deer Park, TX	Manufacturer	none
Nichimen Co.		
New York, NY	Importer	<1000 lb
Crescent Chemical		
Hauppauge, NY	Importer	none

8. Use

Allyl glycidyl ether is used as a reactive diluent for epoxy resins, in copolymers with ethylene oxide and derivatives, and in copolymers with vinyl monomers (Oosterhof, 1975a; Schildknecht, 1978).

The elastomer Parel 58 is a commercially available copolymer of propylene oxide and allyl glycidyl ether. The commercial product is largely amorphous and contains about 5% allyl glycidyl ether (Vandenberg, 1979).

9. Manufacturers and Distributors

SRI International (1980) lists the following manufacturers:

Alcolac Inc.	Sedalia, MO
Shell Chem. Co.	Deer Park, TX

USITC (1980) lists only Alcolac. U.S. EPA (1980) data is listed in Table 1.

Additional distributors include (1980-81 OPD Chemical Buyers Directory, 1980; Chem Sources - USA, 1980):

Aldrich Chem.	MCB Reagents
ARC Chem.	Miki Sangyo Inc.
Chem. Procurement Lab.	Monomer-Polymer and Dajac Lab.
Columbia Organics	Pfaltz and Bauer
CPS Chem.	Polysciences Inc.
Gallard-Schelsinger	Tridom Chem.
Howard Hall and Co.	Westco Chem.
ICN/K and K	

10. Manufacturing Processes

Allyl glycidyl ether is manufactured from epichlorohydrin (Oosterhof, 1975a) via condensation with allyl alcohol.

11. Impurities or Additives

There is no evidence in the literature searched to indicate the presence of impurities or deliberate additives in commercially produced allyl glycidyl ether.

12. Occupational Exposure

The National Occupational Hazard Survey indicates that 2792 workers are potentially exposed to allyl glycidyl ether.

13. Control Technology and Work Practices

Specific factors that may contribute to or prevent employee exposure to allyl glycidyl ether were not found in the literature searched.

14. Biological Effects

A detailed discussion of the toxicological information on allyl glycidyl ether will not be presented here, since this information is available in the NIOSH (1978) criteria document on occupational exposure to glycidyl ethers. Allyl glycidyl ether has an oral LD50 value of 1.60 g/kg body weight in rats, and 0.39 g/kg body weight in mice. The LC50 value for rats and mice is 3120 and 1260 mg/m^3, respectively. This compound is a moderate skin and severe eye irritant, and causes sensitization following skin application. In the Ames assay for mutagenicity, allyl glycidyl ether is positive in the absence of a mammalian metabolic activation system.

15. Ongoing Studies

The National Toxicology Program (NTP, 1980) has scheduled allyl glycidyl ether for mutagenesis testing in the Ames Salmonella assay. Carcinogenicity testing of allyl glycidyl ether in rats and mice exposed via inhalation has been started by the National Toxicology Program (NTP, 1980); prechronic testing is currently in progress.

16. Exposure Standards

The present U.S. federal ceiling limit for allyl glycidyl ether is 45 mg/m^3 (NIOSH, 1978), which is the same as the value recommended by the American Conference of Governmental Industrial Hygienists (ACGIH, 1980). ACGIH (1981) has also recommended a time-weighted average limit (TWA) of 22 mg/m^3. A

number of foreign maximum allowable concentrations (MACs) for occupational exposure to allyl glycidyl ether are reported in NIOSH (1978). These standards include 100 and 200 mg/m^3 for the average and maximum limits, respectively, in Rumania, 45 mg/m^3 in Yugoslavia and the Federal Republic of Germany, and 22 mg/m^3 in Australia, Belgium, Finland, Netherlands, and Switzerland.

17. Sources of Additional Relevant Information

No sources of additional relevant information were identified.

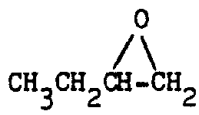
18. Other Pertinent Data

No other information that would aid in the assessment of allyl glycidyl ether as an occupational hazard was found in the literature searched.

C. 1,2-BUTYLENE OXIDE

1. Chemical Name: 1,2-Butylene Oxide

2. Chemical Structure:



3. Synonyms: 1,2-Butane oxide
1-Butene oxide
N-Butene-1,2-oxide
alpha-Butylene oxide
1,2-Epoxybutane
Ethyl ethylene oxide
Ethyl oxirane
Oxirane, ethyl

4. Chemical Abstracts Service (CAS) Number: 106-88-7

5. Registry of Toxic Effects of Chemical Substances (RTECS) Number:

EK3675000

6. Chemical and Physical Properties:

Description:	nearly colorless liquid
Molecular Weight:	72.107
Boiling Point:	63.4°C
Melting Point:	-129.28°C
Vapor Pressure:	176 mm Hg (25°C)
Solubility:	9.5 g/100 g water (25°C); completely soluble in acetone, benzene, carbon tetrachloride, diethyl ether, and methanol
Specific Gravity:	0.826
Stability:	highly flammable; autoignition temperature 822°F; Flash point: -7°F; flammability limits, % by volume in air: 1.9-19

7. Production

Cosslett and Gerry (1976) estimated that approximately 7 million pounds of n-butene were used in synthesis of butylene oxide in 1974; this would correspond to a butylene oxide production of roughly 8 million pounds assuming a 90% yield. Likewise, in 1977, an estimated 6.2 million pounds of butene were

used to make butylene oxide (Hoff et al., 1978), which would correspond to an approximate production of 7 million pounds.

The U.S. EPA (1980) reports that Dow Chemical produced between 1 and 10 million pounds of butylene oxide in 1977 and that BASF Wyandotte imported 0.1 to 1.0 million pounds.

Domestic production of butylene oxide is expected to decline (Cosslett and Gerry, 1976). The main use of butylene oxide is to stabilize chlorinated solvents such as trichloroethylene and 1,1,1-trichloroethane. A projected decline in the use of these chlorinated solvents appears to be part of the reason for the predicted decline in domestic butylene oxide production. Another reason is that Dow's patents on butylene oxide production expired in 1979, allowing the Showa Denko Chemical Company of Japan to build a butylene oxide facility with a 4.4 million pounds/year capacity (Chemical Engineering, 1978; Chemical Age 1978). This could effectively reduce Dow's overseas market for butylene oxide.

8. Use

Currently, more than 95% of the butylene oxide produced annually is used as a stabilizer in chlorinated solvents such as 1,1,1-trichloroethane (methyl chloroform) and trichloroethylene (Taylor, 1978). Depending upon the solvent's use, butylene oxide is added to the chlorinated solvent from as little as a fraction of a percent to as high as 8% of the total solvent make-up. Inclusion of about 0.25 to 0.5% butylene oxide, based on the solvent weight, during preparation of vinyl chloride and copolymer resin solutions minimizes container corrosion, that may be detrimental to resin color and properties (Hoff et al., 1978).

There are several minor uses of butylene oxide. For example, it is used to reduce corrosion in oil and gas well casings (Dow, 1977). Other

current commercial applications include use in production of pharmaceuticals, surfactants, and agrichemicals (Chemical Engineering, 1978).

Exports of butylene oxide are not listed separately by the Department of Commerce (Bureau of the Census). It was suggested, however, that Dow Chemical enjoyed a virtual world monopoly on 1,2-butylene oxide production due to patent restrictions, which expired in 1979 (Chemical Engineering, 1978). Under these circumstances, it seems likely that a sizeable portion of Dow's production is exported.

9. Manufacturers and Distributors

The only commercial manufacturer of 1,2-butylene oxide in the United States is Dow Chemical in Midland, MI (SRI International, 1980; USITC, 1980; U.S. EPA, 1980).

Distributors include (Chem Sources - USA, 1980):

BASF Wyandotte
Chemical Procurement Lab
ICN/K and K
Lachat Chem.
Polysciences Inc.

10. Manufacturing Processes

1,2-Butylene oxide is commercially prepared from 1-butene (Cosslett and Gerry, 1976). It is manufactured by Dow Chemical using chlorohydrin technology (Hoff et al., 1978). Assuming this technology is similar to the ethylene oxide-chlorohydrin technology as described by Schultze (1965), the process would first involve conversion of 1-butene to butylene chlorohydrin with hypochlorous acid. The chlorohydrin would then be converted to butylene oxide by dehydrochlorination with slaked lime.

The butene is injected into a reactor containing a hypochlorous acid medium formed from chlorine and water. The aqueous chlorohydrin thus formed is then mixed with a 10% solution of milk of lime at the inlet to the hydrolyzer.

The crude butylene oxide product from the hydrolyzer will contain primarily butylene oxide along with water, chlorinated organics (such as dichlorobutanes and butyl ethers), and butyraldehyde. The crude product is then refined in a distillation system. The basic process operations are outlined in Figure 1.

11. Impurities or Additives

Dow's specifications for butylene oxide are given below (Dow, 1977):

Assay, (IR), min.	99.0%
Chloride ion, max.	0.05%
Aldehydes as butyraldehyde, max.	0.05%
Acidity as butyric acid, max.	0.01%
Water, max.	0.10%
Isobutylene oxide, (IR), max.	0.30%
Color, APHA, max.	10

12. Occupational Exposure

The National Occupational Hazard Survey does not provide an estimate of the number of workers who are potentially exposed to 1,2-butylene oxide.

13. Control Technology and Work Practices

Specific factors that may contribute to or prevent employee exposure to butylene oxide were not found in the literature searched.

14. Biological Effects

a. Animal Studies

(1) Acute Exposures

In a series of range-finding toxicological studies (Table 2), Smyth and coworkers (1962) determined that the LD50 value for a single oral dose of butylene oxide was approximately 1170 mg/kg in male Wistar rats. Five non-fasted rats were used in the study.

The LD50 for dermal application was determined to be approximately 1174 mg/kg when butylene oxide was applied for 24 hours to the

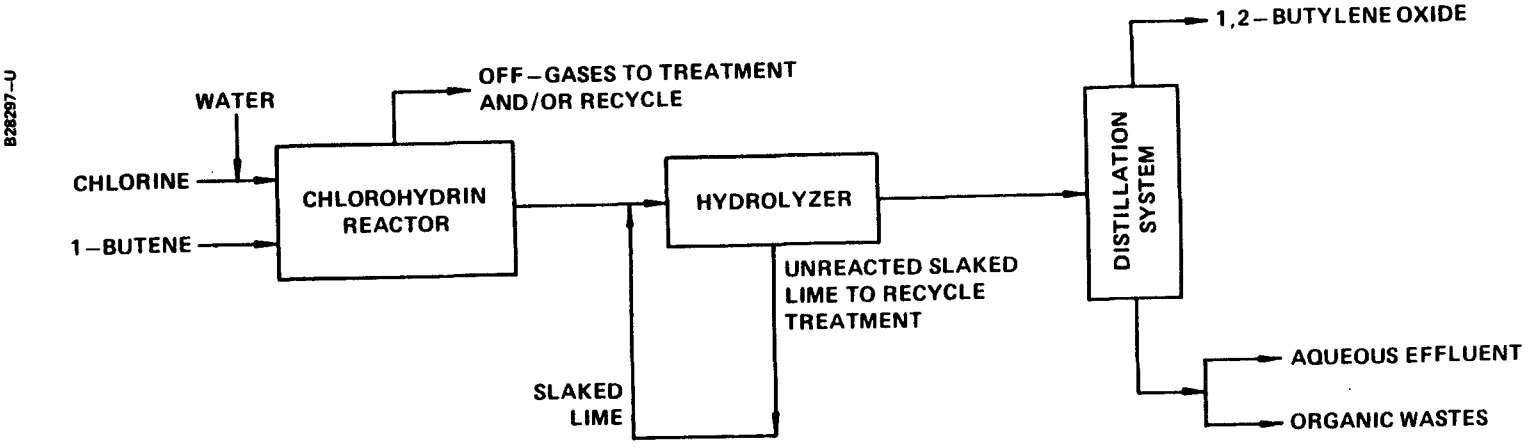


Figure 1. Manufacture of 1,2-butylene oxide via chlorohydrination.

Table 2. Acute Toxicity of Butylene Oxide

Route	Species	Sex	Strain	Dose	Response	Reference
oral	rats	M	Wistar	1170 mg/kg	LD50	Smyth et al., 1962
inhalation	rats	M,F	Wistar	4000 ppm/4h[a]	LCLo	Smyth et al., 1962
dermal	rabbits	M	New Zealand	1740 mg/kg	LD50	Smyth et al., 1962

[a] h=hour.

clipped skin of New Zealand rabbits. The dose was applied under an impervious plastic film, and the animals were observed for 14 days. Dermal irritation to the shaved skin using a 1-day uncovered application was found to be insignificant; however, it was not clear as to whether the pure compound or a dilution of the compound was used. Corneal injury produced in rabbit eyes indicated that butylene oxide could induce corneal burns with sufficient duration of exposure.

On inhalation exposure, a 4000 ppm concentration of butylene oxide vapor for 4 hours resulted in the death of 1 of 6 Wistar rats; double this concentration caused the death of all 6 animals. Hine and Rowe (1973) reported that 12-minute exposures to an atmosphere saturated with butylene oxide vapor caused the death of all rats; when rats were exposed for 6 minutes, deaths were delayed and caused by secondary pneumonia.

(2) Subchronic Exposures

Hine and Rowe (1973) reported that rats, guinea pigs, and rabbits tolerated repeated (number of repetitions not mentioned) 7-hour exposures to butylene oxide at a concentration of 400 ppm.

(3) Chronic Exposures

No information was found in the literature searched.

(4) Carcinogenicity

The carcinogenicity of butylene oxide was studied by Van Duuren and coworkers (1967) in skin painting studies. Approximately 10 mg of butylene oxide (10% in acetone) was applied 3 times weekly for 540 days to the clipped skin of ICR/Ha Swiss mice. This treatment schedule resulted in no toxicity to the test animals, and no skin tumors were observed among the 30 test animals during the period of the experiment.

(5) Mutagenicity

The mutagenic effects of butylene oxide in microbial assays are summarized in Table 3.

Investigation of the mutagenicity of butylene oxide in the Ames assay was performed by Speck and Rosenkranz (1976). Butylene oxide (14 μg) was incorporated into the agar overlay and produced a 6-fold increase in revertants over the levels in control plates when tester strain TA100 was used and metabolic activation was not employed. Other work from this laboratory demonstrated the mutagenic potential of comparable concentrations of butylene oxide in tester strain TA1530, but not in strain G46 (Chen et al., 1975). A recent report by Rosenkranz and Poirier (1979) showed a dose-dependent increase in mutations from butylene oxide in the Ames assay using tester strain TA1535. Addition of an S-9 metabolic activating system prepared from the livers of uninduced rats produced a decrease in mutation frequency at all concentrations of butylene oxide. McCann et al. (1975), however, obtained only weak mutagenic activity in strain TA1535 in the absence of metabolic activation. In addition, Simmon (1979a) was unable to show mutagenic activity with butylene oxide in any of the S. typhimurium tester strains (TA1538, TA1535, TA1537, TA1536, TA98, and TA100) either with or without metabolic activation at concentrations of butylene oxide as high as 500 μg/plate.

Simmon (1979b) showed an increase in mutations in the yeast Saccharomyces cerevisiae D3 after treatment with 0.6% butylene oxide. Inclusion of an S-9 metabolic activation system prepared from livers of Aroclor-pretreated rats reduced the number of observed mutations. Butylene oxide has also been tested for its ability to modify DNA in E. coli DNA polymerase-deficient strains (Rosenkranz and Poirier, 1979). Comparison of the zones of inhibition produced by application of butylene oxide (50 μg/ml) to E. coli

Table 3. Mutagenic Activity of Butylene Oxide in Microbial *In Vitro* Assays

Type of Assay	Organism	Strain	Dose/Plate	With Metabolic Activation	Results	Reference
reverse mutation	*S. typhimurium*	TA100	14 µg	no	+	Speck and Rosenkranz, 1976
reverse mutation	*S. typhimurium*	TA1535	820 µg	yes/no	+	Rosenkranz and Poirier, 1979
		TA1535				
		TA1538		yes/no	+	
reverse mutation	*S. typhimurium*	TA1530	16,500 µg	no	+	Chen *et al.*, 1975
		G46		no	-	
reverse mutation	*S. typhimurium*	TA1538	500 µg	no	-	Simmon, 1979a
		TA1535		no	-	
		TA1537		no	-	
		TA1536		no	-	
		TA98		no	-	
		TA100		no	-	
reverse mutation	*S. typhimurium*	TA1535	4,200 µg	no	-	McCann *et al.*, 1975
mitotic recombination	*S. cerevisiae*	D3	12,400 µg	yes/no	+	Simmon, 1979b
DNA modification	*E. coli*	pol A$^-$	8,250 µg	no	-[a]	Rosenkranz and Poirier, 1979
DNA modification (liquid suspension)	*E. coli*	pol A$^-$	41,300 µg	no	-[a]	Rosenkranz and Poirier, 1979

[a] Preferential killing of pol A$^-$ strain observed, but the results were not considered positive

strains with or without DNA-repair enzyme indicates that the compound does damage DNA. This assay correlates well with the mutagenic activity determined by the Ames Salmonella assay.

(6) Teratogenicity

Teratology assays of butylene oxide in rats and rabbits exposed via inhalation were completed by the National Toxicology Program in Fiscal Year 1980 (NTP, 1980). Exposures and detailed results of the assays were not reported, but material toxicity appeared to be the only effect observed.

(7) Reproductive Effects

No information was found in the literature searched.

(8) Other Relevant Information

No information was found in the literature searched.

b. Human Studies

(1) Pharmacokinetics

No information was found in the literature searched.

(2) Health Effects

No information was found in the literature searched.

(3) Target Organ Toxicity

No information was found in the literature searched.

(4) Epidemiology

No information was found in the literature searched.

15. Ongoing Studies

The National Toxicology Program (NTP, 1980) reports that there are reproduction and fertility assays reported or in progress for Fiscal Year 1980-1981 on butylene oxide. These assays include: Drosophila sex-linked recessive lethal, rat bone marrow cytology, mouse sperm head morphology, rat dominant lethal, and in vitro unscheduled DNA synthesis. Also, NTP (1980)

reported that a teratogenicity in rats and rabbits using inhalation exposure has recently been completed.

16. Exposure Standards

No recommended or promulgated occupational exposure standards for butylene oxide were found.

17. Sources of Additional Relevant Information

Bogyo et al. (1980) have prepared a review of the health and environmental effects of organic oxides for the U.S. Environmental Protection Agency. Butylene oxide is one of the compounds covered in this review.

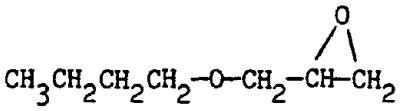
18. Other Pertinent Data

No other information that would aid in the assessment of butylene oxide as an occupational hazard was found in the literature searched.

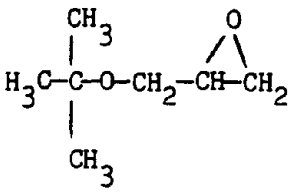
D. BUTYL GLYCIDYL ETHER

1. Chemical Name: Butyl Glycidyl Ether

2. Chemical Structure:



(normal)



(tert)

3. Synonyms: BGE
1,2-Epoxy-3-butoxypropane
2,3-Epoxypropyl butyl ether
Ether, butyl 2,3-epoxypropyl-
Glycidyl butyl ether
Oxirane, (butoxymethyl)-
Propane, 1-butoxy-2,3-epoxy-

4. Chemical Abstract Service (CAS) Number: 2426-08-6 (normal)
7665-72-7 (tert)

5. Registry of Toxic Effects of Chemical Substances (RTECS) Number:

TX4200000 (normal)

6. Chemical and Physical Properties:

Description:	colorless liquid
Molecular Weight:	130.21
Boiling Point:	164-168°C
Melting Point:	---
Vapor Pressure:	3.2 mm Hg (25°C)
Solubility:	2 g/100 ml water (20°C)
Specific Gravity:	0.908^{25}_{4}
Stability:	combustible

7. Production

An exact production figure for butyl glycidyl ether is not available. In 1973, less than 5 million pounds of butyl glycidyl ether were produced (SRC Estimate; Oosterhof, 1975a).

Butyl glycidyl ether has not been listed as a commercially produced chemical by the USITC (U.S. International Trade Commission) since 1974.

Data available from the U.S. EPA (1980) regarding producers of butyl glycidyl ether and production volumes are presented in Table 4.

8. Use

Butyl glycidyl ether has been used as a reactive diluent for epoxy resins (Oosterhof, 1975a). For example, 10-12% butyl glycidyl ether was added as a reactive diluent in Dow Chemical's liquid resin D.E.R. 334, a diglycidyl ether of bisphenol A used in structural applications for castings, caulkings, and sealants. This type of resin has been discontinued (Oosterhof, 1975b).

9. Manufacturers and Distributors

SRI International (1980) lists the following manufacturers:

AZS Corp.	Atlanta, GA
CPS Chem. Co.	Old Bridge, NJ
Dow Chem.	Freeport, TX
Shell Chem.	Deer Park, TX

Data available from the U.S. EPA (1980) regarding producers of butyl glycidyl ether and production volumes are presented in Table 1.

Other distributors include (1980-81 OPD Chemical Buyers Directory, 1980; Chem Sources - USA, 1980):

Ciba-Geigy Corp.	Monomer-Polymer and Dajac Lab.
Electron Microscopy Sci.	Pfaltz and Bauer
Howard Hall and Co.	Polysciences
ICN/K and K	R.T. Vanderbilt and Co.

10. Manufacturing Processes

n-Butyl glycidyl ether is made from epichlorohydrin (Oosterhof, 1975a) via condensation with n-butyl alcohol.

Table 4. Producers of n-Butyl Glycidyl Ether and Production Ranges (U.S. EPA, 1980)

Producer	Type of Production	1977 Production Range
		For CAS No. 2426-08-6
AZS Chemical Co. Atlanta, GA	Manufacturer	0.1-1.0 million lb
Eastman Kodak Rochester, NY	Manufacturer	none
Haven Chemical Co. Philadelphia, PA	Manufacturer	1-10 thousand lb
AZ Products Eaton Park, FL	Manufacturer	1-10 million lb
Shell Chemical Deer Park, TX	Manufacturer	confidential
Wilmington Chemical Co. Wilmington, DE	Manufacturer	10-100 thousand lb
Celanese Polymer Specialties Louisville, KY	Manufacturer	0.1-1.0 million lb
Marubeni America Corp. New York, NY	Importer	none
The Sieflor Corp. Los Angeles, CA	Importer	confidential
		For CAS No. 7665-72-7
Dow Chemical Freeport, TX	Manufacturer	1-10 thousand lb

11. Impurities or Additives

There is no evidence in the literature searched to indicate the presence of impurities or deliberate additives in commercially produced butyl glycidyl ether.

12. Occupational Exposure

The National Occupational Hazard Survey indicates that 19,862 workers are potentially exposed to n-butyl glycidyl ether.

13. Control Technology and Work Practices

Specific factors that may contribute to or prevent employee exposure to n-butyl glycidyl ether were not found in the literature searched.

14. Biological Effects

A detailed discussion of the toxicological information on butyl glycidyl ether will not be presented here, since this information is available in the NIOSH (1978) criteria document on occupational exposure to glycidyl ethers. Butyl glycidyl ether has an oral LD50 value of between 2.05 and 3.43 g/kg body weight in rats, and 1.53 g/kg body weight in mice. The LC50 value for rats and mice is 5,480 mg/m^3 and greater than 18,600 mg/m^3, respectively. This compound is a moderate to severe skin irritant and can cause mild to moderate eye irritation. Sensitization can occur following repeated skin applications. In the Ames assay for mutagenicity, butyl glycidyl ether is positive in the absence of a mammalian metabolic activation system.

15. Ongoing Studies

No current toxicological or environmental studies of butyl glycidyl ether were found.

16. Exposure Standards

The ACGIH currently recommends a Time-Weighted Average (TWA) Threshold Limit Value (TLV) of 25 ppm for n-butyl glycidyl ether (ACGIH, 1981).

OSHA (1976) has promulgated a standard of 50 ppm for the compound. A number of foreign maximum allowable concentrations (MACs) for occupation exposure to butyl glycidyl ether are reported in NIOSH (1978). These standards include: 100 and 200 mg/m^3 for the average and maximum limits, respectively, in Rumania, and 270 mg/m^3 in Australia, Belgium, Finland, Netherlands, Switzerland, and Yugoslavia.

17. Sources of Additional Relevant Information

No sources of additional relevant information were identified.

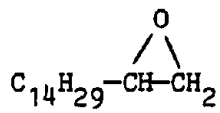
18. Other Pertinent Data

No other information that would aid in the assessment of butyl glycidyl ether as an occupational hazard was found in the literature searched.

E. 1,2-EPOXY HEXADECANE

1. Chemical Name: 1,2-Epoxy hexadecane

2. Chemical Structure:



3. Synonyms: Hexadecene epoxide
alpha-Olefin Epoxide 16
Oxirane, tetradecyl-

4. Chemical Abstract Service (CAS) Number: 7320-37-8

5. Registry of Toxic Effects of Chemical Substances (RTECS) Number:

ML9450000

6. Chemical and Physical Properties:

Description:	liquid
Molecular Weight:	240.48
Boiling Point:	314.8°C
Melting Point:	15.7°C
Vapor Pressure:	<0.01 mm Hg (20°C)
Solubility:	<0.01% by weight in water
Specific Gravity:	0.8399^{20}_{20}
Stability:	combustible

7. Production

Production figures are not available from the U.S. EPA (1980).

8. Use

1,2-Epoxyhexadecane is used as an intermediate for making surfactants and as an acid scavenger (Union Carbide, 1977).

9. Manufacturers and Distributors

1,2-Epoxyhexadecane is manufactured by Union Carbide Corp. in Taft, LA and by Viking Chemical Co. in Blooming Praire, MN (U.S. EPA, 1980; SRI International, 1980). Union Carbide's product is commercially known as alpha-olefin epoxide 16 or as olefin C16 epoxide.

Distributors of 1,2-epoxy hexadecane include (Chem Sources -USA, 1980):

Chemsampco Co.

10. Manufacturing Processes

1,2-Epoxyhexadecane can be prepared by the action of 1-hexadecene with peracetic acid (Jacobson, 1959). The product mixture of the reaction is poured into cold water and extracted with ether. The extract is washed with water and the ether is evaporated. The residue is distilled and additionally purified by dissolving it in petroleum ether and passing the solution through a column of silicic acid. Evaporation of the eluted ether leaves pure 1,2-epoxyhexadecane.

11. Impurities or Additives

There is no evidence in the literature searched to indicate the presence of impurities or deliberate additives in commercially produced 1,2-epoxyhexadecane.

12. Occupational Exposure

The National Occupational Hazard Survey does not provide an estimate of the number of workers who are potentially exposed to 1,2-epoxyhexadecane.

13. Control Technology and Work Practices

Specific factors that may contribute to or prevent employee exposure to 1,2-epoxyhexadecane were not found in the literature searched.

14. Biological Effects

The only information found in the literature searched on the toxicity of 1,2-epoxyhexadecane was two cancer bioassays. The first report by Koten and Falk (1963) provides little experimental detail, with neither the route of administration, nor the periodicity of dosing, nor the tumor incidence in control animals clearly enumerated. The incidence of tumors in treated C_3H mice

was 7 malignant lymphomas in 30 animals. The authors indicate that this was a tumorogenic response. In the second study, Van Durren et al. (1967) treated 41 female 1CR/Ha Swiss mice 3 times a week for 598 days by skin painting with approximately 10 mg of 1,2-epoxyhexadecane. Neither solvent-treated nor non-treated control mice (100 animals per group) developed tumors. In the test group, 2 of the 41 animals developed papillomas and 1 developed a carcinoma of the skin. The authors claim that these results indicate a weak carcinogenic response. The same results have been reported in Van Durren (1969), however, this report contains less experimental detail.

15. Ongoing Studies

The National Toxicology Program (NTP, 1980) has scheduled 1,2-epoxyhexadecane for mutagenicity testing using the Ames Salmonella assay in the fiscal year 1981.

The NTP (1980) also reports that a carcinogenicity bioassay in rats and mice that is presently in the chronic testing phase. In this study, 1,2-epoxyhexadecane is being administered by skin painting.

16. Exposure Standards

No recommended or promulgated occupational exposure standards for 1,2-epoxyhexadecane were found.

17. Sources of Additional Relevant Information

No sources of additional relevant information were identified.

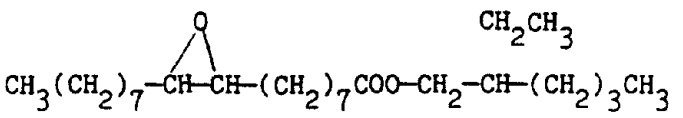
18. Other Pertinent Data

No other information that would aid in the assessment of 1,2-epoxyhexadecane as an occupational hazard was found in the literature searched.

F. 9,10-EPOXYOCTADECANOIC ACID, 2-ETHYLHEXYL ESTER

1. Chemical Name: 9,10-Epoxyoctadecanoic Acid, 2-Ethylhexyl Ester

2. Chemical Structure:



3. Synonyms: 2-Ethylhexyl epoxy stearate
Oxiraneoctanoic acid, 3-octyl, 2-ethylhexyl ester

4. Chemical Abstract Service (CAS) Number: 141-38-8

5. Registry of Toxic Effects of Chemical Substances (RTECS) Number:

Not listed

6. Chemical and Physical Properties:

Description:	---
Molecular Weight:	410.67
Boiling Point:	---
Melting Point:	---
Vapor Pressure:	---
Solubility:	---
Specific Gravity:	---
Stability:	combustible

7. Production

Data available from the U.S. EPA (1980) regarding producers of 9,10-epoxyoctadecanoic acid, 2-ethylhexyl ester and production volumes are presented below.

Henkel Inc.
Importer
1977 production of less than 1000 lb

Witco Chemical Corp. Taft, LA
Manufacturer
1977 production of 10 to 100 thousand lb

8. Use

The Witco Chemical plant which manufactures 9,10-epoxyoctadecanoic acid, 2-ethylhexyl ester produces epoxidized plasticizers (SRI International, 1980).

9. Manufacturers and Distributors

See Section 7, Production.

10. Manufacturing Processes

The commercial process is not available from the literature searched; however, this compound can be made by epoxidation of 2-ethylhexyl oleate.

11. Impurities or Additives

There is no evidence in the literature searched to indicate the presence of impurities or deliberate additives in commercially produced 9,10-epoxyoctadecanoic acid, 2-ethylhexyl ester.

12. Occupational Exposure

The National Occupational Hazard Survey does not provide an estimate of the number of workers who are potentially exposed to 9,10-epoxyoctadecanoic acid, 2-ethylhexyl ester.

13. Control Technology and Work Practices

Specific factors that may contribute to or prevent employee exposure to 9,10-epoxyoctadecanoic acid, 2-ethylhexyl ester were not found in the literature searched.

14. Biological Effects

No information was found in the literature searched.

15. Ongoing Studies

No current toxicological or environmental studies of 9,10-epoxyoctadecanoic acid, 2-ethylhexyl ester were found.

16. Exposure Standards

No recommended or promulgated occupational exposure standards for 9,10-epoxyoctadecanoic acid, 2-ethylhexyl ester were found.

17. Sources of Additional Relevant Information

No sources of additional relevant information were identified.

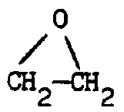
18. Other Pertinent Data

No other information that would aid in the assessment of 9,10-epoxyoctadecanoic acid, 2-ethylhexyl ester as an occupational hazard was found in the literature searched.

G. ETHYLENE OXIDE

1. Chemical Name: Ethylene Oxide

2. Chemical Structure:



3. Synonyms: Anprolene
Dimethylene oxide
EO
1,2-Epoxyethane
ETO
NCI-C50088
Oxacyclopropane
Oxane
Oxidoethane
Oxiran
Oxirane
Oxirene, dihydro

4. Chemical Abstracts Service (CAS) Number: 75-21-8

5. Registry of Toxic Effects of Chemical Substances (RTECS) Number:

KX2450000

6. Chemical and Physical Properties:

Description:	colorless gas at ordinary temperatures; mobile colorless liquid at low temperatures
Molecular Weight:	44.053
Boiling Point:	10.5°C
Melting Point:	-112.44°C
Vapor Pressure:	1095 mm Hg
Solubility:	completely soluble in water, acetone, benzene, carbon tetrachloride, diethyl ether, methanol
Specific Gravity:	0.8694
Stability:	highly reactive chemically; vapors are flammable and explosive; autoignition temperature 804°F; Flash point: -69°F; Flammability limits, % by volume in air: 3-100

7. Production

Recent production volumes of ethylene oxide are as follows (USITC, 1976-1980):

Year	Production in Millions of Pounds
1979	5665
1978	5012
1977	4364
1976	4184
1975	4467
1974	4200

CMR (1979) estimates the future growth of ethylene oxide to be 5% through 1982. Key Chemicals (1980a) has projected the 1980 production of ethylene oxide to be 6% less than in 1979.

Imports of ethylene oxide are in the range of several million pounds per year (Blackford, 1976), which is only a small fraction of domestic production. In 1978, 76 million pounds of ethylene oxide were exported (Bureau of the Census, 1979). Key Chemicals (1980a) has reported that foreign trade of ethylene oxide (import, export) is very small.

Data available from the U.S. EPA (1980) regarding producers of ethylene oxide and production volumes are presented in Table 5.

8. Use

The following tabulation presents the percentage of the total amount of ethylene oxide produced that is used in each of the applications listed:

	Percentage of Total	
	(Lawler, 1977)	(CMR, 1978)
Ethylene glycol	63	60
Nonionic surface-active agents	11	11
Glycol ethers	6	7
Diethylene glycol	5	-

Table 5. Producers of Ethylene Oxide and Production Ranges (U.S. EPA, 1980)

Producer	Type of Production	1977 Production Range
Olin Corp.		
Brandenburg, KY	Manufacturer	50-100 million lb
Dow Chemical		
Plaquemine, LA	Manufacturer	100-500 million lb
Freeport, TX	Manufacturer	100-500 million lb
Midland, MI	Importer	1-10 million lb
PPG Industries		
Beaumont, TX	Manufacturer	100-500 million lb
Ponce, PR	Manufacturer	100-500 million lb
Texas Eastman		
Longview, TX	Manufacturer	100-500 million lb
Union Carbide Corp.		
Ponce, PR	Manufacturer	500-1000 million lb
Hahnville, LA	Manufacturer	confidential
Port Lavaca, TX	Manufacturer	confidential
BASF Syandotte		
Geismar, LA	Manufacturer	100-500 million lb
Shell Chemical		
Geismar, LA	Manufacturer	100-500 million lb
Sunolin Chemical		
Claymont, DE	Manufacturer	50-100 million lb
Northern Petrochemical		
Morris, IL	Manufacturer	10-50 million lb
Celanese Chemical		
Pasedena, TX	Manufacturer	100-500 million lb
Calcasieu Chemical		
Lake Charles, LA	Manufacturer	50-100 million lb
Continental Oil Co.		
Westlake, TX	Manufacturer	0.1-1 million lb
Jefferson Chemical		
Port Neches, TX	Manufacturer	confidential

	Percentage of Total	
	(Lawler, 1977)	(CMR, 1978)
Ethanolamines	5	7
Triethylene glycol	2	-
Polyethylene glycol	2	-
Exports	2	-
Miscellaneous	4	16

A very large percentage of ethylene oxide production is used captively by the manufacturers.

The miscellaneous uses, not individually listed above, can represent rather sizeable consumption volumes. The largest amount in the miscellaneous group goes into production of polyether polyols for flexible polyurethane foams. In 1975, about 75 million pounds of ethylene oxide were consumed in these polyols (Blackford, 1976).

Approximately 13 to 18 million pounds of ethylene oxide are used annually to make the medicinals choline and choline chloride (Blackford, 1976).

Approximately 10 million pounds of ethylene oxide are used annually in the manufacture of hydroxyethyl starch, which is a semi-synthetic gum used in textile sizing and adhesives (Blackford, 1976).

Arylethanolamines are made by reacting ethylene oxide with either aniline or aniline derivatives. It is estimated that 3 million pounds of ethylene oxide were used for arylethanolamines in 1974 (Blackford, 1976). They are used as intermediates for monoazo dyestuffs.

Acetal copolymer resins are produced by copolymerizing 1,3,5-trioxane with a cyclic ether having at least two adjacent carbon atoms (e.g., ethylene oxide) in the presence of a catalyst. Ethylene oxide consumption for these resins is believed to have amounted to about 2 to 3 million pounds per year in 1972 to 1975. Acetal copolymer resins are made by Celanese Plastics at Bishop, Texas, under the trade name Celcon ® (Blackford, 1976).

Like nonionic surface-active agents, ethylene oxide is used to produce ethoxylated cationic surface-active agents. Several million pounds of ethylene oxide are used annually to produce these cationic agents such as ethoxylated (coconut oil alkyl) amine, ethoxylated (tallow alkyl) amine, and various ethoxylated fatty acid amino amides (Blackford, 1976).

Small amounts of ethylene oxide are also consumed as a fumigant, as a food and cosmetic sterilant, and in hospital sterilization (Gilmour, 1978). In 1975, an estimated 0.1 million pounds of ethylene oxide were used for fumigant purposes (Landels, 1976).

9. Manufacturers and Distributors

Table 5 lists the manufacturers that produce ethylene oxide at the indicated sites. With a few exceptions, production is concentrated in the major industrial chemical centers of Texas and Louisiana.

The manufacturers of ethylene oxide are the major users and distributors of the compound. Additional distributors of ethylene oxide include the following (1980-81 Chemical Buyers Directory, 1980; Chemical Week: 1981 Buyers' Guide Issue, 1980; Chem Sources - USA, 1980):

Airco Industrial Gases	Fisher Sci.
Air Products and Chems.	ICN/K and K
Arc Chem. Corp.	Ideal Gas Prod.
Atlantic Chem.	Matheson Gas Prod.
Atomergic Chemetals	MG Sci. Gases
Bentley Chem.	Nippon Soda Co. Ltd.
Bio-Lab	Pfaltz and Bauer
Conoco	Precision Gas Prod.
Devon Chem. Inc.	Scientific Gases
Diamond Shamrock	Tridom Chem.
EM Lab	Warren Chemical Co.

10. Manufacturing Processes

Two major processes have been used to manufacture ethylene oxide in large, commercial quantities: the direct oxidation of ethylene and the chlorohydrination of ethylene.

In 1975, about 99 percent of all ethylene oxide was produced by the direct oxidation method (Blackford, 1976). This is commercially carried out in the vapor phase using either air or tonnage oxygen and a silver catalyst. Approximately 65% of industry capacity is based upon air and the remainder uses tonnage oxygen. There is a trend toward oxygen to increase yields (Blackford, 1976).

The overall reaction may be represented as follows:

$$CH_2{=}CH_2 + 1/2O_2 \xrightarrow{Ag} CH_2 - CH_2 \quad (O)$$

One of the by-products of ethylene oxidation is ethylene glycol (Blackford, 1976); ethylene glycol is not a serious impurity because many of the ethylene oxide manufacturers use the oxide to produce this glycol. Some carbon dioxide and water is formed by complete oxidation of ethylene (Lowenheim and Moran, 1975).

Figure 2 diagrams the process flow for production of ethylene oxide via oxidation. Ethylene (95% to 98% purity) and air are mixed in a volume ratio of 1:8 and passed over a catalyst of silver oxide deposited on an inert carrier. The catalyst is usually replaced every 18 months. Generally, an anticatalyst such as ethylene dichloride is added to the ethylene feed to suppress CO_2 formation. With process conditions consisting of atmospheric pressure and a temperature of 270°C to 290°C, a reactor contact time of one second converts about 60% of the ethylene to the oxide. The effluent gases from the reactor are washed with water under pressure in an absorber. The aqueous ethylene oxide solution is sent to a vacuum stripping column where ethylene oxide is liberated from solution and passed overhead to a fractionating column for final purification (Lowenheim and Moran, 1975).

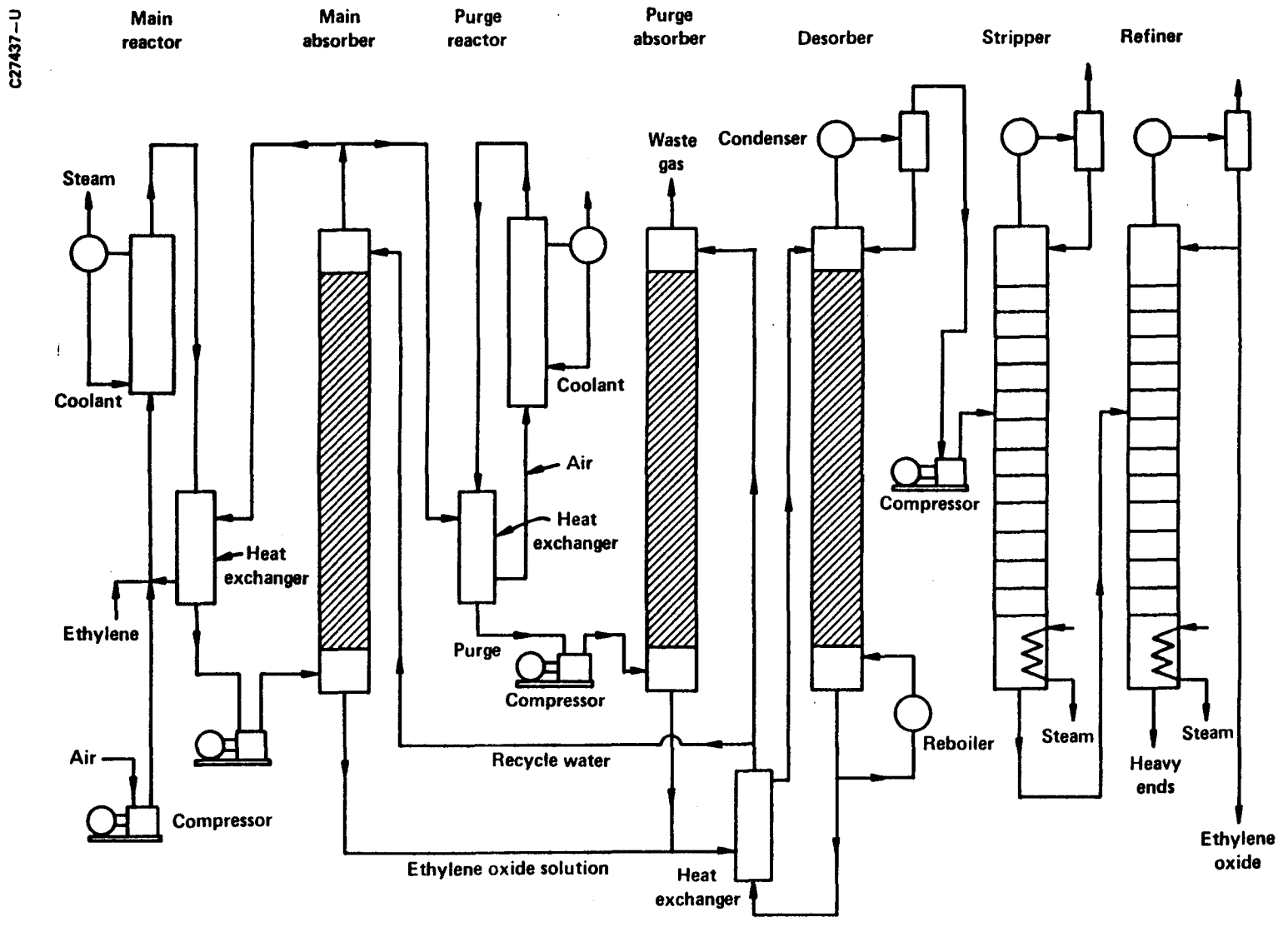


Figure 2. Direct-oxidation process for manufacturing ethylene oxide (Schultze, 1965).

Reactor design and process operations are not standardized throughout the ethylene oxide oxidation industry, so variations of the described process are in use (Lowenheim and Moran, 1975). The average industrial yield of ethylene oxide from ethylene is about 64% of theoretical yield (Blackford, 1976).

The chlorohydrin process was the main method of ethylene oxide manufacture until 1957. In 1972, Dow Chemical converted the remaining chlorohydrin capacity to the production of propylene oxide, and the process was not used again for ethylene oxide production until 1975. Dow has built-in flexibility for using the chlorohydrin process to produce either propylene oxide or ethylene oxide. Since 1975, part of this capacity has been used for ethylene oxide. During 1975, Dow produced between 25 to 50 million pounds of ethylene oxide via the chlorohydrin process (Blackford, 1976), which represented about 1% of total production. The chlorohydrin process is attractive commercially only when good supplies of captive low-cost chlorine and lime or caustic soda are available. In addition, satisfactory markets or disposal facilities are needed for the by-products produced (Schultze, 1965).

The chlorohydrin process starts with converting ethylene to ethylene chlorohydrin with hypochlorous acid. The chlorohydrin is converted to ethylene oxide by dehydrochlorination with slaked lime. A simplified diagram of a typical chlorohydrin process ethylene oxide plant is depicted in Figure 3. The reactor is usually a corrosion-resistant tower measuring 4 feet in diameter and 50 feet high. Its lower section contains spargers and porous plates for the effective dispersion of chlorine into water and for injecting ethylene into the hypochlorous acid medium. Ethylene chlorohydrin formation proceeds rapidly in the lower section of the tower. Gases are separated from the dilute chlorohydrin solution in the top section and the vent gases from the condensing apparatus pass in series to acid-proof water and caustic scrubbers, where residual chlorine and

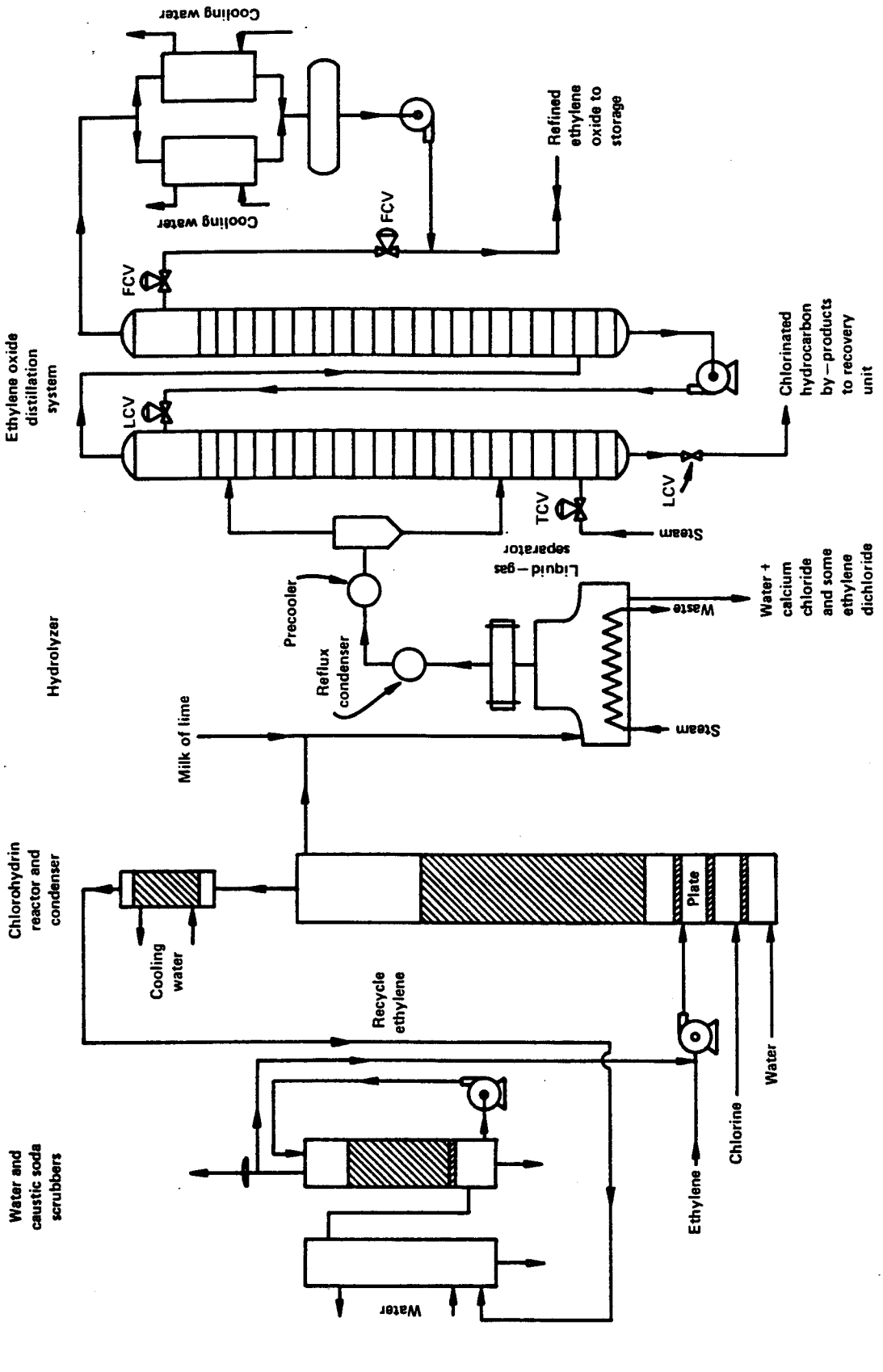


Figure 3. Chlorohydrin process for manufacturing ethylene oxide (Schultze, 1965).

HCl gases are removed before recycling the unreacted ethylene. The aqueous chlorohydrin solution is mixed with a 10% solution of milk of lime at the inlet to the hydrolyzer (Schultze, 1965).

The crude ethylene oxide product from the hydrolyzer contains about 77.5% ethylene oxide, 10% water, 12% chlorinated organic compounds (principally 1,2-dichloroethane and bis(2-chloroethyl)ether), and 0.5% acetaldehyde together with small amounts of hydrocarbon gases. This crude ethylene oxide is refined in two columns; the first column removes chlorinated hydrocarbons and the second removes acetaldehyde.

The manufacture of ethylene oxide is a closed-system operation. Since ethylene oxide has a high vapor pressure, atmospheric emissions appear a more likely environmental entry source than does waste disposal. Ethylene oxide can be lost from the vapor phase as fugitive emissions or with vented gases.

Pervier et al. (1974) have surveyed air emissions from ethylene oxide production plants and have estimated that the total annual emission of air pollutants in 1980 will be roughly 120 million pounds with the following composition:

hydrocarbons	118.6 million pounds
nitrogen oxides	0.45 million pounds
sulfur oxide	0.14 million pounds

Most of the emissions are released by vents on process equipment. The authors reported no details on the contribution of ethylene oxide to this total. Most of the emission appears to be ethylene gas.

11. Impurities or Additives

Commercially available ethylene oxide has a purity greater than 99.9%. The manufacturers specifications are given in Table 6.

Table 6. Manufacturers' Specifications for Ethylene Oxide[a]

	BASF	Celanese	Dow	Jefferson	Shell	Wyandotte
Purity, wt. % min.	99.95	99.95	---	---	---	---
Water, wt. % max.	0.005	0.02	0.03	0.03	0.03	---
Aldehydes, as acetaldehyde, wt. % max.	0.005	0.01	0.005	0.025	0.010	0.003
Acidity as acetic acid, wt. % max.	0.002	0.002	0.002	0.005	0.0020	0.002
CO_2, wt. % max.	0.005	---	0.002	---	---	0.005
Total Cl as Cl^-, wt. % max.	0.005	---	0.005	nil	---	0.0005
Nonvolatile residue, g/100 ml, max.	0.010	0.01	0.01[b]	0.01	0.010	0.01
Color, APHA, max.	10	10	5	---	10	10
Residual odor	---	none	---	none	none	mild
Appearance	---	clear	---	clear	clear	---
Acetylene, max.	---	---	0.0005	nil	---	---

[a]This information was obtained from the respective manufacturer's product data sheets, available from each manufacturer on request.

[b]Presently 0.005 g/100 ml in Dow ethylene oxide (Kurginski, 1979).

12. Occupational Exposure

The National Occupational Hazard Survey indicates that 144,152 workers are potentially exposed to ethylene oxide.

13. Control Technology and Work Practices

NIOSH (1977) has suggested work practices and control technology for the use of ethylene oxide as a sterilant in medical facilities. It is suggested that exposure of workers to ethylene oxide should be kept at a minimum. Ethylene oxide sterilization and aeration operations should be isolated from the rest of the workplace and the room kept under negative pressure. In areas of potential leaks, local pick-up exhaust systems can prevent contamination of the work room air. Before emitting to the environment, exhaust air should be decontaminated. To prevent fire or explosion, ignition sources should be controlled, including sources of static electrical sparks, and fans in the ventilation system should be made of non-sparking material. Impervious clothing is not effective against ethylene oxide penetration and personal protection is most effectively achieved by adherence to appropriate sanitation practices. In case of spills, all non-essential workers should be evacuated and clean-up personnel should be equipped with the appropriate self-contained breathing apparatus equipped with a full-face shield.

14. Biological Effects

a. Animal Studies

(1) Acute Exposures

The acute toxicity of ethylene oxide is summarized in Table 7. Exposure of mice, rats, guinea pigs, rabbits, and dogs to lethal levels of ethylene oxide has produced symptoms of salivation, nausea, vomiting, diarrhea, respiratory irritation, cardiac arrhythmia, incoordination, and convulsions (Hine and Rowe, 1973; Sexton and Henson, 1949). Animals that survived

Table 7. Acute Toxicity of Ethylene Oxide

Route[a]	Species	Sex	Dose (mg/kg)	Response	Reference
oral	rat (Wistar)	M	330	LD50	Smyth et al., 1941
oral	guinea pig	M,F	270	LD50	Smyth et al., 1941
oral	rabbit	M,F	631	LD50	Woodward and Woodward, 1971
i.p.	rat	M,F	178	LD50	Bruch, 1973
i.p.	mouse	M,F	178	LD50	Bruch, 1973
i.p.	rabbit	M,F	251	LD50	Woodward and Woodward, 1971
s.c.	rabbit	M,F	200	LD50	Woodward and Woodward, 1971
i.v.	rat	M	355	LD50	Bruch, 1973
i.v.	rabbit	M,F	178	LD50	Woodward and Woodward, 1971
i.v.	dog	---	125	LD50	Patty, 1973
inhalation	rat (Sherman)	M,F	4000 ppm/4 h[b]	LD50	Carpenter et al., 1949
inhalation	mouse	F	835ppm/4 h	LD50	Jacobsen et al., 1956
inhalation	guinea pig	---	7000 ppm/ 2-1/2 h	LCLo	Waite et al., 1930
inhalation	dog	M	960 ppm/4 h	LD50	Jacobsen et al., 1956

[a] i.p. = intraperitoneal; s.c. = subcutaneous; i.v. = intravenous.
[b] h = hour.

the initial exposures showed subsequent bronchitis, lobar and lobular pneumonia, and loss of appetite, with delayed symptoms of apathy, dyspnea, vomiting, hind leg paralysis, periodic convulsions, and death (Waite et al., 1930; Hollingsworth et al., 1956).

Pathological findings following lethal exposure to ethylene oxide in mice, rats, and guinea pigs showed congestion of the lungs, hyperemia of the liver and kidneys, and gray discoloration of the liver (Waite et al., 1930). Pathological findings after delayed death caused by ethylene oxide included emphysema of the lungs, fatty degeneration of the liver, cloudy swelling of the kidney tubules, and congestion of the spleen and brain (Hollingsworth et al., 1956). Intravenously-administered ethylene oxide caused congestion in all organs of the rabbit (Greaves-Walker and Greeson, 1932). Zamlauski and Cohen (1976) have reported that infusion of ethylene oxide in the rat at blood levels of 0.45 to 4.5 mg/ml produced a significant decrease (≈30%) in glomerular filtration rate, which indicates effects of ethylene oxide on kidney function.

Ethylene oxide in 10% and 50% aqueous solutions produced hyperemia and edema in shaved rabbit skin when applied through cotton pads for 1 to 60 minutes (Hollingsworth et al., 1956). Bruch (1973) studied the dermal irritation properties of 2% to 10% aqueous ethylene oxide solutions in guinea pigs and rabbits. Subcutaneous injection in the guinea pig resulted in acchymoses and skin thickening, while intradermal injection and topical application in the rabbit resulted in mild irritation.

McDonald and coworkers (1977) studied the ocular effects of varied concentrations of ethylene oxide in saline applied repeatedly over a 6-hour period to the eyes of rabbits. They observed a dose-dependent increase in congestion, swelling, discharge, iritis, and corneal cloudiness that

indicated the irritating effect of ethylene oxide on mucous membranes and corneal epithelium. The maximum nondamaging concentration for this time period was 0.1% ethylene oxide. In another study of ocular irritation in rabbit eyes, Woodward and Woodward (1971) found slight irritation following a single application of 10% aqueous ethylene oxide (duration of exposure unknown), and a no-effect concentration of 2.1% ethylene oxide was determined. The higher values determined in this study are probably the result of a different mode of application and, therefore, different duration of exposure.

(2) Subchronic Exposures

The subchronic toxicity of ethylene oxide has been investigated in a variety of different animal species (Table 8). The symptoms of poisoning were similar to those observed in acute studies with lung, kidney, and liver damage occurring, and with neuropathy of the hind quarter being present in some species. In addition, hematological changes were observed in dogs (Jacobson et al., 1956; Woodward and Woodward, 1971). Woodward and Woodward (1971) demonstrated a dose-related increase in anemia in dogs receiving 6 to 36 mg/kg ethylene oxide in 30 daily injections. Balazs (1976) was unable to repeat these findings in beagle dogs, however, with an ethylene oxide-glucose solution administered intravenously over the same concentration range in a 21-day study.

Hollingsworth et al. (1956) observed neurotoxic effects in animals following inhalation exposure to 357 ppm ethylene oxide vapor for several weeks (the exposure for each species is presented in Table 4). Rats, rabbits, and monkeys showed paralysis and atrophy of the muscles of the hind limbs. These effects were reversible after discontinuation of exposure for 100 to 132 days. Special studies on monkeys were carried out with repeated (38 to 94) exposures to this level of ethylene oxide. Knee jerk reflexes became very weak, pain perception in the hind quarters decreased, the cremasteric reflex was

Table 8. Subchronic Toxicity of Ethylene Oxide

Route[a]	Species	Concentration	Number of Exposures[b]	Toxic Symptoms	Reference
oral	rats	100 mg/kg	15 (5 d/wk)	Weight loss, gastric irritation and slight liver damage.	Hollingsworth et al., 1956
oral	rats	30 mg/kg	22 (5 d/wk)	No observed effect.	Hollingsworth et al., 1956
s.c.	rats	54 mg/kg	30	Weight loss, injection site hemorrhage and inflammation.	Hollingsworth et al., 1956
s.c.	rats	18 mg/kg	30	No observed effect.	Hollingsworth et al., 1956
s.c.	dogs	36 mg/kg	30	Anemia, hyperplastic bone marrow, and ectopic hematopoiesis.	Woodward and Woodward, 1971
i.v.	dogs	36 mg/kg	21	No observed anemia, other observations not mentioned.	Balazs, 1976
inhalation	rats guinea pigs mice rabbits monkeys	841 ppm	8 (7 h each)	Death, pathologic changes in lungs, liver, and kidneys similar to those in acute poisoning.	Hollingsworth et al., 1956
inhalation	rats mice	357 ppm	33-38 (7 h each)	Death caused by secondary respiratory infections, impairment of sensory and motor function prior to death.	Hollingsworth et al., 1956

Table 8. Subchronic Toxicity of Ethylene Oxide (Cont'd)

Route	Species	Concentration	Number of Exposures	Toxic Symptoms	Reference
inhal-lation	rats	204 ppm	127-133 (7 h each)	Weight loss, some deaths with effects on lungs, kidneys, and testes.	Hollingsworth et al., 1956
inha-lation	mice rats	400 ppm	30 (6 h/d; 5 d/wk)	Weight loss, reddish nasal discharge, diarrhea, labored breathing, weakness of the hind legs, and some deaths (13 of 20 rats and 24 of 30 mice).	Jacobsen et al., 1956
inha-lation	guinea pigs	357 ppm	123 (7 h each)	Growth depression, degeneration of the testicular tubules (males), slight fatty degeneration of the adrenal cortex (females).	Hollingsworth et al., 1956
inha-lation	dogs	290 ppm	30 (6 h/d; 5 d/wk)	Vomiting, slight tumors, transient weakness of the hindlegs, and decreases in red blood cells, hemoglobin, and hematocrit.	Jacobsen et al., 1956
inha-lation	monkeys	357 ppm	38-94 (7 h each)	Paralysis and muscular atrophy of the hind limbs.	Hollingsworth et al., 1956

[a] s.c. = subcutaneous; i.v. = intravenous.
[b] d = day; wk = week; h = hour.

elicited, and the extensor reflex of the palms of the hind feet was abolished. Impairment of both sensory and motor functions at the lumbar and sacral level of the spinal cord was indicated. Exposure of monkeys to a lower level of ethylene oxide (2.4 ppm for 176 to 226 days) produced partial paralysis and some muscular atrophy of the hind legs with moderate suppression of the leg reflexes. The Babinski reflex was present after this lower level exposure to ethylene oxide.

(3) Chronic Exposures

No information was found in the literature searched.

(4) Carcinogenicity

The carcinogenic effects of ethylene oxide are summarized in Table 9.

In a study of the carcinogenicity of ethylene oxide, Walpole (1958) dissolved the compound in arachis oil and injected rats subcutaneously with a maximum total dose of 1 g/kg over 94 days (dosing schedule not specified). Rats were observed for their lifetime following treatment, and no tumors were detected. Since the amount administered and the frequency of injection was not specified, it is difficult to evaluate these negative results. In a study by Dunkelberg (1979), 100 NMRI female mice were given 0.1, 0.3, and 1.0 mg ethylene oxide by subcutaneous injection weekly. At the time of this preliminary report after 91 weeks of treatment, 25% of the animals remained alive. There was a dose-dependent occurrence of local sarcomas at the site of injection in the experimental animals; no tumors appeared at the injection site in the control animals. The tumor incidence in organs distant from the site of injection was not statistically greater than the incidence in control animals.

Lifetime skin painting studies with 10% ethylene oxide in acetone (3 times weekly) were performed on female mice by Van Duuren et al. (1965). Application of 0.1 ml of ethylene oxide solution to the clipped dorsal

Table 9. Carcinogenic Effects of Ethylene Oxide.

Route	Species, Sex	Dosage	Duration of Treatment (weeks)	Duration of Observation	Type of Tumors	Number of Tumors	Reference
s.c.[a]	Rat M,F	1000 mg total (oil)	94	Lifetime	Sarcoma	0	Walpole, 1958
s.c.	Mouse F	1.0 mg/wk[b] 0.3 mg/wk 0.1 mg/wk	91	91 wk	Sarcoma at injection site	12 8 6	Dunkelberg, 1979
dermal	Mouse F	10 mg/animal	3 time/wk life	Lifetime (493 d)	Papilloma Carcinoma	0 0	Van Duuren et al., 1965

[a] s.c. = subcutaneous.
[b] wk = week.

skin produced no tumors. Median survival time for the mice was 493 days. The investigators indicated that rapid evaporation of the compound from the skin could have been responsible for the negative results observed.

Reyniers and coworkers (1964) conducted a retrospective study on female germ-free mice that developed tumors after being exposed to ethylene oxide-treated groundcorncob bedding for 150 days. Ovarian, lymphoid, and pulmonary tumors developed in these animals after they had been moved to untreated bedding. Colony mates maintained on nontreated bedding did not develop tumors. All the males exposed to ethylene oxide-treated bedding died, and necropsy showed massive hemorrhage. The causative agent may not have been ethylene oxide, and identification by chemical analysis of the bedding was not done.

Union Carbide has reported preliminary results of an inhalation study in rats (Pestic. Toxic Chem. News, 1979). An increased incidence in tumors was reported in animals exposed to 100 ppm, the highest concentration employed. These observations were from gross examination and definitive conclusions await completion of the study.

(5) Mutagenicity

Ethylene oxide has been shown to be mutagenic in the Ames Salmonella assay. The bacteria have been exposed to the compound in the vapor phase (strains TA100, TA1535) (Taylor, 1979) and in liquid media (strain TA1535) (Rannug et al., 1976). Ethylene oxide was a direct acting mutagen in these assays, but addition of an S-9 mix substantially increased the number of revertant colonies. This increase indicates that a mutagenic metabolite of ethylene oxide may have been formed by the liver enzyme system.

Experiments by Kauhanen (1977) at the Stanford Research Institute also indicate that ethylene oxide gives positive results in the Ames

mutagenesis assay in a dose-dependent manner in tester strains TA1535 and TA100. Ethylene oxide concentrations from 0.01% to 0.1% produced mutations without S-9 mix. Preliminary results reported by Embree and Hine (1975) indicated that ethylene oxide produced base-pair substitution type mutations in the Ames system in tester strain TA1535 without activation.

Ethylene oxide has also been shown to produce mutations in a wide variety of other test systems. Tanooka (1979) has shown a time-dependent killing by ethylene oxide of spores of Bacillus subtilis deficient in DNA polymerase-I as compared to control wild type spores, and a time-dependent increase in back mutations to histidine positive in this organism. In both experiments, the spores were exposed, in the dry state, to an atmosphere of 27.3% ethylene oxide and 72.7% freon (v/v). Back mutations (≈1000) were induced at the adenine locus of Neurospora crassa by a 15-minute exposure of the mold to 0.025 M ethylene oxide (Kolmark and Westergaard, 1953).

Studies with Drosophila melanogaster (Fahmy and Fahmy, 1970) have shown that ethylene oxide (114 mM) microinjected into adults produces point mutations, chromosome deletions, and chromosome breaks. Ethylene oxide (0.8%) injected into Drosophila has also been shown to increase the number of lethal mutations observed (Bird, 1952).

The mutagenicity of ethylene oxide has been evaluated by Embree and Hine (1975) in several mammalian assay systems. Rats exposed by inhalation to ethylene oxide for 4 hours at 1000 ppm showed mutagenic effects in the dominant lethal assay. Ethylene oxide produced an increase in the ratio of dead implants to total implants but did not increase preimplantation losses. Rats exposed to 250 ppm ethylene oxide by inhalation 7 hours per day for 3 days showed mutagenic effects in bone marrow samples. Twenty-four hours after exposure, these bone marrow samples showed increased chromatid and isochromatid

gaps, increased breaks, rearrangements and exchanges, and increased chromatid rings. Total aberrations were increased from 6% to 84% in metaphases examined. Examination of erythrocytes indicated that ethylene oxide induced an increase in red blood cells with micronuclei following a single 4-hour exposure to concentrations of 50 to 1000 ppm. Experiments conducted by Appelgren and coworkers (1978) using this micronucleus test indicated ethylene oxide-induced mutations in both mice and rats. Ethylene oxide (aqueous) administered intravenously twice (30 hours and 6 hours before sacrifice) at a dose of 100 mg/kg also increased ($P > 0.05$) the proportion of polychromatic erythrocytes showing micronuclei in the test animals. This effect was shown to be dose dependent in mice. Severe bone marrow depression in rats prevented testing of ethylene oxide over an extended concentration range.

Strekalova (1971) reported that oral administration of 9 mg/kg aqueous ethylene oxide produced increased chromosomal fragments and bridges in rat femur bone marrow at 24 and 48 hours following exposure.

(6) Teratogenicity

In an inhalation teratogenicity study, Snellings and coworkers (1979) exposed rats from day 6 to day 15 of gestation to 10 to 100 ppm ethylene oxide (6 hours/day). Evaluation of day 20 fetuses showed no developmental effects other than a reduced body weight in the 100 ppm group.

Kimmel and Laborde (1979) injected ethylene oxide intravenously into the tail veins of female mice at doses of 75 mg/kg and 150 mg/kg daily for 3 days at 4 periods during gestation: days 4-6, 6-8, 8-10, and 10-12. Mice receiving 150 mg/kg showed toxic symptoms (unspecified) during treatment, but they recovered and showed no ultimate change in maternal weight gain during pregnancy. Litters were examined at day 17 of gestation. Animals treated during the first and last gestation periods with ethylene oxide showed an

increase in the percentage of resorptions, and a significant increase in malformations were seen in animals treated on days 6-10 of gestation at the high (150 mg/kg) ethylene oxide level. Malformations noted included fused vertebral arches, fused and branched ribs, scrambled sternabrae, and some exencephaly. Embryotoxicity and teratogenicity as a result of this route of exposure to ethylene oxide are thus indicated.

(7) Reproductive Effects

In chronic inhalation studies, Strekalova and coworkers (1975) continuously exposed male rats to 2 ppm and 62 ppm ethylene oxide for 66 days. Both levels produced an increase in fetal deaths in untreated pregnant rats.

In the study by Snellings et al. (1979) (Section 14.a.(6)), reproductive effects were studied following exposure of male and female weanling rats to 10 to 100 ppm ethylene oxide 6 hours per day, 5 five days per week, for 12 weeks. Animals were mated and ethylene oxide exposure was continued through day 19 of gestation. Female rats exposed to 100 ppm ethylene oxide had a longer gestation period, reduced fertility index, and significantly fewer pups per litter. No differences were found for gestation survival or postpartum survival. The effects seen are probably the result of the nonspecific toxicity produced by this level of ethylene oxide inhalation.

(8) Other Relevant Information

The distribution of inhaled ethylene oxide was studied in mice with radioactively labeled (1,2-^{3}H)ethylene oxide by Ehrenberg et al. (1974). Following exposure of mice to 1.1 ppm labeled ethylene oxide for 75 minutes, high levels of radioactivity were measured in the lungs, kidney, liver, testis, and moderate levels in the brain and spleen. Approximately 80% of the radioactivity absorbed was excreted in the urine within 48 hours, indicating

rapid urinary elimination. The only urinary metabolite characterized was 1-hydroxyethyl guanine which accounted for a minor amount (0.007%) of the total urinary radioactivity. Tissue proteins isolated from lung, liver, kidney, spleen, and testis were alkylated *in vivo* by ethylene oxide, as was a nucleic acid fraction of the kidneys. Thus, ethylene oxide distributes and reacts extensively throughout the body. A biological half-life for ethylene oxide following intraperitoneal injection was determined to be 9 minutes.

Martis *et al.* (1979) reported that 24 hours were required for complete elimination in dogs of intravenously administered (25 and 75 mg/kg) ethylene oxide.

Appelgren and coworkers (1977) carried out whole body autoradiography on mice that were injected intravenously with radioactive [^{14}C]ethylene oxide (label position unspecified). Preliminary inhalation studies with labeled ethylene oxide showed a similar tissue distribution of the compound as that seen following intravenous injection, except for a high initial labeling of respiratory mucosa (data not shown). Concentrations of radioactivity 2 to 3 times those seen in the blood were observed after 2 minutes in the liver, kidney, and pancreas. Tissue labeling after 20 minutes to 4 hours showed high levels in the liver, kidney, lung, intestinal mucosa, epididymis, cerebellum, and testes. Twenty-four hours after injection, radioactivity was still found in the liver, intestinal mucosa, epididymis, cerebellum, bronchi, and bone marrow. Since these observations were made on autoradiographs, quantitative results were not reported.

b. Human Studies

(1) Pharmacokinetics

No information was found in the literature searched.

(2) Health Effects

Ethylene oxide toxicity following acute vapor exposure has been reviewed in several sources (Hollingsworth et al., 1956; Curme and Johnston, 1952). In cases of industrial exposure that caused systemic poisoning, workers complained of headache, vomiting, dyspnea, diarrhea, and respiratory irritation (von Oettingen, 1939; Blackwood and Erskine, 1938; Ind. Hyg. Newsletter, 1947). Symptoms of poisoning have been reported to be delayed by several hours following exposure (Sexton and Henson, 1949). When exposed workers were examined for hematological changes, elevated leukocyte counts have been observed (von Oettingen, 1939; Sexton and Henson, 1949). Thiess (1963) reported that high concentrations of ethylene oxide for brief periods produced bronchitis, pulmonary edema, and emphysema in industrial accidents. In a controlled investigation of the effects of ethylene oxide on human volunteers, Greaves-Walker and Greeson (1932) observed that ethylene oxide at approximately 2200 ppm was slightly irritating to 4 subjects. At a 5-fold higher concentration, the compound had a definite irritating effect on nasal mucosa within about 10 seconds.

The dermatological effects of ethylene oxide contact were reviewed by Taylor (1977). Pure ethylene oxide evaporates rapidly from the skin and produces a freezing effect. Burns ranging from first degree through third degree severity have been seen after exposure to ethylene oxide solutions. Skin exposed to 1% ethylene oxide developed large vesiculated blisters without significant erythema (Sexton and Henson, 1949). Burns have also been caused by residual ethylene oxide in clothing or foot wear that was either treated with the compound or accidentally contaminated with ethylene oxide (Phillips and Kay, 1949; Royce and Moore, 1955; Biro et al., 1974; Adams, 1976). Sexton and Henson (1950) tested human subjects for dermal reactions to aqueous ethylene oxide

solutions. The most severe development of characteristic bullae (blisters) was with a 50% ethylene oxide solution. Three of 8 volunteers showed signs of delayed skin sensitization.

In a study of chemical burns of the human cornea, McLaughlin (1946) reported an acute case induced by ethylene oxide; prompt healing was observed in the 48 hours following a corneal denudement procedure. Theiss (1963) described two cases of accidental eye injury with ethylene oxide. A nurse was exposed to a direct blast of ethylene oxide from a sterilizer cartridge and developed an epithelial keratitis of the cornea within 3 hours. Within 24 hours, the eye was entirely normal. The second case involved a patient who received a squirt of liquid ethylene oxide (concentration not stated) in the eye. After extensive washing, irritation of the conjunctivae followed and persisted for about 1 day.

Clinical reports of hemolysis following use of ethylene oxide-sterilized plastic tubings have been made by Hirose and coworkers (1953) and Clarke and coworkers (1966). Ethylene oxide, rather than a chemical reaction product, was implicated since this type of effect can be prevented by extensive aeration of ethylene oxide-sterilized plastic devices.

Anaphylactic reactions have been observed in patients using ethylene oxide-sterilized plastic tubing for hemodialysis (Poothullil et al., 1975; Bell and Dolovich, 1978) or cardiac catherization (Pessayre and Trevoux, 1978). These symptoms included uticaria, breathlessness, and hypotension. In a follow-up study on a patient apparently sensitized to contact with hemodialysis tubing, Dolovich and Bell (1978) illustrated that this patient showed a positive skin test response to ethylene oxide-serum albumin conjugate and produced in vitro histamine release to this antigen. This response indicates that a specific IgE antibody to ethylene oxide had been induced in this patient.

(3) Target Organ Toxicity

Gross et al. (1978, 1979) have reported on 4 cases of sensory-motor peripheral neuropathy following exposure to ethylene oxide from a defective sterilizer. The workers were exposed from 2 weeks to 2 months to intermittent concentrations of greater than 700 ppm ethylene oxide. Neurological symptoms included weakness, a decrease in deep tendon reflexes, decreased sensation in the lower extremities, and abnormal nerve conduction. There was symptomatic improvement 2 weeks after cessation of ethylene oxide exposure; however, 2 patients showed no improvement in nerve conductivity after nearly 1 year of follow-up examination. Jensen (1977, unpublished) reports that 3 workers using an ethylene oxide sterilizer were hospitalized for neuropathy of the lower limbs. Follow-up indicated these effects were reversible.

(4) Epidemiology

An investigation of health incidents in Veterans Administration hospitals (162 hospitals and 7 outpatient clinics) using ethylene oxide sterilization equipment indicated that, in an 8-year period, several employees suffered watering eyes, nausea, and skin irritation (Glazer, 1977).

Joyner (1964) conducted a retrospective morbidity study of 37 male employees at an ethylene oxide production plant. These 29- to 56-year old male workers were exposed to 5 to 10 ppm for a period of 5 to 16 years. Controls consisted of operators assigned to other production units, with no indication of types of chemical exposure in these units. Three ethylene oxide operators refused to participate in the study, but their previous medical records were used in the overall evaluation. Workers exposed to ethylene oxide who had left the plant were not included. No significant increase in health problems relative to controls was found. This evaluation should identify major toxic effects of ethylene oxide, but the size of the group studied, the exposure

duration, and the duration of observation preclude any evaluation of more subtle toxic or carcinogenic responses.

Hematological and chromosomal studies were performed on all factory workers (male) in a Swedish ethylene oxide production factory during 1960 and 1961 (Ehrenberg and Hallstrom, 1967). Workers were classified in one of the following three groups: 66 persons not in contact with ethylene oxide, 86 persons in permanent contact, and 8 persons exposed to high accidental concentrations of ethylene oxide. The comparison of exposed and control groups indicated certain differences. Certain cellular abnormalities, such as 3 cases of anisocytosis and 1 case of leukemia, were observed in the exposed group. Lower hemoglobin values were found in the exposed group. The high ethylene oxide (accident) exposure group showed higher numbers of chromosomal aberrations. Statistical evaluation of these findings was not available for examination. A follow-up of this study is planned.

Recently, a study of 230 Swedish factory workers exposed to 20 $\pm$ 10 ppm (TWA) ethylene oxide over a 9-year period was reported (Hogstedt et al., 1979a). Three cases of leukemia were found in the 236 workers compared with an expected 0.2 case incidence in this population. The gas used for sterilization of hospital products was an equal mixture of ethylene oxide and methyl formate. Leakage from gas-sterilized storage boxes located in a working-hall area could have produced local levels of 150 ppm. Monitoring of ethylene oxide levels was done only recently, and correlation with levels several years previously may be poor. Methyl formate may have contributed to the effects seen, but it is less volatile than ethylene oxide and less reactive chemically. Latency time for the 3 leukemia cases was 4 years, 6 years, and 8 eight years, respectively.

Hogstedt et al. (1979b) have also studied a cohort of workers in a Swedish ethylene oxide production plant. The cohort was subdivided into a control group that was not exposed to ethylene oxide, a group only intermittently exposed, and a high exposure group. The high exposure group showed an increase in total deaths and an increase in deaths caused by tumors and circulatory disease. This increase was apparent when the high exposure group was compared with either the control group or the national age specific death rate for Sweden. Excessive incidences of both leukemia and stomach tumors were noted. The increased incidence of cancer could not be attributed solely to ethylene oxide because workers were also exposed to the known carcinogens ethylene dichloride, bis(2-chloroethyl)ether, and chloroform in this production facility.

Yakubova and coworkers (1976) reported that pregnant workers in ethylene oxide production facilities were prone to miscarriages and toxicosis in the second half of pregnancy. Levels of exposure and quantitation of effects were not available for analysis.

15. Ongoing Studies

Carcinogenicity testing of ethylene oxide in mice exposed via inhalation is currently being conducted by the National Toxicology Program (NTP, 1980). Mutagenicity testing of ethylene oxide (mouse sperm head morphology assay) is also in progress (NTP, 1980).

Chronic toxicity testing of ethylene oxide in rats and monkeys at dose levels of 50 and 100 ppm is currently being sponsored by the Division of Biomedical and Behavioral Science of NIOSH (SSIE, 1981); exposures are for 6 to 7 hours daily, 5 days per week for 18 months. A teratogenicity reproductive effects study of ethylene oxide is also planned by this a division of NIOSH (SSIE, 1981).

ICRDB (1980a, 1980b) has reported on two epidemiology studies on groups exposed to epoxides. Thiess et al. are conducting a survey of the health effects in the chemical industry in Germany, and Rinsky and Oser are studying mortality of workers exposed to ethylene oxide in the United States. It has been reported in Tox-Tips (1980) that Union Carbide Corporation is studying mortality patterns of employees exposed to ethylene oxide in its Kanawha Valley plant.

16. Exposure Standards

The ACGIH currently recommends a Time-Weighted Average (TWA) Threshold Limit Value (TLV) of 10 ppm for ethylene oxide (ACGIH, 1981). A reduction of the recommended standard to 5 ppm has been proposed, however, because the compound is suspect of carcinogenic potential for man. OSHA (1976) has promulgated a standard of 50 ppm for occupational exposure to ethylene oxide.

In 1965, the Dow Chemical Company provided some estimates for ethylene oxide limits (Kereluk, 1971).

Exposure	Ethylene Oxide
Daily, up to 8 hours	50 ppm
Single, for several hours	150 ppm
Single, for 1 hour	500 ppm

17. Sources of Additional Relevant Information

Bogyo et al. (1980) have prepared a review of the health and environmental effects of organic oxides for the U.S. Environmental Protection Agency. Ethylene oxide was one of the compounds covered in this review.

NIOSH Health Hazard Evaluations (HHEs) relating to ethylene oxide have been conducted at the following facilities:

	HHE No.
Hospal Medical Corp. Littleton, CO	78-70-528
Swedish Hospital Seattle, WA	78-42-498
Boulder Memorial Hospital Boulder, CO	TA/78-36
Xomed Co. Cincinnati, OH	TA/77-32
Harpers Ferry Center Museum Laboratory Harpers Ferry, WV	TA/76-92

The industries that produce and use ethylene oxide have formed the Ethylene Oxide Industry Council to develop scientific data and provide information on the safe manufacturing and use of this compound (Occupational Health and Safety, 1981).

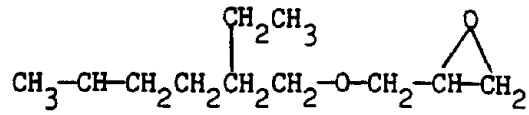
18. Other Pertinent Data

American Hospital Supply filed evidence with the U.S. Environmental Protection Agency that a statistically significant difference was observed in chromosomal aberrations in individuals exposed to ethylene oxide (Pestic. Toxic Chem. News, 1980; NTP, 1980).

H. 2-ETHYLHEXYL GLYCIDYL ETHER

1. Chemical Name: 2-Ethylhexyl Glycidyl Ether

2. Chemical Structure:



3. Synonyms: Glycidyl 2-ethylhexyl ether
1-Glycidyloxy-2-ethylhexane
Oxirane, (2-ethylhexyloxy)methyl-

4. Chemical Abstract Service (CAS) Number: 2461-15-6

5. Registry of Toxic Effects of Chemical Substances (RTECS) Number:

Not listed

6. Chemical and Physical Properties:

Description:	colorless liquid
Molecular Weight:	186.29
Boiling Point:	118-120°C (20 mm Hg)
Melting Point:	---
Vapor Pressure:	---
Solubility:	---
Specific Gravity:	0.893^{20}_{4}
Stability:	combustible

7. Production

Data available from the U.S. EPA (1980) regarding producers of 2-ethylhexyl glycidyl ether and production volumes are presented in Table 10.

8. Use

Patent literature indicates that ethylhexyl glycidyl ether is useful in the production of surfactants and resins.

9. Manufacturers and Distributors

See Table 10.

Table 10. Producers of 2-Ethylhexyl Glycidyl Ether and Production Ranges (U.S. EPA, 1980)

Producer	Type of Production	1977 Production Range
AZS Chemical Co. Atlanta, GA	Manufacturer	none
AZ Products Eaton Park, FL	Manufacturer	1-10 thousand lb
Wilmington Chemical Co. Wilmington, DE	Manufacturer	10-100 thousand lb
Marubeni America Corp. New York, NY	Importer	none

10. Manufacturing Processes

The specific manufacturing process is not available; however, glycidyl ethers are commonly made via condensation reactions with epichlorohydrin (Oosterhof, 1975a).

11. Impurities or Additives

There is no evidence in the literature searched to indicate the presence of impurities or deliberate additives in commercially produced 2-ethylhexyl glycidyl ether.

12. Occupational Exposure

The National Occupational Hazard Survey does not provide an estimate of the number of workers who are potentially exposed to 2-ethylhexyl glycidyl ether.

13. Control Technology and Work Practices

Specific factors that may contribute to or prevent employee exposure to 2-ethylhexyl glycidyl were not found in the literature searched.

14. Biological Effects

No information was found in the literature searched.

15. Ongoing Studies

No current toxicological or environmental studies of 2-ethylhexyl glycidyl ether were found.

16. Exposure Standards

No recommended or promulgated occupational exposure standards for 2-ethylhexyl glycidyl ether were found.

17. Sources of Additional Relevant Information

No sources of additional relevant information were identified.

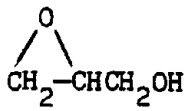
18. Other Pertinent Data

No other information that would aid in the assessment of 2-ethylhexyl glycidyl ether as an occupational hazard was found in the literature searched.

I. GLYCIDOL

1. Chemical Name: Glycidol

2. Chemical Structure:



3. Synonyms: Epihydrin alcohol
2,3-Epoxy-1-propanol
Glycide
Glycidyl alcohol
3-Hydroxy-1,2-epoxypropane
3-Hydroxypropylene oxide
Methanol, oxiranyl-
Oxirane methanol

4. Chemical Abstract Service (CAS) Number: 556-52-5

5. Registry of Toxic Effects of Chemical Substances (RTECS) Number:

4B4375000

6. Chemical and Physical Properties:

Description:	colorless, slightly viscous liquid
Molecular Weight:	74.08
Boiling Point:	162-167°C (with decomposition)
Melting Point:	81°C
Vapor Pressure:	0.9 mm Hg (25°C)
Solubility:	soluble in water, alcohol, and ether
Specific Gravity:	1.1143^{25}_{4}
Stability:	combustible

7. Production

Glycidol is commercially produced as either an on-plant site intermediate for the production of glycerin or as an end-use product. FMC Corp. (Bayport, TX) manufactures glycerin via an allyl alcohol-peracetic acid-glycidol to glycerine process at a 40 million pounds per year plant (SRI International, 1980); capacity to produce glycidol is, therefore, on the order of 32 million

pounds. As an end-use product for sale, glycidol is commercially available in developmental quantities (Riesser, 1979).

8. Use

The largest volume use of glycidol is an on-site intermediate in the production of glycerin.

As an end-use product, glycidol is used as a stabilizer for natural oils, as a demulsifier, as a dye leveling agent, as a stabilizer for vinyl polymers (Hawley, 1977), as a sterilant for aqueous drug compositions (Doyle, 1969), and in the synthesis of hydraulic fluids with toluenediamine (Milligan and Gilbert, 1978).

9. Manufacturers and Distributors

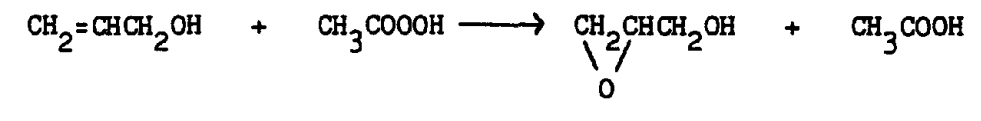
FMC Corp. (Bayport, TX) manufactures glycidol as an on-site intermediate for glycerin production (SRI International, 1980). As an end-use product, glycidol is manufactured by Dixie Chemical Co. in Bayport, TX (SRI International, 1980; USITC, 1980).

Distributors include (1980-81 OPD Chemical Buyers Directory, 1980; Chem Sources - USA, 1980):

Aldrich Chem.	Eastman Kodak
Bio-Clinical Lab.	EM Lab
Chem. Procurement Lab.	Fisher Sci.
Chem. Services	ICN/K and K
Columbia Organics	MCB Reagents
Degussa Corp.	Pfaltz and Bauer
Dynamit Nobel	Polysciences
Eastern Chem.	Tridom Chem.

10. Manufacturing Processes

As an on-site intermediate, glycidol is produced as shown in the following equation (Oosterhof, 1976):



allyl alcohol peracetic acid glycidol acetic acid

The glycidol is then converted to glycerin via hydrolysis.

As an end-use product, glycidol is produced by isolating the products of mild saponification of either isomeric monochlorohydrin with alkaline catalysts (Riesser, 1979).

11. Impurities or Additives

Technical grade glycidol contains varying amounts of polymer (Aldrich, 1980).

12. Occupational Exposure

The National Occupational Hazard Survey indicates that 36,697 workers are potentially exposed to glycidol.

13. Control Technology and Work Practices

Specific factors that may contribute to or prevent employee exposure to glycidol were not found in the literature searched.

14. Biological Effects

a. Animal Studies

(1) Acute Exposures

The acute toxicity of glycidol is summarized in Table 11. Hine et al. (1956) described the effects of oral exposure to glycidol as central nervous system depression with animals being comatose at death. Animals that survived treatment showed heightened central nervous system activity with tremors and hypersensitivity to sound. On inhalation exposure, dyspnea, lacrimation, salivation, nasal discharge, and aerophagia were observed prior to depression in lethal exposure.

Hine et al. (1956) also reported that glycidol was a moderate skin and severe eye irritant in rabbits.

Table 11. Acute Toxicity of Glycidol

Route	Species	Sex	Dose	Response	Reference
oral	rats	M	850 mg/kg	LD50	Hines et al. (1956)
oral	mice	M	450 mg/kg	LD50	Hines et al. (1956)
i.p.[a]	rats	M	466 mg/kg	LD50	Andersen et al. (1980)
i.p.[a]	mice	NS	500-1000 mg/kg	LD50	Beck et al. (1936)
i.p.[a]	mice	NS	431 mg/kg	LD50	Ivanov et al. (1980); Mel'nikova and Klyachkina (1979)
inhalation	rats	NS	1260 mg/m^3 for 4 h[b]	LC50	Ivanov et al. (1980); Mel'nikova and Klyachkina (1979)
inhalation	mice	NS	1069 mg/m^3 for 4 h[b]	LC50	Ivanov et al. (1980); Mel'nikova and Klyachkina (1979)
inhalation	mice	M	1362 mg/m^3 for 4 h[b]	LC50	Hines et al. (1956)
inhalation	mice	M	1755 mg/m^3 for 8 h[b]	LC50	Hines et al. (1956)
percutaneous	rabbit	M	1980 mg/kg	LD50	Hines et al. (1956)

[a] i.p. = intraperitoneal

[b] h = hour

(2) Subchronic Exposures

Hine et al. (1956) exposed 10 rats to repeated 7 hour exposure of 1211 mg/m^3 (400 ppm) for 5 days per week for 10 weeks. Treatment related deaths were not reported, and changes in weight gain, organ weights (kidneys, liver and lungs), and organ to body weight ratios were not observed. There was a slight but significant increase in hemoglobin.

(3) Chronic Exposure

No information was found in the literature searched.

(4) Carcinogenicity

Van Duuren et al. (1967) treated 20 1CR/Ha female Swiss mice with glycidol by skin painting. The mice were painted with approximately 5 mg of the compound in acetone 3 times per week for a total of 520 days. Glycidol did not produce a carcinogenic response in this study. The same results have been reported in Van Duuren (1967); however, this report contains less experimental detail.

(5) Mutagenicity

Glycidol has been assayed for mutagenicity in both bacteria and yeast; the results of these assays are summarized in Table 12. Positive results were obtained with both organism in the absence of a mammalian metabolic activation system. Although positive results have also been demonstrated with mammalian activation (Rosenkranz and Poirier, 1979), the mutagenic response was lower.

Hemminki (1979) and Hemminki et al. (1980) have obtained DNA adducts when glycidol was incubated at a high concentration with either single or double stranded DNA or with deoxyguanosine. The reaction proceeds faster with single stranded DNA than with double stranded DNA. Using

Table 12. Mutagenicity of Glycidol

Type of Assay	Organism	Strain	With Mammalian Metabolic Activation	Dose/Plate	Results	References
reverse mutation	S. typhimurium	TA1535	no	500 μg	+	McCann et al., 1975
reverse mutation	S. typhimurium	TA1535	no	200 μg	+	Wade et al., 1978
		TA100	no	200 μg	+	
reverse mutation	S. typhimurium	TA100	yes/no	100 μg	+	Wade et al., 1979
		TA98	yes/no	500 μg	-	
reverse mutation	S. typhimurium	TA1535	no	50 μg	+	Simmon, 1979a
		TA100	no	50 μg	+	
reverse mutation	S. typhimurium	TA1535	yes/no	10,000 μg	+	Rosenkranz and Poirer, 1979
mitotic recombination	S. cerevisiae	D3	yes/no	0.25% vol/vol	+	Simmon, 1979b
forward mutation	S. cerevisiae	NS	no	10%	-	Izard and Libermann, 1978
reverse mutation	S. cerevisiae	S211	no	10%	+	Izard and Libermann, 1978
		S138	no	10%	-	
reverse mutation	N. crassa	W40	no	0.5 M	+	Kolmark and Giles, 1955
DNA modification	E. coli	pol A^-	no	10 μl	+	Rosenkranz and Poirier, 1979

Pol A^-, Rosenkranz and Poirier (1979) have demonstrated that this strain of *E. coli* can modify DNA in living bacteria after exposure to glycidol.

(6) Teratogenicity

No information was found in the literature searched.

(7) Reproductive Effects

Glycidol has been shown to cause reversible sterility in male rats (Jackson *et al.*, 1970; Cooper *et al.*, 1974). Rats were treated orally for 5 consecutive days with glycidol at a dose of 100 or 200 mg/kg. After treatment, the males were tested for fertility by weekly mating with proven females. Sterility was 100% for 3 weeks from the initial dose, with fertility returning on week 4. Treatment related epididymal spermatociles were observed in some animals. Lower doses of 40 mg/kg caused preimplantation losses of 40% in the first week and 95% in the second week. At 20 mg/kg, the treated animals were identical to controls. Brown-Woodman *et al.* (1979) treated male rats with glycidol by intraperitoneal injection for 14 days at a dose of 3.4 mg/kg. Although fertility was not affected, sperm mobility was decreased and the epididymide to body weight ratio increased significantly over control values.

(8) Other Relevant Information

No information was found in the literature searched.

b. Human Studies

(1) Pharmacokinetics

No information was found in the literature searched.

(2) Health Effects

No information was found in the literature searched.

(3) Target Organ Toxicity

No information was found in the literature searched.

(4) Epidemiology

No information was found in the literature searched.

15. Ongoing Studies

The National Toxicology Program (NTP, 1980) has reported that glycidol is in the testing phase of a carcinogenicity bioassay.

16. Exposure Standards

The American Conference of Governmental Industrial Hygienists (ACGIH, 1981) has recommended a Threshold Limit Value (TLV) for glycidol of 75 mg/m^3 and a Short Term Exposure Limit (STEL) of 300 mg/m^3. The promulgated Occupational Safety and Health Administration Standard for glycidol is 150 mg/m^3 (OSHA, 1976).

17. Sources of Additional Relevant Information

No sources of additional relevant information were identified.

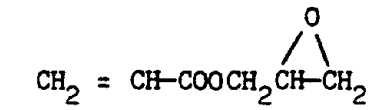
18. Other Pertinent Data

No other information that would aid in the assessment of glycidol as an occupational hazard was found in the literature searched.

J. GLYCIDYL ACRYLATE

1. Chemical Name: Glycidyl Acrylate

2. Chemical Structure:



3. Synonyms: Acrylic acid, 2,3-epoxypropyl ester
2,3-Epoxypropyl acrylate
Glycidyl propenoate
1-Propanol, 2,3-epoxyacrylate
2-Propenoic acid, oxiranylmethyl ester

4. Chemical Abstract Service (CAS) Number: 106-90-1

5. Registry of Toxic Effects of Chemical Substances (RTECS) Number:

AS9275000

6. Chemical and Physical Properties:

Description:	liquid
Molecular Weight:	128.14
Boiling Point:	57°C (2 mm Hg) with polymerization
Melting Point:	-41.5°C
Vapor Pressure:	---
Solubility:	insoluble in water
Specific Gravity:	1.1074^{20}_{20}
Stability:	combustible

7. Production

The U.S. EPA (1980) reports that Thiokol Chemical Division produced between 0.1 and 10 million pounds of glycidyl acrylate in 1977.

8. Use

Glycidyl acrylate is used as a monomer in the manufacture of thermosetting acrylic surface coating resins (Hawley, 1977).

9. Manufacturers and Distributors

Glycidyl acrylate is manufactured by Sartomer Industries in Essington and West Chester, PA (SRI International, 1980) and by Thiokol Chemical in Calvert City, KY (U.S. EPA, 1980).

Distributors of glycidyl acrylate include (Chem Sources - USA, 1980):

Chemical Procurement Lab
Columbia Organics
ICN/K and K
Monomer-Polymer and Dajac Lab
Pfaltz and Bauer
Tridom Chem.

10. Manufacturing Processes

Glycidyl methacrylate is made from epichlorohydrin and methyl methacrylate (Oosterhof, 1975b). Therefore, it is likely that glycidyl acrylate is made from epichlorohydrin and methyl acrylate.

11. Impurities or Additives

There is no evidence in the literature searched to indicate the presence of impurities or deliberate additives in commercially produced glycidyl acrylate.

12. Occupational Exposure

The National Occupational Hazard Survey does not provide an estimate of the number of workers who are potentially exposed to glycidyl acrylate.

13. Control Technology and Work Practices

Specific factors that may contribute to or prevent employee exposure to glycidyl acrylate were not found in the literature searched.

14. Biological Effects

a. Animal Studies

(1) Acute Exposures

The lethal doses of glycidyl acrylate was determined in rats by Smyth et al. (1962) following oral, dermal, and inhalation exposure. Potential for eye and skin irritation also was reported. Similar data is presented in a Union Carbide Corporation (1968) data sheet. A summary of this information is presented in Table 13. No information was found in the literature searched on the symptoms of acute exposure to glycidyl acrylate.

(2) Subchronic Exposure

No information was found in the literature searched.

(3) Chronic Exposure

No information was found in the literature searched.

(4) Carcinogenicity

No information was found in the literature searched.

(5) Mutagenicity

Hendry et al. (1951) administered glycidyl acrylate at a dose of 5 mg/kg by intraperitoneal injection to rats implanted with a Walker tumor. The animals were sacrificed 24 hours after treatment and the tumor cells and bone marrow cells were examined for chromosomal damage. The tumor cells had a 2% increase of anaphase cells with damaged chromosomes, and qualitatively, a few "sticky" chromosome bridges were observed in the bone marrow cells. Hendry et al. (1951) considered glycidyl acrylate to be inactive in this assay system.

(6) Teratogenicity

No information was found in the literature searched.

(7) Reproductive Effects

No information was found in the literature searched.

Table 13. Acute Toxicity of Glycidyl Acrylate

Route	Species	Sex	Dose	Response	Reference
oral	rat	M	232 mg/kg	LD50	Smyth et al. (1962)
oral (1% solution)	rat	---	214 mg/kg	LD50	Union Carbide (1968)
inhalation	rat	M	concentrated vapor for 30 min	maximum for no deaths	Smyth et al. (1962)
inhalation	rat	M	62.5 ppm for 4 h[a]	no deaths	Smyth et al. (1962); Union Carbide (1968)
inhalation	rat	M	125 ppm for 4 h[a]	killed all animals	Smyth et al (1962); Union Carbide (1968)
dermal	rabbit	M	440 mg/kg	LD50	Smyth et al. (1962); Union Carbide (1968)
dermal	rabbit	M	0.1 ml undiluted	necrosis of the skin	Smyth et al. (1962)
ocular	rabbit	M	0.5 ml of a 1% solution	severe burns	Smyth et al. (1962); Union Carbide (1968)

[a] h = hour.

(8) Other Relevant Information

No information was found in the literature searched.

b. Human Studies

(1) Pharmacokinetics

No information was found in the literature searched.

(2) Health Effects

No information was found in the literature searched

(3) Target Organ Toxicity

No information was found in the literature searched.

(4) Epidemiology

No information was found in the literature searched.

15. Ongoing Studies

No current toxicological or environmental studies of glycidyl acrylate were found.

16. Exposure Standards

No recommended or promulgated occupational exposure standards for glycidyl acrylate were found.

17. Sources of Additional Relevant Information

No sources of additional relevant information were identified.

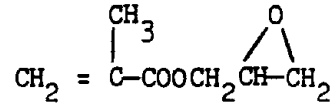
18. Other Pertinent Data

No other information that would aid in the assessment of glycidyl acrylate as an occupational hazard was found in the literature searched.

K. GLYCIDYL METHACRYLATE

1. Chemical Name: Glycidyl Methacrylate

2. Chemical Structure:



3. Synonyms: CP 105
2,3-Epoxypropyl methacrylate
Glycidyl alpha-methyl acrylate
GMA
Methacrylic acid, 2,3-epoxy propyl ester
1-Propanol, 2,3-epoxy-, methacrylate
2-Propenoic acid, 2-methyl-, oxiranylmethyl ester

4. Chemical Abstract Service (CAS) Number: 106-91-2

5. Registry of Toxic Effects of Chemical Substances (RTECS) Number:

OZ4375000

6. Chemical and Physical Properties:

Description:	liquid
Molecular Weight:	142.17
Boiling Point:	189°C
Melting Point:	83°C
Vapor Pressure:	---
Solubility:	---
Specific Gravity:	1.042
Stability:	combustible

7. Production

An exact production figure is not available; however, Blemmer Chemical operates a 3 million pound per year capacity plant (Oosterhof, 1975b).

Data available from the U.S. EPA (1980) regarding producers of glycidyl methacrylate and production volumes are presented in Table 14.

8. Use

Glycidyl methacrylate is used in radiation-cured liquid coatings for plastics and metals, intended primarily for the automobile industry (Oosterhof, 1975b).

Table 14. Producers of Glycidyl Methacrylate and Production Ranges (U.S. EPA, 1980)

Producer	Type of Production	1977 Production Range
Thiokol Chemical Div. Calvert City, KY	Manufacturer	0.1-1.0 million lb
Sartomer Co. Div. West Chester, PA	Manufacturer	confidential
Plant Site Not Listed	---	0.1-1.0 million lb

Glycidyl methacrylate is also used as a functional monomer for copolymerizations (Kine and Novak, 1978). It is used in the production of resins for restorative dental fillers (Paffenbarger and Rupp, 1979) and for hydrogel contact lenses (Refojo, 1979).

9. Manufacturers and Distributors

Glycidyl methacrylate is manufactured by (SRI International, 1980):

Blemmer Chem. Corp.	Bayport, TX
Sartomer Indust.	Essington, PA West Chester, PA

The U.S. EPA (1980) also listed Thiokol Chemical as a manufacturer.

In addition to the manufacturers, the distributors include (1980-81 OPD Chemical Buyers Directory, 1980; Chemical Week: 1981 Buyers Guide Issue, 1980; Chem Sources - USA, 1980):

Accurate Chem.	Columbia Organics
Aceto Chem.	ICN/K and K
Alcolac Inc.	Mitsubishi Gas Chem.
Aldrich Chem.	Monomer-Polymer and Dajac Lab.
Chemical Dynamics	Pfaltz and Bauer
Chem. Procurement Lab.	Tridom Chem.
Chugai International	George Uhe and Co.

10. Manufacturing Processes

Glycidyl methacrylate is manufactured from epichlorohydrin and methyl methacrylate (Oosterhof, 1975b).

11. Impurities and Additives

Commercial grade glycidyl methacrylate may contain an inhibitor of 50 ppm hydroquinone monomethyl ether (Aldrich, 1980).

12. Occupational Exposure

The National Occupational Hazard Survey indicates that 40,700 workers are potentially exposed to glycidyl methacrylate.

13. Control Technology and Work Practices

Specific factors that may contribute to or prevent employee exposure to glycidyl methacrylate were not found in the literature searched.

14. Biological Effects

a. Animal Studies

(1) Acute Exposures

There is little information on the effects of acute exposure to glycidyl methacrylate except for the reports of lethal doses by Smyth et al. (1969) and Petrove (1973). The data from these two studies is presented in Table 15.

(2) Subchronic Exposures

A study determining the maximum tolerated dose for a cancer bioassay was reported by Hadididian et al. (1968). Weanling male rats were treated by gavage 5 times per week for 8 weeks at doses of 300, 100, 30, 3, 1.0, 0.3, and 0.1 mg/animal. Of the 3 animals in each group, all died at doses of 1.0 mg/animal or greater, while none died at 0.3 mg/animal.

(3) Chronic Toxicity

No information was found in the literature searched.

(4) Carcinogenicity

Hadidian et al. (1968) treated 3 male and 3 female rats per dose group with glycidyl methacrylate by gavage. The doses used were 0.3, 0.1, 0.03, and 0.001 mg/animal. The animals were treated 5 times per week for 52 weeks, followed by an additional observation period of 26 weeks. The incidence of tumors observed in the treated animals was not considered different from the incidence in control animals.

Table 15. Acute Toxicity of Glycidyl Methacrylate

Route	Species	Sex	Dose	Response	Reference
oral	rat	M	800 mg/kg	LD50	Smyth et al. (1969)
oral	rat	---	290 mg/kg	LD50	Petrov (1973)
oral	mice	---	1050 mg/kg	LD50	Petrov (1973)
inhalation	rat	M	concentrated vapor for 2 h[a]	maximum dose for no deaths	Smyth et al. (1969)
dermal	rabbit	M	470 mg/kg	LD50	Smyth et al. (1969)
ocular	rabbit	---		severe burns	Smyth et al. (1969)

[a] h = hour.

(5) Mutagenicity

Hendry et al. (1951) administered glycidyl methacrylate at a dose of 300 mg/kg by intraperitoneal injection to rats implanted with a Walker tumor. The animals were sacrificed 24 hours after treatment and the tumor cells and bone marrow cells were examined for chromosomal damage. The tumor cells had a 1% increase of anaphase cells with damaged chromosomes, and qualitatively, a few pyknotic nuclei and "sticky" chromosome bridges were observed in the bone marrow cells.

(6) Teratogenicity

No information was found in the literature searched.

(7) Reproductive Effects

No information was found in the literature searched.

(8) Other Relevant Information

No information was found in the literature searched.

b. Human Studies

(1) Pharmacokinetics

No information was found in the literature searched.

(2) Health Effects

No information was found in the literature searched.

(3) Target Organ Toxicity

No information was found in the literature searched.

(4) Epidemiology

No information was found in the literature searched.

15. Ongoing Studies

No current toxicological or environmental studies of glycidyl methacrylate were found.

16. Exposure Standards

No recommended or promulgated occupational exposure standards for glycidyl methacrylate were found.

17. Sources of Additional Relevant Information

No sources of additional relevant information were identified.

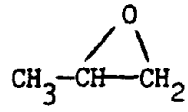
18. Other Pertinent Data

No other information that would aid in the assessment of glycidyl methacrylate as an occupational hazard was found in the literature searched.

L. PROPYLENE OXIDE

1. Chemical Name: Propylene Oxide

2. Chemical Structure:



3. Synonyms: 1,2-Epoxypropane
Ethylene oxide, methyl-
Methyl oxirane
NCI-C50099
Propene oxide
1,2-Propylene oxide

4. Chemical Abstracts Service (CAS) Number: 75-56-9

5. Registry of Toxic Effects of Chemical Substances (RTECS) Number:

TZ2975000

6. Chemical and Physical Properties:

Description:	colorless liquid, ethereal odor
Molecular Weight:	58.08
Boiling Point:	34.2°C
Melting Point:	-104°C to -112°C
Vapor Pressure:	445 mm Hg
Solubility:	59 g/100 g water; completely soluble in acetone, benzene, carbon tetrachloride, diethyl ether, and methanol
Specific Gravity:	0.826
Stability:	flammable; chemically reactive; auto-ignition temperature 869°F; flash point: -41°F; flammability limits, % by volume in air: 2.3-37

7. Production

Recent production volumes of propylene oxide are as follows (USITC, 1976-1980):

Year	Production in Million of Pounds
1979	2248
1978	2047
1977	1866
1976	1823
1975	1524
1974	1756

CMR (1979) estimates the future growth of propylene oxide to be 5.5 to 6.0% per year through 1983.

Imports of propylene oxide ranged from 20 to 33 million pounds per year from 1971 to 1975 (Blackford, 1976b); no export data for that time period were available. In 1978, 75 million pounds of propylene oxide were exported (Bureau of the Census, 1979). For 1980, exportation of propylene oxide was expected to be about 160 million pounds, with importation of approximately 40 million pounds (Key Chemicals, 1980b).

Data available from the U.S. EPA (1980) regarding producers of propylene oxide and production volumes are presented in Table 16.

8. Use

The following tabulation presents the percentage of the total amount of propylene oxide produced that is used in each of the applications listed (Lawler, 1977; Blackford, 1976b; SRC estimate):

	Percentage of Total
Polyurethane polyols	54.5
Propylene glycol	19.5
Non-urethane polyether polyols	6
Exports	6-7
Surface-active agents	4
Dipropylene glycol	2.5
Glycerine	2
Glycol ethers	2
Miscellaneous	2.5-3.5

Miscellaneous uses, not individually listed above, can represent sizeable consumption volumes. It was estimated that, in 1975, from 10 to 15 million pounds of propylene oxide were consumed in the production of isopropanol-

Table 16. Producers of Propylene Oxide and Production Ranges (U.S. EPA, 1980)

Producer	Type of Production	1977 Production Range
Olin Corp.		
Brandenburg, KY	Manufacturer	50-100 million lb
Dow Chemical		
Freeport, TX	Manufacturer	confidential
Plaquemine, LA	Manufacturer	100-500 million lb
Midland, MI	Importer	10-50 million lb
Oxirane Chemical		
Pasadena, TX	Manufacturer	500-1000 million lb
Channelview, TX	Manufacturer	50-100 million lb
BASF Wyandote		
Wyandotte, MI	Manufacturer	confidential
Jefferson Chemical		
Port Neches, TX	Manufacturer	confidential

amines (Blackford, 1976b), which are used to make isopropanolamides and isopropanolamine soaps.

Approximately 1 to 2 million pounds per year of propylene oxide are used to make propylene carbonate, which is used in solvent extractions, plasticizers, syntheses, and natural gas purification (Blackford, 1976b).

Propylene oxide has other minor applications in production of hydroxypropyl cellulose and starch and many miscellaneous chemicals. Hercules Incorporated makes a sulfur-vulcanizable elastomer from propylene oxide and allyl glycidyl ether that is trade-named Parel® and is used in automotive engine mounts. Propylene oxide is also used as a low-boiling solvent for nitrocellulose adhesives, as a fumigant, and as a food preservative (Blackford, 1976b).

9. Manufacturers and Distributors

Table 16 lists the manufacturers that produce propylene oxide at the indicated sites. As with ethylene oxide, a large percentage of the production is concentrated in the Texas and Louisiana areas.

The manufacturers of propylene oxide are the major distributors of the compound. Additional distributors of propylene oxide include the following (1980-81 OPD Chemical Buyers Directory, 1980; Chemical Week: 1981 Buyers' Guide Issue, 1980; Chem Sources - USA, 1980):

Accurate Chem.	Fisher Sci.
Aldrich Chem.	Gallard-Schelsinger
Alfa Prod.	J.F. Henry Chem.
Anachemia Chem.	Lachat Chem.
Ashland Chem.	LaPine Sci.
Atomergic Chemetals	Mallinckrodt
Bio-Clinical Lab	MC/B Reagents
J.T. Baker Chem.	McKesson Chem.
Chem Services	Pfaltz and Bauer
Eastman Kodak	Toyomenka
Electron Microscopy	Tridom Chem.
EM Lab.	Worth Chem.

10. Manufacturing Processes

Two major processes are used to manufacture propylene oxide from propylene in large quantities: peroxidation and chlorohydrination. In 1978, about 41% of the total nameplate capacity for propylene oxide was based on the peroxidation of propylene and the remainder on chlorohydrination (Blackford, 1976b).

The chlorohydrination processes for propylene oxide and ethylene oxide are somewhat similar. A typical propylene chlorohydrin plant produces, for every 100 kg of propylene oxide, about 9 kg of propylene dichloride, 2 kg of dichloropropyl ethers, and 215 kg of calcium chloride brine (Lowenheim and Moran, 1975).

The overall reaction of the chlorohydrin process for production of propylene oxide can be represented by the following sequence:

$$CH_2{=}CHCH_3 + HOCl \longrightarrow ClCH_2\underset{OH}{\overset{CH_3}{CH}}$$

$$2ClCH_2\underset{OH}{\overset{CH_3}{CH}} + Ca(OH)_2 \longrightarrow 2CH_2\underset{O}{CHCH_3} + CaCl_2 + 2H_2O$$

A diagram of a typical chlorohydrin propylene oxide plant is depicted in Figure 4. Operation is similar to that of a chlorohydrin ethylene oxide plant. While yield varies from plant to plant, the industrial average is estimated as 77% of theoretical propylene oxide from propylene yield (Blackford, 1976b).

The peroxidation of propylene to propylene oxide can be represented by the following reactions:

$$2(CH_3)_3CH + 3/2O_2 \longrightarrow (CH_3)_3COOH + (CH_3)_3COH$$

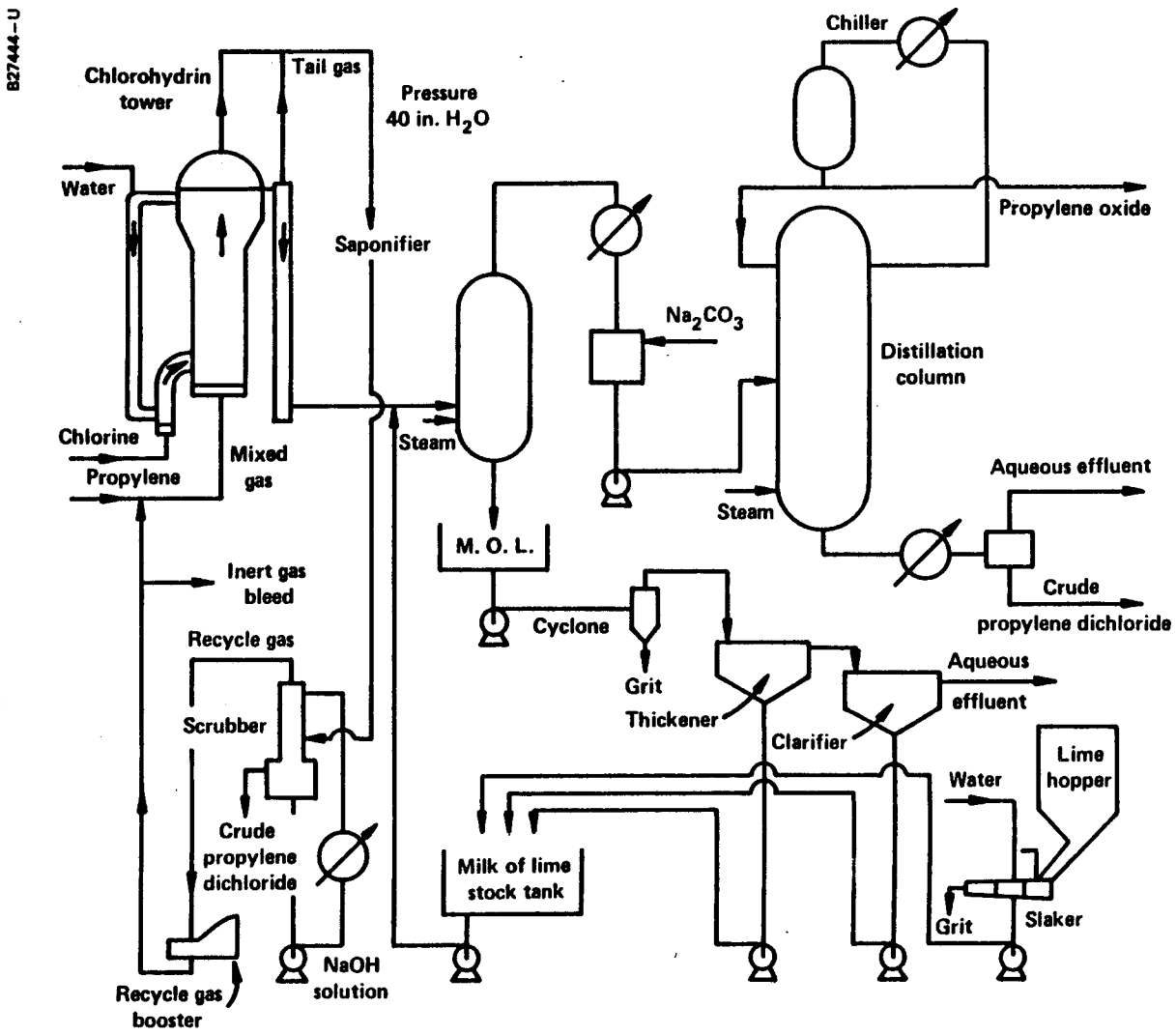


Figure 4. Diagram of a typical chlorohydrin propylene oxide plant (Fyvie, 1964).

$$CH_2CHCH_3 + (CH_3)_3COOH \longrightarrow CH_2\underset{\diagdown O \diagup}{CH}CH_3 + (CH_3)_3COH$$

Propylene oxide is produced by a two-step process. Isobutane is air-oxidized in the liquid phase to tert-butyl hydroperoxide, which is used to oxidize propylene to the oxide; the diagram of this process is shown in Figure 5. The yield of propylene oxide is about 93% of theoretical yield using the peroxidation method; approximately 2.2 kg of tert-butyl alcohol are formed per kilogram of propylene oxide produced (Lowenheim and Moran, 1975). Feeds other than isobutane can be used. For example, in 1977, Oxirane Corporation brought on-stream a 400 million pound per year propylene oxide plant in Texas that uses ethylbenzene feed instead of isobutane. In this process, ethylbenzene hydroperoxide is formed and reacted with propylene to make propylene oxide and methyl phenyl carbinol; the carbinol is used to make styrene (Soder, 1977). Because of the large amounts of coproducts formed, the economics of the peroxidation methods depend as much on the coproducts as on the propylene oxide market.

The manufacture of propylene oxide is a closed-system operation. As in the case of ethylene oxide, the most probable release of propylene oxide into the atmosphere is from fugitive emissions and from vented gases. In addition, liquid wastes from the chlorohydrination manufacturing route may contain propylene oxide.

11. Impurities or Additives

The manufacturers' specifications for commercially available propylene oxide are given in Table 17.

12. Occupational Exposure

The National Occupational Hazard Survey indicates that 268,433 workers are potentially exposed to propylene oxide.

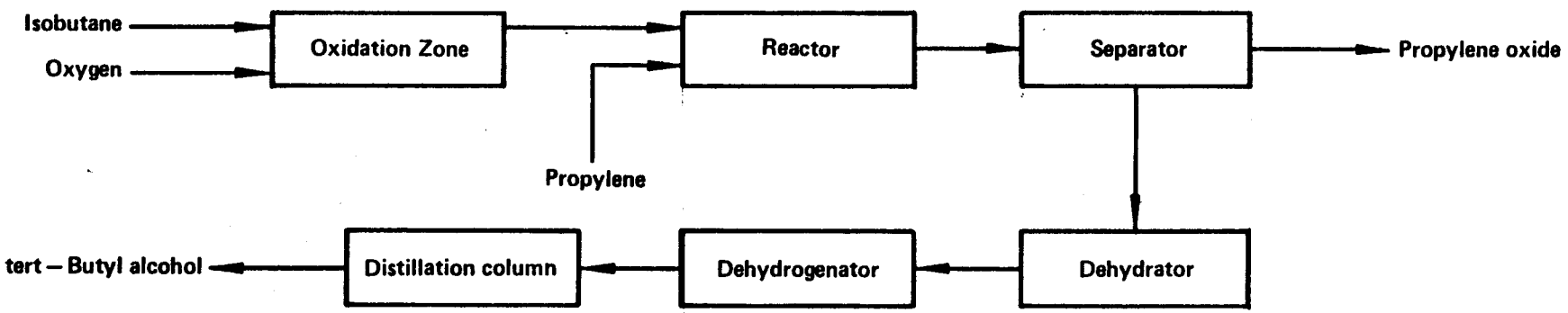


Figure 5. Preparation of propylene oxide by peroxidation of propylene (Lowenhiem and Moran, 1975).

Table 17. Manufacturers' Specifications for Propylene Oxide[a]

	Dow	Jefferson	Oxirane
Specific gravity	0.825-0.827 at 25/25°C	0.829-0.831 at 20/20°C	0.829-0.831 at 20/20°C
Acidity as acetic acid, max.	20 ppm	0.005 wt. %	0.005 wt. %
Water, max.	500 ppm	0.050 wt. %	0.050 wt. %
Chloride ion, max.	40 ppm	---	0.010 wt. %
Color, APHA, max.	5	10	10
Aldehydes, total, max.	100 ppm	0.040 wt. %	0.040 wt. %
Appearance	---	clear	clear

[a]This information was obtained from product data sheets supplied by the manufacturers.

13. Control Technology and Work Practices

Specific factors that may contribute to or prevent employee exposure to propylene oxide were not found in the literature searched.

14. Biological Effects

a. Animal Studies

(1) Acute Exposures

Acute toxicity resulting from exposure to propylene oxide is shown in Table 18. Rowe and coworkers (1956) determined that oral feeding (intubation) of 1000 mg/kg aqueous propylene oxide killed all rats tested, while a single oral dose of 300 mg/kg allowed the survival of all treated animals. Application of undiluted or strong aqueous (10% to 20%) propylene oxide solutions to the skin of rabbits for 6 minutes or longer produced hyperemia and edema. Undiluted propylene oxide produced severe burns when applied directly to the eyes of rabbits (Carpenter and Smyth, 1946).

Rats and guinea pigs exposed to high vapor concentrations of propylene oxide (4000 to 16,000 ppm) developed persistent lung irritation; secondary respiratory infections in these animals often led to death (Rowe et al., 1956). Propylene oxide was shown to have a relatively weak anesthetic effect. Rats were able to tolerate exposure to concentrations of 4000 ppm for 1/2 hour or 2000 ppm for 2 hours without organic damage. Inhalation studies with propylene oxide vapor conducted by Weil and coworkers (1963) showed that exposure of rats to concentrated vapor (a concentration approaching saturation) caused the death of all animals in 5 minutes. A concentration of 4000 ppm propylene oxide killed 4 of 6 rats exposed for a period of 4 hours.

Jacobsen and coworkers (1956) conducted inhalation studies in a number of species with propylene oxide. Symptoms produced in rats, mice, and dogs following acute exposure to propylene oxide vapor for 4 hours were

Table 18. Acute Toxicity of Propylene Oxide

Route	Species	Sex	Strain	Dose	Response	Reference
oral	rats	F	Wistar derived	603 mg/kg	LD50	Smyth et al., 1969
oral	rats	M	Wistar	1140 mg/kg	LD50	Smyth et al., 1941
oral	guinea pigs	M,F	---	690 mg/kg	LD50	Smyth et al., 1941
inhalation	rats	--	Sherman	<4000 ppm/4h[a]	LC50	Smyth and Carpenter, 1948
inhalation	rats	M	---	4000 ppm/4h	LC50	Jacobsen et al., 1956
inhalation	mice	F	---	1740 ppm/4h	LC50	Jacobsen et al., 1956
inhalation	guinea pigs	F	---	4000 ppm/4h	LCLo	Rowe et al., 1956
inhalation	dogs	M	Beagle	2000 ppm/4h	LCLo	Jacobsen et al., 1956
dermal	rabbits	--	---	≈1730 mg/kg	LD50	Smyth and Carpenter, 1948

[a] h = hour.

lacrimation, salivation, nasal discharge, gasping, convulsions, vomiting (in the dogs), and death. Pathologic examination of the dogs showed damage to respiratory epithelium, vascular congestion, and edema of the lungs.

(2) Subchronic Exposures

Rowe and coworkers (1956) performed experiments on repeated inhalation exposure to propylene oxide vapor. Guinea pigs, rabbits, and one monkey survived 79 to 154 7-hour exposures to 457 ppm propylene oxide. Rats showed increased mortality from pneumonia. Pathological examinations performed on these animals revealed slight alveolar hemorrhage and edema, congestion of the lungs, and slight fatty degeneration of the liver (guinea pigs). At the level of 195 ppm, propylene oxide administered for 128 to 154 7-hour exposures did not induce observable toxic effects.

In subchronic vapor inhalation studies conducted by Midwest Research Institute (1976) for Tracor Jitco Inc., mice were exposed for 6 hours per day for 63 days to propylene oxide vapor. At the highest level tested (500 ppm), there were no deaths. A significant ($P > 0.01$) weight loss was observed in these animals, but no histopathologic changes could be seen upon tissue examination. Rats treated under the same schedule also showed total weight loss at the highest level of propylene oxide vapor tested (500 ppm).

Feeding studies with 10% propylene oxide in olive oil were conducted by Rowe et al. (1956). Following 18 doses of 300 mg/kg propylene oxide, rats showed slight weight loss, gastric irritation, and slight liver damage. Administration of 200 mg/kg in comparable studies did not produce observable toxic effects.

(3) Chronic Exposures

No information was found in the literature searched.

(4) Carcinogenicity

Injection of propylene oxide subcutaneously into rats was shown to produce local (injection site) sarcomas (Walpole, 1958). Propylene oxide dissolved in arachis oil or water was injected over 325 days for a total maximum dosage of 1.5 g/kg (schedule not specified). Eight of the animals administered propylene oxide in oil developed tumors between 507 to 739 days. Three of the animals receiving the aqueous solution of the compound developed sarcomas, 1 in 158 days and the other 2 after 737 days. These tumors (except 1 at 158 days) were quite late in developing. Since the schedule of administration is not known and control data were not reported, evaluation of these data is not possible.

Similar results were obtained by Dunkelberg (1979) with female NMRI-mice following subcutaneous injection of 0.1, 0.3, 1.0, and 2.5 mg propylene oxide per animal. Injections were given weekly and preliminary results were reported after 91 weeks. An apparent dose-dependent increase in the appearance of sarcomas at the site of injections was observed. No statistically significant increase in tumors occurred in tissues distant from the injection site.

(5) Mutagenicity

Wade and coworkers (1978) investigated the mutagenicity of propylene oxide in the Ames assay. The compound was dissolved in dimethyl sulfoxide and used in the plate incorporation assay at various concentrations. Both tester strains TA100 and TA1535 showed increased numbers of revertants over controls in the absence of metabolic activation. No dose response data were presented, but values reported were taken from the mid-point of the linear portion of a dose-response curve. Mutagenicity in TA100 was 166 revertants/1500 μg of the compound.

Bootman et al. (1979) examined the genotoxic effects of propylene oxide in both in vitro and in vivo systems. Using S. typhimurium, propylene oxide gave positive results in the spot test, plate-incorporation assay, and by the treat and plate method in strains TA100 and TA1535, but not in strains TA1537, TA1538, or TA98. Metabolic activation with rat liver homogenate had no effect on the results. Similar positive results were obtained using the spot test with E. coli stains WP2, CM871, and CM891. In cultured human lymphocytes, propylene oxide at concentrations of 1.85 and 9.25 μg/ml produced chromosome aberrations. There was no chromosome damage, however, resulting from in vivo (oral and intraperitoneal) administration of nearly lethal doses of propylene oxide to male CD-1 mice. As indirect indicators of chromosome damage, bone marrow cells were examined for micronucleated erythrocytes and male mice were used in a dominant-lethal assay.

Loveless and Wheatley (1966), citing the early studies of Rappaport, reported that propylene oxide will induce sex-linked lethal mutations in Drosophilia. Brief immersion of flies into a 10% propylene oxide solution increased the mutation rate 10-fold. Back mutations at the adenine locus of Neurospora crassa were produced after treatment with 0.5 M propylene oxide (aqueous) for 15 minutes (Kolmark and Giles, 1955).

(6) Teratogenicity

No information was found in the literature searched.

(7) Reproductive Effects

No information was found in the literature searched.

(8) Other Relevant Information

Smyth et al. (1969) examined the joint toxic action in the rat of orally administered propylene oxide in combination with 26 other industrial chemicals. The ratio of predicted to observed LD50 was greater than 1

in 2 cases and less than 1 in 24 cases; the median was 0.58. The two chemicals that produced a greater than additive toxic effect with propylene oxide were carbon tetrachloride (ratio = 1.08) and ethyl acetate (ratio = 1.22). Furthermore, Anderson and Jenkins (1977) demonstrated a 5-fold reduction in the acute oral LD50 of 1,1-dichloroethylene in rats treated with 278 mg/kg propylene oxide 1 hour prior to being challenged with the 1,1-dichloroethylene.

b. Human Studies

(1) Pharmacokinetics

No information was found in the literature searched.

(2) Health Effects

Propylene oxide shares many of the toxic properties of ethylene oxide; injuries to the eyes and skin have been reported (Hine and Rowe, 1973). Based on animal studies, Jacobsen and coworkers (1956) have estimated that propylene oxide is approximately 2 to 3 times less toxic than ethylene oxide.

(3) Target Organ Toxicity

No information was found in the literature searched.

(4) Epidemiology

No information was found in the literature searched.

15. Ongoing Studies

Chronic toxicity testing of propylene oxide in rats and monkeys at dose levels of 100 and 300 ppm is currently being sponsored by the Division of Biomedical and Behavioral Science of NIOSH (SSIE, 1981); exposures are for 6 to 7 hours daily, 5 days per week for 18 months. A teratogenicity/reproductive study of propylene oxide is also planned by this division of NIOSH.

The National Toxicology Program (NTP, 1980) has reported that reproduction and fertility assays on propylene oxide employing the rat dominant

lethal test and the mouse sperm head morphology assay have been reported or are in progress during fiscal year 1980-1981.

The ICRDB (1980a) has reported on an ongoing epidemiological study by Thiess and coworkers in Germany. Workers exposed to ethylene oxide and propylene oxide will be studied for causes of mortality and morbidity. The follow-up will include retired workers and persons who resigned their employment.

16. Exposure Standards

The ACGIH currently recommends a Time-Weighted Average (TWA) Threshold Limit Value of 20 ppm for propylene oxide (ACGIH, 1981). OSHA has promulgated a standard of 100 ppm for propylene oxide (OSHA, 1976).

In 1965, the Dow Chemical Company provided some estimates for propylene oxide limits (Kereluk, 1971).

Exposure	Propylene Oxide
Daily, up to 8 hours	100 ppm
Single, for several hours	400 ppm
Single, for 1 hour	1000 ppm

17. Sources of Additional Relevant Information

Bogyo et al. (1980) have prepared a review of the health and environmental effects of organic oxides for the U.S. Environmental Protection Agency. Propylene oxide was one of the compounds covered in this review.

18. Other Pertinent Data

No other information that would aid in the assessment of propylene oxide as an occupational hazard was found in the literature searched.

Appendix - Epoxy Compounds

The following list includes all of the epoxy compounds considered under the class definition. The compounds in the list were identified primarily from the following sources: U.S. EPA TSCA list and U.S. EPA (1980), USITC (1980), SRI International (1980), Chem Sources - USA (1980), 1980-81 OPD Chemical Buyers Directory (1980), Chemical Week: 1981 Buyers Guide Issue (1980), Kirk-Othmer's Encyclopedia of Chemical Technology, The Merck Index (1976), and Hawley (1977).

The listing has been divided into glycidyl ethers and other non-cyclic epoxy compounds. CAS numbers are given, where available, to help avoid some confusion, as these compounds can be identified by a variety of synonyms.

Glycidyl ethers	CAS No.
Allyl glycidyl ether*	106-92-3
n-Alkyl glycidyl ether*	---
n-Butyl Glycidyl ether*	2426-08-6
tert-Butyl glycidyl ether*	7665-72-7
Dodecyl glycidyl ether	2461-18-9
Ethyl glycidyl ether	4016-11-9
2-Ethylhexyl glycidyl ether*	2461-15-6
Glycidyl ether	2238-07-5
Hexadecyl glycidyl ether	---
Hexyl glycidyl ether	5926-90-9
Isopropyl glycidyl ether	4016-14-2
3-Methyl butyl glycidyl ether	---
Methylethyl glycidyl ether	---
Methyl glycidyl ether	930-37-0
2-Methyl-propyl glycidyl ether	---
Octadecyl glycidyl ether	16245-97-9
Octyl glycidyl ether	3385-66-8
Pentyl glycidyl ether	---
Propyl glycidyl ether	3126-95-2
Other epoxy compounds	
1,2-Butylene oxide*	106-88-7
Diepoxybutane	1464-53-5
Epoxybutane	26249-20-7
2,3-Epoxybutane	---
1,2-Epoxy-3-butene	930-22-3
2,3-Epoxybutyric acid, butyl ester	10138-34-8
2,3-Epoxy-2,3-dimethylbutane	5076-20-0
1,3-Epoxydodecane**	2855-19-8

2,3-Epoxy-2-ethylhexanol	78-72-8
1,2-Epoxyheptadecane**	22092-38-2
1,2-Epoxyhexadecane*	7320-37-8
Epoxyhexane	5063-65-0
1,2-Epoxyhexane	---
3,4-Epoxy-1-hexanol	67663-02-9
cis-7,8-Epoxy-2-methyl octadecane	---
4,5-Epoxy-4-methyl-2-pentyne	---
1,2-Epoxy-2-methylpropane	558-30-5
1,2-Epoxynonadecane**	67860-04-2
1,2-Epoxyoctadecane**	7390-81-0
cis-9.10-Epoxyoctadecanoic acid	24560-98-3
9.10-Epoxyoctadecanoic acid	2443-39-2
9,10-Epoxyoctadecanoic acid, 2-ethylhexyl ester*	141-38-8
Epoxyoctane	28114-20-7
1,2-Epoxyoctane	---
2,3-Epoxyoctane	---
12,13-Epoxyoleic acid	503-07-1
1,2-Epoxypentadecane**	18633-25-5
4,5-Epoxy-2-penten-1-al	---
2,3-Epoxy propionaldehyde	---
1,2-Epoxytetradecane**	3234-28-4
1,2-Epoxy-2,4,4-trimethyl pentane	107-48-2
2,3-Epoxy-2,4,4-trimethyl pentane	96-06-6
Ethylene oxide*	75-21-8
Glycidaldehyde	765-34-4
Glycidol*	556-52-5
Glycidyl acetate	6387-89-9
Glycidyl acrylate*	106-90-1
Glycidyl methacrylate*	106-91-2
Glycidyl oleate	5431-33-4
Glycidyl stearate	7460-84-6
Propylene oxide*	75-56-9

* Individual profile prepared for these compounds. n- and tert-Butyl glycidyl ether are in the same profile.

**Denotes specialty epoxides manufactured by Viking Chemical in Blooming Praire, MN. Data available from the U.S. EPA (1980) has no production volumes available. Production volumes are judged to be small, but these specialty epoxides may have some minor commercial applications.

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