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AR201-13696A

ICCA HPV PROGRAM ON EPICHLOROHYDRIN

Evaluation of acute fish and acute *Daphnia magna* study

Acute fish toxicity and acute toxicity for *Daphnia magna* are both SIDS endpoints, which means that adequate studies need to be available. Based on the evaluation of the available literature only the following reports could satisfy these endpoints:

- Mayes et al. (1982). A study to assess the influence of age on the response of fathead minnows in acute toxicity tests. Internal report of Dow Chemical U.S.A., Midland, Michigan, 30 pages.
- Gersich et al. (1985). The precision of daphnid (Dahnia magna Straus, 1820) static acute toxicity tests. Internal report of Dow Chemical U.S.A., Midland, Michigan, 29 pages.

Please find below an evaluation of these two reports.

Acute fish test

Toxicity data are reported for 3 different life stages of fish: fry, juveniles and subadults. Based on the length of the fish (Table III of the report) the juvenile fish would be the most appropriate category to satisfy the OECD guideline requirement (length of fish: 2 ± 1 cm). For these juvenile fish the pH ranged between 7.5 and 8.3 during the test, while the temperature ranged between 21.3 and 22.2 °C (see Table IV of the report).

In general the test method is described sufficiently for this test with epichlorohydrin and juvenile fish. The test material, dilution water, fish and procedures are presented in the report. The main disadvantages of the study are:

- the exposure is unknown (no analysis of test compound in solutions) and
- the full concentration-response data are not given (NOEC is unknown).

The decrease of the epichlorohydrin concentration in the test solutions can be predicted based on a hydrolysis study that has been conducted (Boelhouwers et al., 2001). This hydrolysis study was performed at 20 ° and at 35 °C. The data at 20 °C are more representative for the fish study. The half-life at 20 °C was 3.9 and 6.8 days at a pH of 7 and 9, respectively. For a pH of 8 the half-life would be equal to (3.9 + 6.8)/2 = 5.35 days. Based on the half-life of 5.35 days the decrease in concentration would be 40 % during the 4-day exposure period of the test. During the algal test the decrease of the test concentration was about 50 %, while this test revealed an EC50 (biomass integral) value of 7.1 mg/l.

The fish test revealed an LC50 value of 10.6 mg/l, which is higher than the EC50 of the algal test. Although the predicted decrease in concentration was 40 % during the fish, it is unlikely that a new fish test with constant exposure would reveal an EC50 that would be lower than the EC50 of the algal toxicity test (7.1 mg/l).

Acute *Daphnia magna* test

In general the test methods are described sufficiently for this test with epichlorohydrin and daphnids. The test material, dilution water, daphnids and procedures are presented in the report. The main disadvantages of the study are:

- the exposure is unknown (no analysis of test compound in solutions) and
- the full concentration-response data are not given (NOEC is unknown).

The decrease of the epichlorohydrin concentration in the test solutions can be predicted based on a hydrolysis study that has been conducted. This hydrolysis study was performed at 20 ° and at 35 °C. The data at 20 °C are more representative for the daphnid study. The half-life at 20 °C was 3.9 and 6.8 days at a pH of 7 and 9, respectively. According to page 8 of the daphnid report the pH fell between 7.7 and 8.3 and for this reason a pH of 8 can be considered a representative value for the daphnid study. For a pH of 8 the half-life would be equal to (3.9 + 6.8)/2 = 5.35 days. Based on the half-life of 5.35 days the decrease in concentration would be 23 % during the 2 day exposure period of the test. During the algal test the decrease of the test concentration was about 50 %, while this test revealed EC50 (biomass integral) value of 7.1 mg/l.

The *Daphnia magna* test revealed an EC50 value of 23.9 mg/l, which is higher than the EC50 of the algal test. Although the predicted decrease in concentration was 23 % for the *Daphnia magna* test, it is unlikely that a new *Daphnia magna* test with constant exposure would reveal an EC50 that would be lower than the EC50 of the algal toxicity test (7.1 mg/l).

Conclusion

According to page 7 of the OECD document "Provisional Guidance for the Initial Assessment of Aquatic Effects" (see http://www.oecd.org/ehs/sidsman.htm) , the lowest $L(E)C_{50}$ of the 3 acute toxicity test is used to derive a PNEC. Although analytical measurements are not available and although there was probably a decrease in the test concentration during the fish test and the *Daphnia magna* test, it is unlikely that new toxicity tests with constant exposure would reveal an EC50 that would be significantly lower than the EC50 of the current algal toxicity test (7.1 mg/l). For this reason an additional test with fish and/or *Daphnia magna* would not significantly change or improve the initial assessment of aquatic effects.

The full concentration-response data are not available for the fish test and the *Daphnia magna* test. However, with the available EC_{50} values we believe that the acute toxicity of epichlorohydrin for *Daphnia magna* and fish has been described sufficiently. With the available studies we are able to predict the acute toxicity on fish and water fleas, when exposure of organisms in the environment to a relatively high concentration occurs (e.g due to an accident).

Based on the previous considerations, we believe there is no need to repeat neither the acute fish study nor the acute *Daphnia magna* study.

Reference

Boelhouwers, E.J. et al. (2001)
Hydrolysis of epichlorohydrin at 20 °C and 35 °C
Solvay Pharmaceuticals Int. Doc. No. 8320/14/01

AR201-13696B

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IUCLID

Data Set

Existing Chemical	:	ID: 106-89-8
CAS No.	:	106-89-8
EINECS Name	:	1-chloro-2,3-epoxypropane
EC No.	:	203-439-8
TSCA Name	:	Oxirane, (chloromethyl)-
Molecular Formula	:	C3H5ClO

Producer related part

Company	:	Epichlorohydrin Task Group, The Society of the Plastics Industry, Inc.
Creation date	:	15.03.2002

Substance related part

Company	:	Epichlorohydrin Task Group, The Society of the Plastics Industry, Inc.
Creation date	:	15.03.2002
Status	:	
Memo	:	
Printing date	:	29.03.2002
Revision date	:	
Date of last update	:	28.03.2002
Number of pages	:	145
Chapter (profile)	:	Chapter: 1, 2, 3, 4, 5, 6, 7, 8, 10
Reliability (profile)	:	Reliability: without reliability, 1, 2, 3, 4
Flags (profile)	:	Flags: without flag, confidential, non confidential, WGK (DE), TA-Luft (DE), Material Safety Dataset, Risk Assessment, Directive 67/548/EEC, SIDS

1.0.1 APPLICANT AND COMPANY INFORMATION

Type	:	cooperating company
Name	:	Resolution Performance Products
Contact person	:	
Date	:	
Street	:	1600 Smith Street, 24th Floor
Town	:	77002 Houston, Texas
Country	:	United States
Phone	:	
Telefax	:	
Telex	:	
Cedex	:	
Email	:	
Homepage	:	

15.03.2002

Type	:	cooperating company
Name	:	Solvay
Contact person	:	
Date	:	01.02.2002
Street	:	Rue du Prince Albert 44
Town	:	B-1050 Brussels
Country	:	Belgium
Phone	:	
Telefax	:	
Telex	:	
Cedex	:	
Email	:	
Homepage	:	

15.03.2002

Type	:	cooperating company
Name	:	The Dow Chemical Company
Contact person	:	
Date	:	28.01.2002
Street	:	2020 Dow Center
Town	:	48674 Midland, MI
Country	:	United States
Phone	:	
Telefax	:	
Telex	:	
Cedex	:	
Email	:	
Homepage	:	

15.03.2002

Type	:	other: Consortia Leader
Name	:	The Society of the Plastics Industry, Inc.
Contact person	:	
Date	:	
Street	:	1801 K Street NW, Suite 600K
Town	:	Washington, DC 20006-1301
Country	:	United States
Phone	:	202-974-5200
Telefax	:	202-296-7005

Telex	:	
Cedex	:	
Email	:	
Homepage	:	

15.03.2002

1.0.2 LOCATION OF PRODUCTION SITE, IMPORTER OR FORMULATOR

Type	:	
Name of plant	:	Daiso
Street	:	
Town	:	Matsuyama
Country	:	Japan
Phone	:	
Telefax	:	
Telex	:	
Cedex	:	
Email	:	
Homepage	:	

15.03.2002

Type	:	
Name of plant	:	Daiso
Street	:	
Town	:	Mizushima
Country	:	Japan
Phone	:	
Telefax	:	
Telex	:	
Cedex	:	
Email	:	
Homepage	:	

15.03.2002

Type	:	
Name of plant	:	The Dow Chemical Company
Street	:	
Town	:	Freeport, TX
Country	:	United States
Phone	:	
Telefax	:	
Telex	:	
Cedex	:	
Email	:	
Homepage	:	

15.03.2002

Type	:	
Name of plant	:	The Dow Chemical Company
Street	:	
Town	:	Stade
Country	:	Germany
Phone	:	
Telefax	:	
Telex	:	
Cedex	:	

Email :
Homepage :

15.03.2002

Type :
Name of plant : Formosa
Street :
Town :
Country : other: Taiwan
Phone :
Telefax :
Telex :
Cedex :
Email :
Homepage :

15.03.2002

Type :
Name of plant : Hanwha Chemical
Street :
Town : Yeochon
Country : other: South Korea
Phone :
Telefax :
Telex :
Cedex :
Email :
Homepage :

15.03.2002

Type :
Name of plant : Kashima Chemical
Street :
Town : Kashima
Country : Japan
Phone :
Telefax :
Telex :
Cedex :
Email :
Homepage :

15.03.2002

Type :
Name of plant : OAO Usolyiechimprom Usolyiechimprom
Street :
Town :
Country : other: Russian Federation
Phone :
Telefax :
Telex :
Cedex :
Email :
Homepage :

15.03.2002

Type :

Name of plant : Orgsintez Sumgait
Street :
Town :
Country : other: Azerbaijan
Phone :
Telefax :
Telex :
Cedex :
Email :
Homepage :

15.03.2002

Type :
Name of plant : Qilu Petrochemical
Street :
Town : Zibo
Country : other: PRC
Phone :
Telefax :
Telex :
Cedex :
Email :
Homepage :

15.03.2002

Type :
Name of plant : Samsung Fine Chemicals
Street :
Town :
Country : other: South Korea
Phone :
Telefax :
Telex :
Cedex :
Email :
Homepage :

15.03.2002

Type :
Name of plant : Resolution Performance Products
Street :
Town : Rotterdam-Pernis
Country : Netherlands
Phone :
Telefax :
Telex :
Cedex :
Email :
Homepage :

15.03.2002

Type :
Name of plant : Showa Denko
Street :
Town : Kawasaki, Kanagawa
Country : Japan
Phone :
Telefax :

Telex	:	
Cedex	:	
Email	:	
Homepage	:	

15.03.2002

Type	:	
Name of plant	:	Solvay Electrolyse Specialitaten - GMBH
Street	:	Xantener Strasse 237
Town	:	47495 Rheinberg
Country	:	Germany
Phone	:	
Telefax	:	
Telex	:	
Cedex	:	
Email	:	
Homepage	:	

15.03.2002

Type	:	
Name of plant	:	Spolek pro Chemickou a Hunti, Vyrobu a.s. Usti nad Labem
Street	:	
Town	:	
Country	:	other: Czech Republic
Phone	:	
Telefax	:	
Telex	:	
Cedex	:	
Email	:	
Homepage	:	

15.03.2002

Type	:	
Name of plant	:	Sumitomo Chemical
Street	:	
Town	:	Niihama
Country	:	Japan
Phone	:	
Telefax	:	
Telex	:	
Cedex	:	
Email	:	
Homepage	:	

15.03.2002

Type	:	
Name of plant	:	Thai Organic Chemical
Street	:	
Town	:	
Country	:	other: Thailand
Phone	:	
Telefax	:	
Telex	:	
Cedex	:	
Email	:	
Homepage	:	

15.03.2002

Type :
Name of plant : Tianjin Dagu
Street :
Town :
Country : other: PRC
Phone :
Telefax :
Telex :
Cedex :
Email :
Homepage :

15.03.2002

Type :
Name of plant : Triplex Chemical
Street :
Town :
Country : other: Taiwan
Phone :
Telefax :
Telex :
Cedex :
Email :
Homepage :

15.03.2002

Type :
Name of plant : Verachim Giurgiu
Street :
Town :
Country : other: Romania
Phone :
Telefax :
Telex :
Cedex :
Email :
Homepage :

15.03.2002

Type :
Name of plant : Zaklady Chemiczne "Organika-Zachem" Bydgoszcz
Street :
Town :
Country : other: Poland
Phone :
Telefax :
Telex :
Cedex :
Email :
Homepage :

15.03.2002

Type :
Name of plant : ZAO Kaustic Sterlitamak, Bashkir
Street :
Town :
Country : other: Russian Federation

Phone	:	
Telefax	:	
Telex	:	
Cedex	:	
Email	:	
Homepage	:	

15.03.2002

Type	:	
Name of plant	:	Resolution Performance Products - Norco Chemical Plant
Street	:	16122 River Road
Town	:	70079 Norco, Louisiana
Country	:	United States
Phone	:	
Telefax	:	
Telex	:	
Cedex	:	
Email	:	
Homepage	:	

15.03.2002

Type	:	
Name of plant	:	Resolution Performance Products - Deer Park Manufacturing Complex
Street	:	5900 Highway 225 East
Town	:	77536 Deer Park, Texas
Country	:	United States
Phone	:	
Telefax	:	
Telex	:	
Cedex	:	
Email	:	
Homepage	:	

15.03.2002

Type	:	
Name of plant	:	Solvay Electrolyse France - Usine de Tavaux
Street	:	1 Avenue de la Republique
Town	:	39501 Travaux
Country	:	France
Phone	:	
Telefax	:	
Telex	:	
Cedex	:	
Email	:	
Homepage	:	

15.03.2002

1.0.3 IDENTITY OF RECIPIENTS

Name of recipient	:	United States Environmental Protection Agency
Street	:	Mail Code 7403, Ariel Rios Bldg., 1200 Pennsylvania Ave., NW
Town	:	20460 Washington, DC
Country	:	United States
Phone	:	
Telefax	:	
Telex	:	

Cedex	:
Email	:
Homepage	:

28.03.2002

1.0.4 DETAILS ON CATEGORY/TEMPLATE

1.1.0 SUBSTANCE IDENTIFICATION

1.1.1 GENERAL SUBSTANCE INFORMATION

Purity type	:	
Substance type	:	organic
Physical status	:	liquid
Purity	:	ca. 99.9 % w/w
Colour	:	
Odour	:	

15.03.2002 (196)

1.1.2 SPECTRA

1.2 SYNONYMS AND TRADENAMES

(Chloromethyl)ethylene oxide

14.03.2002

1,2-Epoxy-3-chloropropane

14.03.2002

1-chloro-2, 3-epoxypropane

14.03.2002

2-(Chloromethyl)oxirane

30.08.1996

2-Chloropropylene oxide

06.02.2002

3-chloro-1,2-epoxypropane

24.01.1994

3-Chlorohydrin-1,2-epoxy propane

14.03.2002

3-Chloropropene-1,2-oxide

30.08.1996

Chloromethyloxirane

28.05.1994

Chloropropylene oxide

15.03.2002

ECH (used as abbreviation)

28.05.1994

EPI [used as abbreviation]

15.03.2002

Epichlorhydrine

24.01.1994

Epichlorohydrin

Remark : Usual name.
14.03.2002

gamma-chloropropylene oxide

09.04.1993

Glycerol epichlorohydrin

14.03.2002

Glycidyl chloride

14.03.2002

1.3 IMPURITIES

Purity :
CAS-No :
EC-No :
EINECS-Name : Chlorinated ethers, chlorinated propenes
Molecular formula :
Value : < 1 % w/w

15.03.2002 (196)

Purity :
CAS-No : 7732-18-5
EC-No : 231-791-2
EINECS-Name : water
Molecular formula :
Value : <= .1 % w/w

15.03.2002 (138)

Purity	:	
CAS-No	:	96-18-4
EC-No	:	202-486-1
EINECS-Name	:	1,2,3-trichloropropane
Molecular formula	:	
Value	:	ca. .01 % w/w

15.03.2002 (137)

1.4 ADDITIVES

1.5 TOTAL QUANTITY

Remark	:	Nameplate capacitiy of plants in Western Europe as of mid-2000.
Result	:	Quantity = 270 thousands of metric tons

15.03.2002 (70)

Remark	:	Nameplate capacity of plants in Eastern Europe as of mid-2000
Result	:	Quantity = 114 thousands of metric tons

15.03.2002 (70)

Remark	:	Nameplate capacity of plants in the United States as of October 2000.
Result	:	Quantity = 1015 million pounds

15.03.2002 (70)

Remark	:	Nameplate capacity of plants in Japan in 2000
Result	:	Quantity = 137 thousands of metric tons

15.03.2002 (70)

Remark	:	Nameplate capacity of plants in the Pacific other than Japan in 1999
Result	:	Quantity = 159 thousands of metric tons in 2000

15.03.2002 (70)

1.6.1 LABELLING

Labelling	:	as in Directive 67/548/EEC
Specific limits	:	yes
Symbols	:	T, , ,
Nota	:	E, C,
R-Phrases	:	(45) May cause cancer (10) Flammable (23/24/25) Toxic by inhalation, in contact with skin and if swallowed (34) Causes burns (43) May cause sensitization by skin contact
S-Phrases	:	(53) Avoid exposure - obtain special instructions before use (44) If you feel unwell, seek medical advice (show the label where possible)

15.03.2002 (154)

Labelling : other, as in legislation: ARD/RID (Europe)
Specific limits :

Remark : Orange panel (ADR)63
6=toxic material
3=flammable material

15.03.2002 (154)

Labelling : other, as in legislation: DOT Regulations (United States)
Specific limits :

Remark : Labels: "Poison" and "Flammable Liquid" per 49 CFR 172.419 and 172.430

Label: "Marine Pollutant" - see 172.203(L)(3) and 171.4(c) for exceptions

DOT placard of "Flammable" for motor vehicles, tank cars or box cars per 172.521 and 172.542

DOT placard of "Empty" per 172.525

DOT markings of "THIS SIDE UP" for hazardous liquids per 172.312

15.03.2002 (135) (154)

1.6.2 CLASSIFICATION

Classified : as in Directive 67/548/EEC
Class of danger : carcinogenic, category 2
R-Phrases : (45) May cause cancer
Specific limits :

15.03.2002

Classified : as in Directive 67/548/EEC
Class of danger : corrosive
R-Phrases : (34) Causes burns
Specific limits :

15.03.2002

Classified : as in Directive 67/548/EEC
Class of danger : toxic
R-Phrases : (23/24/25) Toxic by inhalation, in contact with skin and if swallowed
Specific limits :

15.03.2002

Classified : as in Directive 67/548/EEC
Class of danger :
R-Phrases : (10) Flammable
Specific limits :

15.03.2002

Classified : as in Directive 67/548/EEC
Class of danger :
R-Phrases : (43) May cause sensitization by skin contact
Specific limits :

15.03.2002

1.6.3 PACKAGING

1.7 USE PATTERN

Type of use : type
Category : Non dispersive use

15.03.2002

Type of use : type
Category : Use in closed system

15.03.2002

Type of use : industrial
Category : Basic industry: basic chemicals

15.03.2002

Type of use : industrial
Category : Chemical industry: used in synthesis

15.03.2002

Type of use : industrial
Category : Polymers industry

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Type of use : industrial
Category : other

15.03.2002

Type of use : use
Category : Intermediates

15.03.2002

Type of use : use
Category : Stabilizers

15.03.2002

Type of use : use
Category : Surface-active agents

15.03.2002

1.7.1 DETAILED USE PATTERN

1.7.2 METHODS OF MANUFACTURE

Origin of substance :
Type : Production

Remark : Production processes:

The primary process for producing epichlorohydrin consists of three steps: chlorination of propylene to obtain allyl chloride, reaction of the allyl chloride with hypochlorous acid to produce glycerol dichlorohydrins, and finally reaction of the glycerol dichlorohydrin isomers with sodium hydroxide or calcium hydroxide to produce epichlorohydrin. The reactions yield hydrochloric acid, sodium chloride or calcium chloride, and water. By-products include cis- and trans-1,3-dichloropropene, 1,2-dichloropropane, and 1,2,3-trichloropropane. The reactions are carried out in closed process.

One alternative process includes use of allyl alcohol as a precursor; another uses hydrogen peroxide in the second step described above. The latter process does not appear to be performed on a commercial scale.

Crude epichlorohydrin can be used in glycerin production, or refined to produce other products such as epoxy resins.

15.03.2002 (196)

1.8 REGULATORY MEASURES

1.8.1 OCCUPATIONAL EXPOSURE LIMIT VALUES

Type of limit : MAK (DE)
Limit value : mg/m3

Remark : Skin, carcinogen
15.03.2002 (39) (115)

Type of limit : TRK (DE)
Limit value : 3 other: ppm

15.03.2002 (44)

Type of limit : other: LTEL (UK)
Limit value : 8 mg/m3

Remark : 2 ppm (8 mg/m3)
Short term exposure limit 5 ppm
Skin
15.03.2002 (115)

Type of limit : other: MAC-TGG (NL)
Limit value : 4 mg/m3

Remark : 1 ppm (4 mg/m3)
Listed as carcinogenic
MAC-K 4ppm

Skin notation

15.03.2002 (115)

Type of limit : other: PEL-TWA (US-OSHA)
Limit value : 1.9 mg/m3
Short term exposure limit value
Limit value :
Time schedule : 8 hour(s)
Frequency : times

Remark : 1.9 mg/m3 (5 ppm)
Skin Notation

15.03.2002 (115) (154)

Type of limit : other: TLV-TWA (US - ACGIH)
Limit value : 1.9 mg/m3
Short term exposure limit value
Limit value :
Time schedule : 8 hour(s)
Frequency : times

15.03.2002 (154)

1.8.2 ACCEPTABLE RESIDUES LEVELS

1.8.3 WATER POLLUTION

1.8.4 MAJOR ACCIDENT HAZARDS

1.8.5 AIR POLLUTION

1.8.6 LISTINGS E.G. CHEMICAL INVENTORIES

1.9.1 DEGRADATION/TRANSFORMATION PRODUCTS

1.9.2 COMPONENTS

1.10 SOURCE OF EXPOSURE

Remark : Exposure:
During production, engineering controls are in place, and established exposure guidelines are typically not exceeded. Closed system operations allow for the safe handling of epichlorohydrin. Sampling may introduce the potential for exposure, but this procedure can be automated. During the transfer of the epichlorohydrin, use of vapor return lines and dry disconnect fittings for transfer hoses will minimize the potential for exposure.

Workers should protect themselves by using appropriate respiratory

protection when required, and minimize skin contact by wearing protective clothing. Protective goggles, boots, gloves, and safty hats may also be required for certain operations. Workers should be trained in the proper use of machinery and personal protective equipment, as well as know the procedures to follow if exposure should occur.

Continous improvement in production process and incineration of vent gases have led to further decrease of emissions to the environment, namely the atmosphere. Epichlorohydrin will photodegrade by reacting with photochemically produced hydroxyl radicals. Proper transport and handling should minimize potential spills to aquatic or soil environments which could result in exposure to wildlife or other organisms.

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1.11 ADDITIONAL REMARKS

Remark : TRANSPORT INFORMATION

UN Number: 2023
Class: 6.1
Packing Group: II

Sea (IMO)
Class: 6.1 (subsidiary 3)
Packing Group: II
Symbol: Poison and flammable liquid
Marine Pollutant (Y/N): No

Rail/Road (RID/ADR)
Class: 6.1 (subsidiary 3)
Item: 16(b)
Symbol:Poison and flammable liquid
Kemler Plate: 63/2023

Air (IATA/ICAO)
Class: 6.1
Packing Group: II
Symbol: Poison

Proper Shipping Name: Epichlorohydrin

15.03.2002 (44) (153) (154)

Remark : CONVERSION FACTORS (20 deg C, 101.3 kPa):
1 mg/m3 = 0.265 ppm
1 ppm = 3.78 mg/m3

27.03.2002 (196)

1.12 LAST LITERATURE SEARCH

1.13 REVIEWS

2.1 MELTING POINT

Value : = -57.2 °C

03.09.2001 (174)

Value : = -57.1 °C

15.03.2002 (44)

Value : = -57 °C
Sublimation :
Method :
Year :
GLP : no data
Test substance :

17.05.1994 (153) (154) (155) (196)

Result : Range = -25.6 to -58.1 degrees C
28.03.2002 (139)

2.2 BOILING POINT

Value : = 115 °C at

15.03.2002 (196)

Value : = 116 - 117 °C at

03.09.2001 (183)

Value : = 116.1 °C at

03.09.2001 (174)

Value : = 116.2 °C at

03.09.2001 (139)

Result : 116.4 degrees C at 760 mm
15.03.2002 (44)

Result : 116 degrees C at atmospheric pressure
15.03.2002 (136) (153) (154)

2.3 DENSITY

Type : relative density
Value : = 1.18 g/cm³ at 20 °C

27.03.2002 (196)

Type : relative density
Value : = 1.181 g/cm³ at 20 °C
Method :
Year :
GLP : no data
Test substance :

27.03.2002 (55)

Type :
Value : = 1.17 g/cm³ at 25 °C

Test condition : Liquid density
15.03.2002 (153)

Type : relative density
Value : = 3.2 at °C
Method :
Year :
GLP : no data
Test substance :

Test condition : Vapour density (air = 1).
18.05.1994 (136) (154)

Type :
Value : = 3.27 at °C

Test condition : Vapor density (air = 1).
15.03.2002 (44)

2.3.1 GRANULOMETRY

2.4 VAPOUR PRESSURE

Value : = 17 hPa at 20 °C
Decomposition :
Method :
Year :
GLP : no data
Test substance :

18.05.1994 (55) (155) (196)

Value : = 29 hPa at 30 °C
Decomposition :
Method :
Year :
GLP : no data
Test substance :

17.05.1994 (155)

Result : 17 torr at 25 degrees C
15.03.2002 (153)

Result : 17 mbars at 20 degrees C
15.03.2002 (136)

15.03.2002

Result : =3.5 mmHg at 0 degrees C
=17.1 mmHg at 25 degrees C
=62.7 mmHg at 50 degrees C
=452.7 mmHg at 100 degrees C
15.03.2002 (154)

Result : 13.8 mm Hg at 70 degrees F
27.03.2002 (136)

2.5 PARTITION COEFFICIENT

Partition coefficient :
Log pow : = .26 at °C
pH value :

03.09.2001 (174)

Partition coefficient :
Log pow : = .3 at °C
pH value :

17.05.1994 (92) (139) (196)

Partition coefficient :
Log pow : = .45 at °C
pH value :

Remark : Measured value.
17.05.1994 (38)

2.6.1 SOLUBILITY IN DIFFERENT MEDIA

Solubility in :
Value : = 66 g/l at 20 °C
pH value :
concentration : at °C
Temperature effects :
Examine different pol. :
pKa : at 25 °C
Description :
Stable :

03.09.2001 (174) (196)

Solubility in :
Value : = 64 g/l at °C
pH value :
concentration : at °C
Temperature effects :
Examine different pol. :

pKa : at 25 °C
Description :
Stable :

Result : 0 - 25 degrees C
03.09.2001 (139)

Solubility in :
Value : = 60000 mg/l at 20 °C
pH value :
concentration : at °C
Temperature effects :
Examine different pol. :
pKa : at 25 °C
Description :
Stable :

03.09.2001 (183)

Solubility in :
Value : = 66 g/l at 25 °C
pH value : 5 - 6
concentration : 5 vol% at 20 °C
Temperature effects :
Examine different pol. :
pKa : at 25 °C
Description :
Stable :
Deg. product :
Method :
Year :
GLP : no data
Test substance :

18.05.1994 (55)

Solubility in :
Value : = 65 g/l at 20 °C
pH value :
concentration : at °C
Temperature effects :
Examine different pol. :
pKa : at 25 °C
Description :
Stable :
Deg. product :
Method :
Year :
GLP : no data
Test substance :

Remark : pH neutral (aqueous extract).
Soluble in most organic solvents.
18.05.1994 (155)

Solubility in :
Value : = 6.5 other: % at 20 °C
pH value :
concentration : at °C
Temperature effects :
Examine different pol. :
pKa : at 25 °C

Description :
Stable :

15.03.2002 (154)

Solubility in :
Value : = 6.6 other: %wt at 20 °C
pH value :
concentration : at °C
Temperature effects :
Examine different pol. :
pKa : at 25 °C
Description :
Stable :

15.03.2002 (44) (153)

Solubility in :
Value : = 6.69 other: %wt at °C
pH value :
concentration : at °C
Temperature effects :
Examine different pol. :
pKa : at 25 °C
Description :
Stable :

Result : 6.69 %wt. at 68 degrees F
15.03.2002 (136)

2.6.2 SURFACE TENSION

Result : 36.4 Dynes/cm at 25 degrees C
15.03.2002 (44)

Result : 26.3 Dynes/cm at 100 degrees C
15.03.2002 (44)

Result : 0.035 N.m-1 at 20 degrees C
15.03.2002 (154)

Result : 36.36 Dynes/cm at 25 degrees C
28.03.2002 (153)

2.7 FLASH POINT

Value : = 26 °C
Type : closed cup
Method : other: ABEL
Year :
GLP :
Test substance :

15.03.2002 (154)

Value : = 31 °C
Type : closed cup
Method : other: TAG
Year :
GLP : no data
Test substance :

15.03.2002 (44) (153) (154)

Value : = 34 °C
Type : open cup
Method : other
Year :
GLP :
Test substance :

27.03.2002 (196)

Value : = 87 °C
Type : closed cup
Method : other: TAG
Year :
GLP :
Test substance :

15.03.2002 (136)

2.8 AUTO FLAMMABILITY

Value : = 371 °C at

15.03.2002 (153)

Value : = 385 °C at
Method :
Year :
GLP : no data
Test substance :

17.05.1994 (55)

Value : >= 385 °C at
Method :
Year :
GLP : no data
Test substance :

02.06.1998 (154)

Value : = 416 °C at

26.04.1994 (44)

2.9 FLAMMABILITY

Method :
Year :

GLP : no data
Test substance :

Result : Lower limit = 3.8% v/v
Upper limit - 21% v/v
15.03.2002 (44) (136) (137) (153) (154) (196)

2.10 EXPLOSIVE PROPERTIES

Result : not explosive
Method :
Year :
GLP : no data
Test substance :

Remark : Explosion limits in air at 20 degree C and 1 hPa:
- lower : 3.8 vol% = 142 g/m3
- upper : 21 vol% = 785 g/m3.

Vapour-air mixtures may be explosive at high temperatures.
18.05.1994 (55) (155)

2.11 OXIDIZING PROPERTIES

2.12 DISSOCIATION CONSTANT

2.13 VISCOSITY

Result : Viscosity: 1.12 mPa.s at 20 degrees C
15.03.2002 (154) (155)

Result : Viscosity: 1.06 cp at 25 degrees C
15.03.2002 (154)

Value : = - at °C
Result :

Result : Viscosity: 1.086 cp at 25 degrees C
15.03.2002 (44)

2.14 ADDITIONAL REMARKS

3.1.1 PHOTODEGRADATION

Type	:	air
Light source	:	
Light spectrum	:	nm
Relative intensity	:	based on intensity of sunlight
INDIRECT PHOTOLYSIS		
Sensitizer	:	OH
Conc. of sensitizer	:	1500000 molecule/cm³
Rate constant	:	= .0000000000005643 cm³/(molecule*sec)
Degradation	:	% after
Deg. product	:	
Method	:	other (calculated): EPIWIN
Year	:	2000
GLP	:	
Test substance	:	other TS: Epichlorohydrin
Remark	:	Epichlorohydrin does not strongly absorb solar ultraviolet radiation, but photochemical degradation of epichlorohydrin does occur. The EPIWIN V3.05 AOPWIN modeling program that estimates atmospheric oxidation and photodegradation rates predicted the half-life of epichlorohydrin to be 18.953 days in the atmosphere. This assumes that the reaction occurs during a 12-hour day with an average atmospheric concentration of 1.5 E6 OH/cm3. In experimental studies investigating the photodecomposition of epichlorohydrin under simulated atmospheric conditions in the presence of nitric oxide, a half-life of 16 hours was determined. The experimental conditions included a light intensity approximately 2.6 times that occurring at midday in summer, a UV light source at 290 nm, and a relative humidity of 35-40%. In experimental studies using reaction rate constants estimated from structure-activity relationships, the half-life of epichlorohydrin in the atmosphere was estimated to be 2-8 days. Variations in atmospheric conditions such as UV intensity, hydroxyl radicals, humidity, nitric oxide, and temperature can affect the photodecomposition rates of epichlorohydrin.

26.03.2002

Type	:	air
Light source	:	
Light spectrum	:	nm
Relative intensity	:	based on intensity of sunlight
Spectrum of substance	:	lambda (max, >295nm) : 204 nm epsilon (max) : 27 epsilon (295) :
Conc. of substance	:	24.1 mmol/l at °C
INDIRECT PHOTOLYSIS		
Sensitizer	:	OH
Conc. of sensitizer	:	500000 molecule/cm³
Rate constant	:	= .00000000000066 cm³/(molecule*sec)
Degradation	:	ca. 50 % after 24 day(s)
Deg. product	:	
Method	:	other (calculated)
Year	:	1990
GLP	:	
Test substance	:	

Remark : ECH does not strongly absorb solar ultra violet radiation, so that direct photochemical degradation would seem unlikely [Santodonato et al. (1980); Krijgsheld & van der Gen (1986)].

Result : UV/VIS absorption spectrum for 0.25 % ECH in methanol (21.4 mmol/l) gives the following parameters:

- lambda max: 204 nm
- epsilonn max: 27 l/mol.cm

27.03.2002 (4) (43) (92) (145)

Type : air
Light source :
Light spectrum : nm
Relative intensity : based on intensity of sunlight
INDIRECT PHOTOLYSIS
Sensitizer : other: smog chamber with NOx
Conc. of sensitizer :
Rate constant : cm^3/(molecule*sec)
Degradation : % after
Deg. product :
Method : other (measured)
Year :
GLP : no data
Test substance :

Remark : Concentration data are given in ppm as temperature is not defined.

Result : After 24.4 hour irradiation, max. 0.226 ppm ozone are produced; there is no evidence of photoreaction.

Test condition : Initial concentration of ECH: 11.55 ppm; Sensitizer concentration (NOx in smog chamber): 0.427 ppm; Duration of irradiation: 24.4 hour.

26.03.2002 (53)

Type : air
Light source : Sun light
Light spectrum : > 290 nm
Relative intensity : ca. 2.6 based on intensity of sunlight
Conc. of substance : .0378 mg/l at 27 °C
DIRECT PHOTOLYSIS
Halflife t1/2 : = 16 hour(s)
Degradation : % after
Quantum yield :

26.03.2002 (41)

Type : air
Light source :
Light spectrum : nm
Relative intensity : based on intensity of sunlight

Remark : Photooxidation products foreseen by Cuppit (1980) : formaldehyde, glyoxolic acid, chloroacetylformyloxide and by Wolff (1988) : carbon dioxide, water, hydrogen chloride.

26.03.2002 (25) (194)

Type : air
Light source :
Light spectrum : nm
Relative intensity : based on intensity of sunlight

Remark : Epichlorohydrin will degrade by reaction withphotochemically produced hydroxyl radicals (t1/2 4days).

26.03.2002

3.1.2 STABILITY IN WATER

Type : abiotic
t1/2 pH4 : = 7.3 day(s) at 20 °C
t1/2 pH7 : = 3.9 day(s) at 20 °C
t1/2 pH9 : = 6.8 day(s) at 20 °C
Deg. product : no
Method : OECD Guide-line 111 "Hydrolysis as a Function of pH"
Year : 2001
GLP : yes
Test substance : other TS: Epichlorohydrin supplied by Solvay, purity of 99.9%

Result : Half-life (t(1/2) in days or hours at a specific pH (pH 4, 7, 9, and other) and temperature):

Temperature of 20 °C: 7.3 (pH=4), 3.9 (pH=7) and 6.8 (pH=9) days.

Remarks: Breakdown products are not discussed in the report. However, it is known that hydrolysis of epichlorohydrin results in the formation of 1-chloro-2,3-dihydroxypropane (= alpha-monochlorohydrin).
Test condition : Abiotic hydrolysis test at 20 and 35 degrees C
Reliability : (1) valid without restriction
Flag : Critical study for SIDS endpoint
27.03.2002 (8)

Type : abiotic
t1/2 pH4 : = 1.3 day(s) at 35 °C
t1/2 pH7 : = .8 day(s) at 35 °C
t1/2 pH9 : = 1.4 day(s) at 35 °C
Deg. product : no
Method : OECD Guide-line 111 "Hydrolysis as a Function of pH"
Year : 2001
GLP : yes
Test substance : other TS: Epichlorohydrin supplied by Solvay, purity of 99.9%

Result : Half-life (t(1/2) in days or hours at a specific pH (pH 4, 7, 9, and other) and temperature):

Temperature of 35 °C: 1.3 (pH=4), 0.77 (pH=7) and 1.4 (pH=9) days.

Remarks: Breakdown products are not discussed in the report. However, it is known that hydrolysis of epichlorohydrin results in the formation of 1-chloro-2,3-dihydroxypropane (= alpha-monochlorohydrin).
Reliability : (1) valid without restriction
Flag : Critical study for SIDS endpoint
27.03.2002 (8)

Type : abiotic
t1/2 pH4 : = 6.3 day(s) at 20 °C
t1/2 pH7 : = 6.5 day(s) at 20 °C
t1/2 pH9 : = 6.5 day(s) at 20 °C

t1/2 pH 10 : = 6.5 day(s) at 20 °C
Deg. product :
Method : other
Year : 1977
GLP : no
Test substance :

Remark : Calculated half-life values.
Recommended value : t1/2 = 6.5 days.

26.03.2002 (84)

Type : abiotic
t1/2 pH4 : at °C
t1/2 pH7 : = 8 day(s) at °C
t1/2 pH9 : at °C
Deg. product :
Method :
Year :
GLP : no data
Test substance :

Remark : Hydrolysis reaction in distilled water. Main reaction product is 3-chloro-1,2-propanediol.

26.03.2002 (145)

Type : abiotic
t1/2 pH4 : at °C
t1/2 pH7 : = 5.3 day(s) at °C
t1/2 pH9 : at °C
Deg. product :
Method :
Year :
GLP : no data
Test substance :

Remark : Hydrolysis in sea water. Reaction products are 3-chloro-1,2-propandiol and 1,3-dichloro-2-propanol.

26.03.2002 (145)

Type : abiotic
t1/2 pH4 : at °C
t1/2 pH7 : = 6.2 day(s) at 20 °C
t1/2 pH9 : at °C
Deg. product :
Method : other: water-ethanol (9:1) medium
Year :
GLP :
Test substance :

Remark : at concentration of 9.2 mg/l epichlorohydrin
Hydrolysis was also measured at pH of 2.5 and 12 with t1/2 at 3.3 and 2.6 days respectively.

26.03.2002 (126)

Type : abiotic
t1/2 pH4 : at °C
t1/2 pH7 : at °C
t1/2 pH9 : at °C

Remark : In water, evaporation will occur in t1/2=29hours in a model river, hydrolysation will occur in t1/2=8.2 days. In sea water t1.2=5.3 days due to reaction with chloride ions.

26.03.2002 (62)

Deg. product :
Method :
Year :
GLP :
Test substance : other TS: Epichlorohydrin

Remark : Scientific studies conducted, no guideline studies used.
Result : Epichlorohydrin reacts with water and degrades by a hydrolysis reaction. The half-life of epichlorohydrin for the reaction with water at room temperature to form 3-chloro-1,2-propanediol (alpha chlorohydrin) was determined to be 148 hrs, 79 hrs, and 62 hrs in neutral, acidic, and alkaline solutions, respectively. The rate of hydrolysis increased 7-fold when the temperature was increased to 40 deg C. The presence of nucleophilic ions also increased the rate of hydrolysis. The literature generally supports a half-life ranging from 96 hrs to 192 hrs in water due to hydrolysis of epichlorohydrin. The half-life of epichlorohydrin due to hydrolysis in distilled water (pH 7.0) was estimated to be 192 hrs and in seawater (pH 7.0) the half-life was estimated to be 127 hrs.
Reliability : (2) valid with restrictions
26.03.2002

3.1.3 STABILITY IN SOIL

Remark : Due to the physical properties of ECH, the calculated values for the Henry constant (2.43 Pa.m3/mol at 20 degree C), the measured log Pow (0.45), and the application of the fugacity model (stage I), a partitioning in soil or sediment is expected to be negligibly small.
26.03.2002 (38) (74) (101)

Type : other
Radiolabel :
Concentration :
Soil temperature : °C
Soil humidity :
Soil classification :
Year :

Remark : It will evaporate into the atmosphere and leach into the ground. Chemical and biodegradation will occur with rapid hydrolysis also occurring.
26.03.2002 (61)

3.2.1 MONITORING DATA

Type of measurement : background concentration
Media : surface water
Concentration :
Method :

Result : Concentration < 10 microg/l (Japan 1977).
26.03.2002 (52)

Type of measurement : background concentration
Media : sediment
Concentration :

Method :

Result : Concentration < 60 microg/kg (Japan 1977).
26.03.2002 (52)

Type of measurement : concentration at contaminated site
Media : air
Concentration :
Method :

Remark : Following Russian studies conducted in the 1960's and 70's, in which, however, no quantitative data are cited, epichlorohydrin could be detected in the atmosphere at a distance of up to 200 m from the site of a plant (unclear, whether production or processing plant).
Atmospheric epichlorohydrin pollution from the use of epoxy resins has also been reported.
26.03.2002 (145)

Type of measurement : concentration at contaminated site
Media : sediment
Concentration :
Method :

Remark : De Leer (1985) reports on the formation of by-products (polychlorinated ethers and diethers) of the ECH detected in the harbour sediment in the vicinity of a Dutch ECH production plant.
26.03.2002 (32)

Type of measurement : concentration at contaminated site
Media : air
Concentration :
Method :

Remark : According to an EPA (1987) estimation cited by the SAIC (Science Applications International Corporation),
ECH concentrations > 0.05 mg/m3 can be detected in the vicinity of production and processing plants.
26.03.2002 (54)

Type of measurement : concentration at contaminated site
Media : air
Concentration :
Method :

Remark : An American study of potential carcinogens revealed that following the production of ECH, the substance occurs in the ambient air when it is filled into transport tankers.
20 air samples (8-hour TWA) were found to contain concentrations from below the detection limit of 0.05 ppm (= 0.19 mg/m3) up to 2.1 ppm (= 7.94 mg/m3).
By the production of epoxy resins, 39 air samples were found to have an 8-hour TWA of under 0.8 ppm (= 3.0 mg/m3).
26.03.2002 (121)

Type of measurement : concentration at contaminated site
Media : ground water
Concentration :
Method :

Result : Concentration in closest well : 75 mg/l.

Test condition : Accidental spill of ECH (1978) at Point Pleasant, WV, USA (20000 gall spill resulting from train accident).

26.03.2002 (85)

Type of measurement : other
Media : drinking water
Concentration :
Method :

Remark : ECH in the form of residual monomer from polymers used in the processing of drinking water can enter the water in concentrations of 2-5 microg/l. Permitted amounts of monomer residues in such polymers are 0.01-0.025 %.

26.03.2002 (54)

Type of measurement : other
Media : food
Concentration :
Method :

Remark : In migration studies of residual monomers from wine casks coated with epoxy resin (duration of the studies 1-4 years at room temperature) Larroque et al. (1989) found no ECH, since in solution ECH is hydrolytically decomposed.
Van Lierop (1978) studied the migration of ECH in water (10 days at 40 degree C according to a guideline of the Dutch Ministry of Health) from 3 different types of drinking cans and 4 cartons coated with epoxy resin. No information on the amount of the residual ECH was provided. No ECH was detected in the mass fragmentogramme, from which the author concluded, that the concentration of ECH which had migrated into the water must be less than 3 microg/l (method detection limit 6 microg/l).

26.03.2002 (95) (179)

3.2.2 FIELD STUDIES

3.3.1 TRANSPORT BETWEEN ENVIRONMENTAL COMPARTMENTS

Type : adsorption
Media : soil - air
Air : % (Fugacity Model Level I)
Water : % (Fugacity Model Level I)
Soil : % (Fugacity Model Level I)
Biota : % (Fugacity Model Level II/III)
Soil : % (Fugacity Model Level II/III)
Method :
Year :

Remark : log Koc = 1.22

27.03.2002 (195)

Type : volatility
Media : water - air
Air : % (Fugacity Model Level I)
Water : % (Fugacity Model Level I)
Soil : % (Fugacity Model Level I)
Biota : % (Fugacity Model Level II/III)

Soil : % (Fugacity Model Level II/III)
Method :
Year : 1989

Remark : Calculation according to H = p/c.
Result : 2,43 Pa.m3/mol.
27.03.2002 (195)

Type : volatility
Media : water - air
Air : % (Fugacity Model Level I)
Water : % (Fugacity Model Level I)
Soil : % (Fugacity Model Level I)
Biota : % (Fugacity Model Level II/III)
Soil : % (Fugacity Model Level II/III)
Method :
Year :

Remark : EHC is rapidly removed from water and t 1/2 was estimated to be 2.1 days for volatilisation (at 20 degree C, 1 m deep). Experimental data of t 1/2 = 12 hours was also determined.
27.03.2002 (92) (145)

Type : other: Transport between environmental compartments (fugacity)
Media : other: air, water, sediment and soil
Air : % (Fugacity Model Level I)
Water : % (Fugacity Model Level I)
Soil : % (Fugacity Model Level I)
Biota : % (Fugacity Model Level II/III)
Soil : % (Fugacity Model Level II/III)
Method : other: EPIWIN V3.05 (Estimation Program Interface for Windows) (EPA OPPT Model); LEV3EPI fugacity model.
Year : 2000

Attached document : Transport-EPIWIN Fugacity Model.doc
Reliability : (2) valid with restrictions
27.03.2002

3.3.2 DISTRIBUTION

Media : air - biota - sediment(s) - soil - water
Method : Calculation according Mackay, Level I
Year :

Remark : ECH should be distributed more or less evenly between the environmental compartments air (54 %) and water (46 %).
27.03.2002 (100)

3.4 MODE OF DEGRADATION IN ACTUAL USE

3.5 BIODEGRADATION

Type : aerobic
Inoculum : activated sludge, adapted
Contact time :
Degradation : = 75 (±) % after 48 hour(s)
Result :

Deg. product :
Method : OECD Guide-line 301 A (old version) "Ready Biodegradabiltiy: Modified AFNOR Test"
Year :
GLP :
Test substance :

Remark : Result given without strip effect. When stripping is taken into account 91 % degradation occurred.
BOD30 was estimated as 97 % ThOD.

27.03.2002 (127)

Type : aerobic
Inoculum : other
Contact time :
Degradation : = 60 (±) % after 14 day(s)
Result :
Deg. product :
Method : OECD Guide-line 301 C "Ready Biodegradability: Modified MITI Test (I)"
Year :
GLP : no data
Test substance : no data

27.03.2002 (113)

Type : aerobic
Inoculum :
Concentration : 100 mg/l related to
related to
Contact time :
Degradation : = 60 (±) % after 3 day(s)
Result :
Deg. product :
Method : other: modified MITI test
Year :
GLP :
Test substance :

Remark : result in fresh water (in sea water 8 % in 3 days)

27.03.2002 (89)

Type : aerobic
Inoculum : activated sludge, industrial, adapted
Contact time :
Degradation : = 89 (±) % after 24 hour(s)
Result :

Remark : - Degradation measured as COD ($KMnO_4$).
- 73 % degradation is due to abiotic degradation as measured by COD without activated sludge and 16 % COD is due to biological degradation.
- Impact of potential degradation by hydrolysis was not taken into account.

27.03.2002 (103)

Remark : In a laboratory test using sewage see, 3% of the theoretical BOD was consumed in 5 days.

27.03.2002 (58)

Deg. product :
Method :

Year :
GLP :
Test substance : other TS: Epichlorohydrin

Remark : The literature supports that epichlorohydrin undergoes biological degradation under various conditions. Epichlorohydrin was biodegraded slowly by aerobic bacteria from the effluent of a secondary water-treatment plant. Five days after seeding and acclimation, the BOD amounted to 14% of the theoretical oxygen demand. After incubation with activated sludge, 89% of the epichlorohydrin degraded within 24 hours as measured by COD removal efficiency; however, the removal of epichlorohydrin was due to both biotic and abiotic (primarily volatilization) factors in the presence of activated sludge. In a modified Japanese MITI biodegradation test, there was 60% degradation of epichlorohydrin after three days incubation in river water and 8% degradation in seawater following the same incubation time. According to the 1986 MITI list, the degree of epichlorohydrin degradation was 60% following 14 days incubation in an OECD 301C test in freshwater with a mixed microbial culture.

Supplemental literature on biodegradation shows that epichlorohydrin is degraded by microbes that are adapted to epichlorohydrin. The pathway for biodegradation is primarily by dechlorination. Bacterial cultures from freshwater sediments enriched with epichlorohydrin rapidly degraded epichlorohydrin via a dehalogenation reaction. In soil, epichlorohydrin was biodegraded with a half-life ranging from 7 - 28 days depending on pH, temperature and microbial densities.

There are adequate and reliable data in the literature that substantiate that epichlorohydrin is biodegraded. Epichlorohydrin is similar to other chlorinated aliphatic compounds in that biodegradation occurs at different rates in sediments and soils depending on acclimation time, microbial densities, temperature and pH.

Reliability : (2) valid with restrictions
27.03.2002

3.6 BOD5, COD OR BOD5/COD RATIO

BOD5
Method : other
Year :
Concentration : 94 mg/l related to
BOD5 : mg/l
GLP :
RATIO BOD5 / COD
BOD5/COD : = .56

Remark : From petrochemical complex of Japanese Kashima waste water treatment plant :
The calculated elimination rate is 72 % (based on COD) in 24 hours.

27.03.2002 (104)

BOD5
Method : other: APHA standard method No. 219
Year : 1979
Concentration : related to
BOD5 : mg/l
GLP :
COD
Method :

Year :
COD : = 1160 mg/g substance
GLP :
RATIO BOD5 / COD
BOD5/COD : = .026

Result : BOD5 = 0.03 g O2 / g substance
= 3 % ThOD (ThOD = 1.21 g O2 / g substance

COD = 1.16 g O2 / g substance
= 96 % ThOD

Test condition : Inoculum: activated sludge, domestic, non-adapted.
27.03.2002 (11)

3.7 BIOACCUMULATION

Species : other: fish muscle (acc. to method of Neely et al. (1974)
Exposure period : at °C
Concentration :
BCF : ca. 1.02
Elimination : no data
Method : other: estimation
Year : 1980
GLP : no data
Test substance :

27.03.2002 (145)

Remark : Not expected to bioconcentrate appreciably in aquatic organisms. The log BCF has been estimated as 0.66.
27.03.2002 (59)

3.8 ADDITIONAL REMARKS

Remark :
- Photodegradation of epichlorohydrin in the atmosphere should occur within a few days (t1/2: 16h - 24d).
- In water, hydrolysis will take place at environmental pH (5-6) with half-life of 5 to 8 days, leading to the formation of 3-chloro-1,2-propanediol and 1,3-dichloro-2-propanol which are not toxic to aquatic organisms (LC50 > 100 mg/l) but not easily biodegradable.
- Intrinsic biodegradability is not very high (BOD5/ThOD = 0.12 with adapted seeds) but results of ready biodegradation tests (MITI tests) showed good degradation (60 %) in 3 to 14 days.
- Epichlorohydrin evaporates rapidly from water with a half-life between 12 hours and 2 days.

Most of the epichlorohydrin should have disappeared from the environment (either from water or air) within several days and therefore will have no long term effects.

27.03.2002

4.1 ACUTE/PROLONGED TOXICITY TO FISH

Type	:	other: semicontinuous system
Species	:	Rasbora heteromorpha (Fish, marine)
Exposure period	:	48 hour(s)
Unit	:	mg/l
LC50	:	= 36
Limit test	:	no
Analytical monitoring	:	no data
Method	:	other: Working Document No. 6 of the Pesticides Safety Precaution Scheme
Year	:	1966
GLP	:	no
Test substance	:	no data
Method	:	STATISTICAL METHOD: The logarithm of the median time of survival was plotted against the logarithm of the concentration of the test substance and a line fitted to the points by eye; 24 and 48-hour median lethal concentrations were interpolated graphically.
Result	:	RESULT: The LC50 (24h) was 72 mg/l, the LC50 (48h) was 36 mg/l.
Test condition	:	TEST ORGANISMS - Strain: not described - Source/supplier: not described - Age/size/weight/loading: 1.3-3 cm in length - Feeding: not described - Pretreatment: not described - Feeding during test: not described STOCK AND TEST SOLUTION AND THEIR PREPARATION - Vehicle/solvent: not described REFERENCE SUBSTANCE: not described DILUTION WATER - Source: standard quality dilution water - Alkalinity: not described - Hardness: 20 mg/l as CaCO3 - pH: 7.2 - Conductance: not described TEST SYSTEM - Test type: semi continuous, test solutions were replaced at the rate of 100 ml every 10 minutes - Concentrations: series of concentrations - Exposure vessel type: 500 ml flasks - Number of replicates, fish per replicate: not described/10 - Test temperature: 20°C - Dissolved oxygen: not described - pH: not described - Intensity of irradiation: not described - Photoperiod: not described TEST PARAMETER: mortality of test organisms
Reliability	:	(3) invalid Documentation insufficient for assessment, several test conditions not described.

27.03.2002 (1)

Type	:	semistatic
Species	:	Poecilia reticulata (Fish, fresh water)
Exposure period	:	14 day(s)

Unit	:	µmol/l
LC50	:	= .66 measured/nominal
Limit test	:	no
Analytical monitoring	:	yes
Method	:	other: not described
Year	:	
GLP	:	no
Test substance	:	no data

Method : STATISTICAL METHOD: The LC50 value was calculated from log-logit analysis
ANALYTICAL METHOD: gas-liquid chromatography (GLC)

Result : RESULTS EXPOSED: Fish exposed for some time (5-7 days) to lethal concentrations of epichlorohydrin started to swim almost continuously in circles very fast. All fish that showed this behaviour died within 24 h after the first occurrences of these symptoms.
RESULTS OF ANALYSIS: The concentrations of the test compound immediately before renewal of the solutions corresponded to > 50% of the concentration originally added.

Test condition : TEST ORGANISMS
- Strain: not described
- Source/supplier: laboratory reared
- Age/size/weight/loading: 2-3 months old at the start of the experiment
- Feeding: daily with a commercial food (TetraPhyll, Tetra Werke, Germany)
- Pretreatment: The fish were acclimated to the water used in the test for at least 12 days prior to the experiment
- Feeding during test: yes, daily

STOCK AND TEST SOLUTION AND THEIR PREPARATION
- Vehicle/solvent: not described

REFERENCE SUBSTANCE: not described
DILUTION WATER: not described
TEST SYSTEM
- Test type: semi-static with renewal of the test solutions daily
- Concentrations: at least 5, geometrically increasing with a factor of 1.8
- Exposure vessel type: 1.5-l glass vessels containing 1.4 l of the test solution, covered with glass lids
- Number of replicates, fish per replicate: not described/10
- Test temperature: 21-23°C
- Dissolved oxygen: > 4.6 mg/l
- pH: 6.8-7.1
- Intensity of irradiation: not described
- Photoperiod: light-dark cycle of 12h:12h

TEST PARAMETER: mortality of test organisms
MONITORING OF TEST SUBSTANCE CONCENTRATION: at least four times before and four times after renewal of the solutions for 2 concentrations

Reliability : (2) valid with restrictions
Study well docmented, meets generally accepted scientific principles, acceptable for assessment.
Daily renewal of test solutions and chemical analyses were included.

27.03.2002 (37) (38)

Type	:	semistatic
Species	:	Salmo gairdneri (Fish, estuary, fresh water)
Exposure period	:	48 hour(s)
Unit	:	mg/l
LC0	:	= 19
LC100	:	= 38
Limit test	:	no
Analytical monitoring	:	no
Method	:	other: not described
Year	:	
GLP	:	no
Test substance	:	no data

Method : STATISTICAL METHOD: A concentration which caused 100 % mortality in the first 24 hours is the lethal concentration. Concentrations in which the fish showed less than 100 % survival and concentrations in which they died after 24 hours, were called toxic concentrations.
Concentrations in which no mortality was observed were called permissible concentrations.

Result : RESULT: During the test no toxic concentration could be determined.

Test condition : TEST ORGANISMS
- Strain: not described
- Source/supplier: Fishery Experimental Station of the Agricultural College in Cracow
- Age/size/weight/loading: two year old fish were used
- Feeding: meat offal
- Pretreatment: The fish were held for an acclimation period of 10-12 days before using them for tests
- Feeding during test: no

STOCK AND TEST SOLUTION AND THEIR PREPARATION
- Vehicle/solvent: not described

REFERENCE SUBSTANCE: not described

DILUTION WATER
- Source: well water
- Alkalinity: not described
- Hardness: not described
- pH: not described

TEST SYSTEM
- Test type: test solutions were renewed once in 24 hours
- Concentrations: not described
- Exposure vessel type: not described
- Number of replicates, fish per replicate: not described
- Test temperature: 16-21.5°C
- Dissolved oxygen: > 6.0 mg/l
- pH: not described
- Intensity of irradiation: not described
- Photoperiod: not described

TEST PARAMETER: mortality of test organisms

Reliability : (3) invalid
Documentation insufficient for assessment, several test conditions not desribed.

27.03.2002 (99)

Type	:	static
Species	:	Brachydanio rerio (Fish, fresh water)
Exposure period	:	96 hour(s)
Unit	:	mg/l
LC0	:	= 26
LC50	:	= 30.5

LC100	:	= 31
Limit test	:	no
Analytical monitoring	:	no data
Method	:	other: UBA draft test guideline
Year	:	1981
GLP	:	no
Test substance	:	no data
Method	:	STATISTICAL METHOD: not described
Test condition	:	TEST ORGANISMS: Brachydanio rerio, no further details described STOCK AND TEST SOLUTION AND THEIR PREPARATION - Vehicle/solvent: not described REFERENCE SUBSTANCE: not described DILUTION WATER: not described TEST SYSTEM - Test type: static, without aeration of the test solutions - Concentrations: series of concentrations - Exposure vessel type: not described - Number of replicates, fish per replicate: not described - Test temperature/dissolved oxygen: not described - pH: 7.5 without adjustment - Intensity of irradiation and photoperiod: not described TEST PARAMETER: mortality of test organisms
Reliability	:	(3) invalid Documentation insufficient for assessment, several test conditions not described.

27.03.2002 (191)

Type	:	static
Species	:	Carassius auratus (Fish, fresh water)
Exposure period	:	24 hour(s)
Unit	:	mg/l
LC50	:	= 23
Limit test	:	no
Analytical monitoring	:	yes
Method	:	other: American Public Health Association (APHA)
Year	:	1971
GLP	:	no
Test substance	:	no data
Method	:	STATISTICAL METHOD: The results are reported as TLm values, the concentration at which 50% of the fish survive. The TLm was obtained by interpolation from a graph of the logarithm of the concentration versus the percentage mortality. ANALYTICAL METHOD: GC analysis
Test condition	:	TEST ORGANISMS - Strain: not described - Source/supplier: not described - Age/size/weight/loading: Fish of uniform length (average 6.2 ± 0.7 cm) and weight (3.3 ± 1.0 g) and in good health were used as test fish - Feeding: not described - Pretreatment: not described - Feeding during test: not described STOCK AND TEST SOLUTION AND THEIR PREPARATION - Vehicle/solvent: not described REFERENCE SUBSTANCE: not described DILUTION WATER: - Source: local tap water - Alkalinity: not adequately described - Hardness: not described

- pH: 7.8
- Conductance: not described

TEST SYSTEM
- Test type: static with aeration without renewal of test solution
- Concentrations: series of concentrations
- Exposure vessel type: glas tanks measuring 42x28x28 cm containing 25 l of test solution
- Number of replicates, fish per replicate: not described/10
- Test temperature: 20 ± 1°C
- Dissolved oxygen: not described but continuous aeration
- pH: 6-8, if the pH of test solutions was outside this range
  it was adjusted to 7.0
- Intensity of irradiation: not described
- Photoperiod: not described

TEST PARAMETER: mortality of test organisms
MONITORING OF TEST SUBSTANCE CONCENTRATION: before and after
the test

Reliability : (2) valid with restrictions
Analytical measurements were included but several test conditions were not described. Short exposure period.

27.03.2002 (12)

Type : static
Species : Lepomis macrochirus (Fish, fresh water)
Exposure period : 96 hour(s)
Unit : mg/l
LC50 : = 35
Limit test : no
Analytical monitoring : no
Method : other: not described
Year :
GLP : no
Test substance : no data

Method : STATISTICAL METHOD: The LC50 was calculated by plotting survival percentages on semi-logarithmic paper and drawing a straight line "fit" through or near significant points above and below 50 % survival.

Result : RESULTS

Concentration (mg/l)	% Survival after 24h	48h	72h	96h
10	100	100	75	75
32	100	90	80	70
37	100	90	80	60
42	50	0	-	-
56	0	-	-	
-				

Test condition : TEST ORGANISMS
- Strain: not described
- Source/supplier: commercial hatchery (New York)
- Age/size/weight/loading: 33-75 mm in length selected at random, any group showing >5% mortality was not used for testing, 1 gram fish per liter of water.
- Feeding: minced frozen shrimp
- Pretreatment: The fish were held for an acclimation period

of fourteen days prior to testing at a temperature of 23°C
- Feeding during test: fish were not fed for 48 hours prior to testing
STOCK AND TEST SOLUTION AND THEIR PREPARATION
- Vehicle/solvent: not described
REFERENCE SUBSTANCE: not described
DILUTION WATER
- Source: potable well water
- Alkalinity: not described
- Hardness: 55 mg/l as CaCO3
- pH: 7.6-7.9
- Conductance: not described
TEST SYSTEM
- Test type: static with aeration (day 2-4) and without renewal of test solution
- Concentrations: 10, 32, 37, 42 and 56 mg/l
- Exposure vessel type: glass 5 gallon aquaria with a water level of more than 15 centimeters
- Number of replicates, fish per replicate: not described
- Test temperature: 23°C
- Dissolved oxygen: not described
- pH: not described
- Intensity of irradiation: not described
- Photoperiod: not described
TEST PARAMETER: mortality of test organisms

Reliability : (2) valid with restrictions
Standard test species and test duration but several test conditions not described. No chemical analyses.

27.03.2002 (28)

Type : static
Species : Leuciscus idus (Fish, fresh water)
Exposure period : 48 hour(s)
Unit : mg/l
LC0 : = 12
LC50 : = 24
LC100 : = 35
Limit test : no
Analytical monitoring : no
Method : other: DIN 38412, L 15
Year : 1976
GLP : no
Test substance : no data

Test condition : TEST ORGANISMS: Leuciscus idus melanotus, no further details described
STOCK AND TEST SOLUTION AND THEIR PREPARATION: not described
REFERENCE SUBSTANCE: not described
DILUTION WATER: not described
TEST SYSTEM: not described
TEST PARAMETER: mortality of test organisms

Reliability : (3) invalid
Documentation insufficient for assessment. Test conditions not described.

27.03.2002 (81)

Type : static
Species : Menidia beryllina (Fish, estuary, marine)
Exposure period : 96 hour(s)
Unit : mg/l
LC50 : = 18

Limit test : no
Analytical monitoring : no
Method : other: not described
Year :
GLP : no
Test substance : no data

Method : STATISTICAL METHOD: The LC50 was calculated by plotting survival percentages on semi-logarithmic paper and drawing a straight line "fit" through or near significant points above and below 50 % survival.

Result : RESULTS

Concentration (mg/l)	% Survival after 24h	48h	72h	96h
10	90	90	90	90
18	100	90	70	50
32	100	30	0	-

Test condition : TEST ORGANISMS
- Strain: Menidia beryllina (Tidewater silversides)
- Source/supplier: Wild population from "Horseshoe Bay", New Jersey (Gateway National Park)
- Age/size/weight/loading: 40-100 mm in length selected at random, any group showing >5% mortality was not used for testing, 1 gram fish per liter of water.
- Feeding: minced frozen shrimp
- Pretreatment: The fish were held for an acclimation period of fourteen days prior to testing at a temperature of 20°C
- Feeding during test: no

STOCK AND TEST SOLUTION AND THEIR PREPARATION
- Vehicle/solvent: not described

REFERENCE SUBSTANCE: not described

DILUTION WATER
- Source: potable well water was used as the base for a synthetic seawater mix
- Alkalinity: not described
- Hardness: 55 mg/l as $CaCO_3$
- pH: 7.6-7.9
- Conductance: not described

TEST SYSTEM
- Test type: static with aeration and without renewal of test solution
- Concentrations: 10, 18 and 32 mg/l
- Exposure vessel type: glass 5 gallon aquaria with a water level of more than 15 centimeters
- Number of replicates, fish per replicate: not described
- Test temperature: 20°C
- Dissolved oxygen: not described but continuous aeration
- pH: not described
- Intensity of irradiation: not described
- Photoperiod: not described

TEST PARAMETER: mortality of test organisms

Reliability : (2) valid with restrictions
Standard test duration but several test conditions not described. No chemical analyses.

27.03.2002

(28)

Type : static
Species : Pimephales promelas (Fish, fresh water)
Exposure period : 96 hour(s)
Unit : mg/l
LC50 : 12.1
Limit test : no
Analytical monitoring : no data
Method : other: ASTM
Year : 1980
GLP : yes
Test substance : other TS: see freetext

Method : DEVIATIONS FROM GUIDELINE: The dissolved oxygen concentration fell below the recommended limit of 40% saturation. However, the low oxygen concentration did not appear to influence fish mortality.
STATISTICAL METHODS: LC50 and 95% confidence intervals were determined by Thompson's method of moving averages. The LC50 values of the three age groups were combined by calculating the geometric mean.

Result : RESULTS
The following LC50 (96h) with 95% Confidence Intervals were found:
- fry (10-15 day) : 12.7 mg/l (11.5-14.2 mg/l)
- juvenile (30-35 day) : 10.6 mg/l (9.1-12.3 mg/l)
- subadult (65-94 day) : 13.2 mg/l (9.6-18.6 mg/l)

Test condition : TEST ORGANISMS
- Strain: Pimephales promelas Rafinesque
- Source/supplier: not described
- Age/size/weight/loading:

	age (days)	size (mm)	weight (mg)
fry	10-15	9.5	11.6
juvenile	30-35	14.9	76.8
subadult	65-94	28.0	391

- Feeding: Newly hatched fry were fed with Artemia salina (2 times per hour), older fish were fed daily with a synthetic diet
- Pretreatment: All fish were held in 57 liter aquaria with a constant water flow of 0.2 l/minute at a temperature of 25 ± 1°C, illumination of 430-645 lux and a light-dark cycle of 8h:16h. Fish were accclimated to the test temperature of 22 ± 1°C at least 48 hours prior to the start of the test
- Feeding during test: no

STOCK AND TEST SOLUTION AND THEIR PREPARATION
- Vehicle/solvent: not described

REFERENCE SUBSTANCE: not described
DILUTION WATER
- Source: Lake Huron water, carbon filtered and UV irradiated
- Alkalinity: not described
- Hardness: 96-125 mg/l as $CaCO_3$
- pH: 7.9-8.3
- Conductance: 135-215 µmhos/cm

TEST SYSTEM
- Test type: static with aeration and without renewal of test solution

- Concentrations: six exposure concentrations and one control
- Exposure vessel type: round glas vessels measuring 22 cm deep and 24.5 cm in diameter containing 10 liters (juvenile and subadult test) or 3.5 liters (fry test)
- Number of replicates, fish per replicate: Number of replicates is not described, 10 subadults, 10 juveniles or 20 fry
- Test temperature: 21-23°C
- Dissolved oxygen: 2.2-8.7 mg/l
- pH: 7.2-8.4
- Intensity of irradiation: not described
- Photoperiod: 16h:8h light-dark cycle

TEST PARAMETER: mortality of test organisms

Test substance : SOURCE: Eastman Kodak
PURITY: reagent-grade quality
IMPURITIES: not described

Reliability : (1) valid without restriction
GLP guideline study. Although chemical analyses were absent the data of section 3.1.2 (Stability in water) indicate sufficient exposure.

27.03.2002 (105) (106)

4.2 ACUTE TOXICITY TO AQUATIC INVERTEBRATES

Type	:	static
Species	:	Daphnia magna (Crustacea)
Exposure period	:	48 hour(s)
Unit	:	mg/l
EC50	:	= 23.9
Analytical monitoring	:	no
Method	:	other: ASTM Guidelines
Year	:	1980
GLP	:	yes
Test substance	:	other TS: see freetext

Method : DEVIATIONS FROM GUIDELINE: non reportedSTATISTICAL METHODS: The LC50 value and 95% confidence interval were estimated by Thompson's method of moving averages. EC50 data declared as LC50.

Result : RESULTS
A 48h LC50 value of 23.9 mg/l with 95% confidence intervals of 19.4-32.9 mg/l was found. The control mortality was below the validity criterion.

Test condition : TEST ORGANISMS
- Strain: Daphnia magna Straus 1820
- Source/supplier: not described
- Breeding method: the brood stock was maintained at 20 ± 1°C and a light-dark cycle of 16h:8h
- Feeding: Selenastrum capricornutum three times a week (1.25 mg dry wt/L of dilution water)
- Pretreatment: 24 h before testing, multiparous females were isolated and the neonates were used for testing
- Feeding during test: no
- Control group: yes

STOCK AND TEST SOLUTION AND THEIR PREPARATION
- Vehicle/solvent: no data

REFERENCE SUBSTANCE: not described
DILUTION WATER
- Source: Lake Huron water

- Alkalinity: 65 ± 4 mg/l as CaCO3
- Hardness: 157 ± 4 mg/l as CaCO3
- pH: 8.0 ± 0.2
- Conductance: 311 ± 11 µmhos/cm

TEST SYSTEM
- Test type: static without renewal of test solution and without aeration
- Concentrations: not described
- Exposure vessel type: 200 ml test solution in a 250 ml glass beaker
- Number of replicates, individuals per replicate: 3/10
- Test temperature: 19.8-20.9°C
- Dissolved oxygen: > 90% saturation
- pH: 7.7-8.3
- Intensity of irradiation: 970-1250 lumens per m2
- Photoperiod: 16h:8h light-dark cycle

TEST PARAMETER: immobility of test organisms

Test substance : SOURCE: Eastman Kodak
PURITY: Reagent grade
IMPURITIES: not reported

Reliability : (1) valid without restriction
GLP guideline study. Although chemical analyses were absent the data of section 3.1.2 (Stability in water) indicate sufficient exposure.

27.03.2002 (67)

Type : static
Species : Daphnia magna (Crustacea)
Exposure period : 24 hour(s)
Unit : mg/l
EC0 : = 20
EC50 : = 30
EC100 : = 44
Analytical monitoring : no
Method : other: not described
Year :
GLP : no
Test substance : no data

Method : STATISTICAL METHODS: The EC50 (24h) was obtained by interpolation from a graph of the logarithm of the concentration versus the percentage mortality.

Test condition : TEST ORGANISMS
- Source/supplier: wild population
- Breeding method: in 2 l glass beakers with 1.6 l tap-water,
  the brood stock was maintained at 20-22°C and a light-dark cycle of 12h:12h.
- Feeding: daily with Chlorella vulgaris
- Pretreatment: neonates of 0-24 h were isolated daily and used for testing
- Feeding during test: not described
- Control group: not described

STOCK AND TEST SOLUTION AND THEIR PREPARATION
- Vehicle/solvent: no solvent used

REFERENCE SUBSTANCE: not described

DILUTION WATER
- Source: tap-water free from chlorine
- Alkalinity: not described
- Hardness: 16°d.H.
- pH: 7.6-7.7
- Conductance: not described

TEST SYSTEM
- Test type: static without renewal of test solutions
- Concentrations: In first instance, geometrically

increasing
with a factor of 2. If the LC0 and LC100 differed less then three test concentrations, geometrically increasing with a factor 1.3 or 1.1
- Exposure vessel type: 50 ml glass beaker containing 20 ml test solution covered with a filter paper
- Number of replicates, individuals per replicate: 3/10
- Test temperature: 20-22°C
- pH: not described
- Intensity of irradiation: daylight but no direct sunlight
- Photoperiod: not described
TEST PARAMETER: immobility of test organisms

Reliability : (2) valid with restrictions
Documentation sufficient for assessment. However no chemical analyses and test concentrations unknown. Short test duration.

27.03.2002

Type : static
Species : Daphnia magna (Crustacea)
Exposure period : 24 hour(s)
Unit : mg/l
EC0 : = 30
EC50 : = 40
EC100 : = 53
Analytical monitoring : no
Method : other: not described
Year :
GLP : no
Test substance : no data

Method : STATISTICAL METHODS: The EC50 (24h) was obtained by interpolation from a graph of the logarithm of the concentration versus the percentage mortality.

Test condition : TEST ORGANISMS
- Strain: IRCHA
- Source/Supplier: not described
- Breeding method: in 2 l glass beakers with 1.6 l tap-water,
the brood stock was maintained in a thermostated room with a temperature setpoint of 20°C and a light-dark

cycle of 9h:15h
- Feeding: dry algae 'Microzell'
- Pretreatment: neonates of 0-24 h were isolated daily and used for testing
- Feeding during test: not described
- Control group: not described
STOCK AND TEST SOLUTION AND THEIR PREPARATION
- Vehicle/solvent: no solvent used
REFERENCE SUBSTANCE: potassium dichromate
DILUTION WATER
- Source: standardized culture medium
- Alkalinity/hardness: not described
- pH: 8.0 ± 0,2
- Conductance: not described
TEST SYSTEM
- Test type: Static without renewal of test solutions
- Concentrations: In first instance, geometrically increasing
with a factor of 2. If the LC0 and LC100 differed less then three test concentrations, geometrically increasing

with a factor 1.4 or 1.1
- Exposure vessel type: 50 ml glass beaker containing 20 ml test solution covered with a filter paper
- Number of replicates, individuals per replicate: 2/10
- Test temperature: 20°C
- Dissolved oxygen/pH: not described
- Intensity of irradiation/photoperiod: not described

TEST PARAMETER: immobility of test organisms

Reliability : (2) valid with restrictions
Documentation sufficient for assessment. However no chemical analyses and test concentrations unknown. Short test duration.

27.03.2002 (19)

4.3 TOXICITY TO AQUATIC PLANTS E.G. ALGAE

Species	:	Scenedesmus quadricauda (Algae)
Endpoint	:	biomass
Exposure period	:	8 day(s)
Unit	:	mg/l
Toxicity threshold	:	= 5.4
Limit test	:	no
Analytical monitoring	:	no
Method	:	other: not described
Year	:	
GLP	:	no
Test substance	:	no data

Method : STATISTICAL METHODS: The concentration epichlorohydrin at which 3 % growth inhibition (EC3) occurs, is calculated. This value is called toxicity threshold.

Test condition : TEST ORGANISMS
- Strain/Source: no data
- Method of cultivation: algae are incubated in 100 ml Erlenmeyer flasks containing 20 ml at 27°C with continuous illumination and transferred every 10 days into fresh medium
- Controls: yes
- Initial cell concentration: not described

STOCK AND TEST SOLUTION AND THEIR PREPARATION
- Vehicle, solvent: not described

GROWTH/TEST MEDIUM CHEMISTRY
- Medium used: standardized medium

TEST SYSTEM
- Test type: static without renewal of test solution
- Concentrations: geometrically increasing with a factor of 2
- Exposure vessel type: 10 ml in a culture tube (18 x 180 mm) stoppered with cotton-lined metal caps
- Number of replicates: triplicate
- Test temperature: 27°C
- pH: not described
- Intensity of irradiation: not described
- Photoperiod: continuous
- Shaking: once a day

TEST PARAMETER: inhibition of cell multiplication

Reliability : (3) invalid
Long test duration and no chemical analyses and therefore probably no exposure at the end of the test. This is

significant methodological deficiency. Some test conditions are lacking.

27.03.2002 (16) (17)

Species : Selenastrum capricornutum (Algae)
Endpoint : biomass
Exposure period : 72 hour(s)
Unit : mg/l
NOEC : = 1.7 measured/nominal
EC50 : = 7.1 measured/nominal
Limit test : no
Analytical monitoring : yes
Method : OECD Guide-line 201 "Algae, Growth Inhibition Test"
Year : 1984
GLP : yes
Test substance : other TS: see freetext

Method : DEVIATIONS FROM GUIDELINE: none reported
STATISTICAL METHODS: The EC50 (0-72 hour) was calculated using linear interpolation. The NOEC based on biomass integral at test termination calculated with Williams' Test
ANALYTICAL METHODS: Gas chromatography

Result : RESULTS: EXPOSED AND CONTROL

-Nominal conc.	measured conc.	mean cell density (day3)
- 0	not detected	110 x 10E+4
1.0	0.87	103 x 10E+4
2.2	1.7	110 x 10E+4
5.0	3.9	91.6 x 10E+4
11	8.4	44.8 x 10E+4
25	19	5.86 x 10E+4
55	40	1.90 x 10E+4

-
- Growth curves: Logarithmic growth until end of the test (72 h)

Test condition : TEST ORGANISMS
- Strain: ATCC 22662
- Source/Supplier: Culture Collection of Algae and Protozoa, Ambleside, Cumbria, UK
- Laboratory culture: yes
- Method of cultivation: algae are incubated at 23°C with continuous illumination and weekly transferred into fresh medium
- Controls: yes (sixfold)
- Initial cell concentration: 1x10E+4

STOCK AND TEST SOLUTION AND THEIR PREPARATION
- Vehicle, solvent: no solvent used

GROWTH/TEST MEDIUM CHEMISTRY
- Medium used: according to OECD 201

TEST SYSTEM
- Test type: static without renewal of test solution
- Concentrations: 0, 1.0, 2.2, 5.0, 11, 25 and 55 mg/l
- Exposure vessel type: 100 ml medium in a 250 ml Erlenmeyer flask with a cap that allows ventilation
- Number of replicates: triplicate
- Test temperature: 22.3-23.4°C
- pH: 8.0 at start and 8.4 at end of the test
- Intensity of irradiation: about 4400 lx

- Photoperiod: continuous
- Shaking: about 100 rpm
TEST PARAMETER: inhibition of cell multiplication
MONITORING OF TEST SUBSTANCE CONCENTRATION: after 0, 24, 48 and 72 hours of exposure

Test substance : SOURCE: Solvay Elektrolysespezialitäten, Rheinberg, Germany
PURITY: 99.9%
IMPURITIES: not reported

Reliability : (1) valid without restriction
GLP guideline study

27.03.2002 (30)

Species : Selenastrum capricornutum (Algae)
Endpoint : growth rate
Exposure period : 14 day(s)
Unit : mg/l
Limit test : no
Analytical monitoring : no
Method : other: EPA-600/9-78-018
Year : 1978
GLP : yes
Test substance : other TS: see freetext

Method : DEVIATIONS FROM GUIDELINE: none reported
STATISTICAL METHODS: A 96-hour EC50 value for growth inhibition was calculated using Finney's method of probit analysis

Remark : A second definitive test was conducted with epichlorohydrin to determine the precision of the test method. Test conditions were the same as described for the first test. The second test lasted 7 days. The 96-hour EC50 based on growth inhibition was 17 mg/l.

Result : RESULTS: EXPOSED AND CONTROLS
- The EC50 (96h) based on growth inhibition was 16 mg/l
- Cell density data: not individually reported
- Growth curves: The growth curves show that the control growth had peaked by the 5th day, growth in the exposed flasks continued to the end of the test (at a reduced rate)

Test condition : TEST ORGANISMS
- Strain: not described
- Source/Supplier: U.S. EPA, Corvalis, Oregon
- Laboratory culture: yes
- Method of cultivation: not described
- Controls: yes (triplicate)
- Initial cell concentration: 1x10E+4
STOCK AND TEST SOLUTION AND THEIR PREPARATION
- Vehicle, solvent: no solvent used
GROWTH/TEST MEDIUM CHEMISTRY
- Medium used: Algal assay medium
TEST SYSTEM
- Test type: static without renewal of test solution
- Concentrations: 0, 2.5, 4.1, 6.9, 11.5, 19 and 32 mg/l
- Exposure vessel type: 50 ml in 125 ml Erlenmeyer flasks, free gas exchange through the foam plugs
- Number of replicates: triplicate
- Test temperature: 24 ± 2°C
- pH: not described
- Intensity of irradiation: 400 ± 80 fc
- Photoperiod: continuous
- Shaking: 100 rpm

Test substance	:	TEST PARAMETER: inhibition of cell multiplication SOURCE: Eastman Kodak PURITY: reagent grade IMPURITIES: not reported
Reliability	:	(2) valid with restrictions GLP guideline study. However, long test duration and no chemical analyses and therefore probably no exposure at the end of the test. This is significant methodological deficiency. The 96-hour data are considered "reliable with restrictions".

27.03.2002 (40)

4.4 TOXICITY TO MICROORGANISMS E.G. BACTERIA

Type	:	aquatic
Species	:	Chilomonas paramaecium (Protozoa)
Exposure period	:	48 hour(s)
Unit	:	mg/l
Toxicity threshold	:	= 29
Analytical monitoring	:	no
Method	:	other: not described
Year	:	
GLP	:	no
Test substance	:	no data
Method	:	STATISTICAL METHODS: The toxicity treshold can be considered as the concentration which results in a 5 % reduction in cell counts after 48 hours of exposure
Test condition	:	TEST ORGANISMS - Strain: Chilomonas paramaecium Ehrenberg - Source/Supplier: not described - Method of cultivation: in 300 ml Erlenmeyer flasks with standardized bacteria-free organic mineral medium at a temperature of 20°C in the dark - Feeding: organic material present in the organic mineral medium - Pretreatment: organisms are kept for 72-96 hours at a temperature of 20°C. The organisms are used as test organisms after a microscopic control - Control group: not described STOCK AND TEST SOLUTION AND THEIR PREPARATION - Vehicle/solvent: no solvent used GROWTH/TEST MEDIUM CHEMISTRY - Medium used: bacteria-free standardized organic mineral test medium - pH: 6.9 TEST SYSTEM - Concentrations: geometrically increasing with a factor of 2 - Exposure vessel type: 300 ml Erlenmeyer flasks containing 20 ml testsolution covered with a metal cap - Number of replicates, individuals per replicate: 2/15000 organisms/ml - Test temperature: 20°C - Photoperiod: 24h dark TEST PARAMETER: quantitative determination of the protozoa and of the multiplication of protozoan cells
Reliability	:	(2) valid with restrictions No chemical analysis but test conditions described in

sufficient detail.

27.03.2002 (20)

Type : aquatic
Species : Entosiphon sulcatum (Protozoa)
Exposure period : 72 hour(s)
Unit : mg/l
Toxicity threshold : = 35
Analytical monitoring : no
Method : other: not described
Year :
GLP : no
Test substance : no data

Method : STATISTICAL METHODS: The toxicity treshold can be considered as the concentration which results in a 5 % reduction in cell counts after 72 hours of exposure

Test condition : TEST ORGANISMS
- Strain: Entosiphon sulcatum Stein
- Source/Supplier: not described
- Method of cultivation: in 300 ml Erlenmeyer flasks with standardized culture medium at a temperature of 25°C in the dark
- Feeding: Escherichia coli: stock cultures are fed with live bacteria, and test cultures with inactivated bacteria to prevent metabolization of the test substance
- Pretreatment: organisms are kept for 72 hours at a temperature of 25°C. The organisms are used as test organisms after a microscopic control
- Control group: no data

STOCK AND TEST SOLUTION AND THEIR PREPARATION
- Vehicle/solvent: no solvent used

REFERENCE SUBSTANCE: not described
GROWTH/TEST MEDIUM CHEMISTRY
- Medium used: standardized mineral test medium
- pH: 6.9

TEST SYSTEM
- Concentrations: geometrically increasing with a factor of 2
- Exposure vessel type: 300 ml Erlenmeyer flasks containing 20 ml test solution covered with a metal cap
- Number of replicates, individuals per replicate: 2/15000 organisms/ml
- Test temperature: 25°C
- Photoperiod: 24h dark

TEST PARAMETER: quantitative determination of the protozoa and of the multiplication of protozoan cells

Reliability : (2) valid with restrictions
No chemical analysis but test conditions described in sufficient detail.

27.03.2002 (14)

Type : aquatic
Species : Microcystis aeruginosa (Bacteria)
Exposure period : 8 day(s)
Unit : mg/l
Toxicity threshold : = 6
Analytical monitoring : no

Method : other: not described
Year :
GLP : no
Test substance : no data

Method : STATISTICAL METHODS: The concentration epichlorohydrin at which 3 % growth inhibition (EC3) occurs, is calculated. This value is called toxicity threshold.

Test condition : TEST ORGANISMS
- Strain/Source: not described
- Method of cultivation: not described
- Pretreatment: not described
- Control group: yes, 12 tubes

STOCK AND TEST SOLUTION AND THEIR PREPARATION
- Vehicle, solvent: not described

GROWTH/TEST MEDIUM CHEMISTRY
- Medium used: standardized medium

TEST SYSTEM
- Test type: static without renewal of test solution
- Concentrations: geometrically increasing with a factor of 2
- Exposure vessel type: 10 ml in a culture tube stoppered with cotton-lined metal caps
- Number of replicates: triplicate
- Test temperature: 27°C
- pH: 7.0
- Photoperiod: continuous
- Shaking: once a day

TEST PARAMETER: inhibition of cell multiplication

Reliability : (3) invalid
Long test duration and no chemical analyses and therefore probably no exposure at the end of the test. This is significant methodological deficiency. Some test conditions are lacking.

27.03.2002 (13) (15)

Type : aquatic
Species : Photobacterium phosphoreum (Bacteria)
Exposure period :
Unit :
Analytical monitoring : no
Method : other: not described
Year :
GLP : no
Test substance : no data

Method : METHOD: Initial light measurements were made, hereafter the test substance was added to the cuvettes and after 5 min, 15 min and 30 min, light measurements were made for each cuvette. The control group was used to correct the sample for time-dependant drift in light output.
STATISTICAL METHOD: Percent inhibition was plotted as a function of sample concentration on log-log graph paper. The concentration that inhibited luminescence by 50% (EC50) was determined by the intersection of the best fit line.

Result : RESULTS:
Luminescence EC50
5 min : 2,310 mg/l
15 min: 1,160 mg/l
30 min: 670 mg/l

Test condition : TEST ORGANISMS
- Strain: a lyophilized strain of marine bacteria most

closely resembling Photobacterium phosphoreum
- Source/Supplier: not described
- Cultivation method: not described
- Pretreatment: not described
- Control group: yes
STOCK AND TEST SOLUTION AND THEIR PREPARATION
- Vehicle/solvent: no solvent used
DILUTION WATER: not described
TEST SYSTEM
- Test type: static
- Concentrations: five concentrations
- Exposure vessel type: cuvettes containing 1 ml solution
- Number of replicates, individuals per replicate: 2/10E+8 bacteria/ml
- Test temperature: 15°C
- Photoperiod: not described
TEST PARAMETER: luminescence

Reliability : (3) invalid
Documentation insufficient for assessment and test procedure is not a standard method.

27.03.2002 (6)

Type : aquatic
Species : Pseudomonas putida (Bacteria)
Exposure period : 16 hour(s)
Unit : mg/l
Toxicity threshold : = 55
Analytical monitoring : no
Method : other: not described
Year :
GLP : no
Test substance : no data

Method : STATISTICAL METHODS: The concentration epichlorohydrin at which 3 % growth inhibition (EC3) occurs, is calculated. This value is called toxicity threshold.

Test condition : TEST ORGANISMS
- Strain/Source: not described
- Method of cultivation: organisms are incubated for 24 hours at 25°C, hereafter the organisms are kept in stock. The organisms are transferred weekly into fresh medium.
- Pretreatment: organisms are kept for 24 hours at a temperature of 25°C.
- Control group: not described
STOCK AND TEST SOLUTION AND THEIR PREPARATION
- Vehicle, solvent: not described
GROWTH/TEST MEDIUM CHEMISTRY
- Medium used: standardized medium
TEST SYSTEM
- Test type: static without renewal of test solution
- Concentrations: geometrically increasing with a factor of 2
- Exposure vessel type: 100 ml test solution in an 300-ml Erlenmeyer flask stoppered with cotton filled synthetic material
- Number of replicates: 3
- Test temperature: 25°C
- pH: not described
- Photoperiod: not described
- Shaking: not described
TEST PARAMETER: inhibition of cell multiplication

Reliability : (2) valid with restrictions
No chemical analysis but test conditions described in sufficient detail.

27.03.2002 (15) (16)

Type : aquatic
Species : Uronema parduzci (Protozoa)
Exposure period : 20 hour(s)
Unit : mg/l
Toxicity threshold : = 57
Analytical monitoring : no
Method : other: not described
Year :
GLP : no
Test substance : no data

Method : STATISTICAL METHODS: The toxicity treshold can be considered as the concentration which results in a 5 % reduction in cell counts after 20 hours of exposure

Test condition : TEST ORGANISMS
- Strain: Uronema parduczi Chatton-Lwoff
- Source/Supplier: not described
- Method of cultivation: in 300 ml Erlenmeyer flasks with standardized culture medium at a temperature of 25°C in the dark
- Feeding: Escherichia coli: stock cultures are fed with live bacteria, and test cultures with inactivated bacteria to prevent metabolization of the test substance
- Pretreatment: organisms are kept for 22 hours at a temperature of 25°C. The organisms are used as test organisms after a microscopic control
- Control group: not described

STOCK AND TEST SOLUTION AND THEIR PREPARATION
- Vehicle/solvent: no solvent used

REFERENCE SUBSTANCE: not described
GROWTH/TEST MEDIUM CHEMISTRY
- Source: standardized mineral test medium
- pH: 6.9

TEST SYSTEM
- Test type: static without renewal of test solutions
- Concentrations: geometrically increasing with a factor of 2
- Exposure vessel type: 300 ml Erlenmeyer flasks containing 20 ml test solution covered with a metal cap
- Number of replicates, individuals per replicate: 2/15000 organisms/ml
- Test temperature: 25°C
- Photoperiod: 24h in the dark

TEST PARAMETER: quantitative determination of the protozoa and of the multiplication of protozoan cells

Reliability : (2) valid with restrictions
No chemical analysis but test conditions described in sufficient detail.

27.03.2002 (18)

4.5.1 CHRONIC TOXICITY TO FISH

4.5.2 CHRONIC TOXICITY TO AQUATIC INVERTEBRATES

4.6.1 TOXICITY TO SEDIMENT DWELLING ORGANISMS

4.6.2 TOXICITY TO TERRESTRIAL PLANTS

Species	:	other terrestrial plant: Gossypium hirsutum
Endpoint	:	other: abscission
Exposure period	:	
Unit	:	
Remark	:	Far-red light treatment caused greater abscission increases than plants kept in darkness room-light or red light.
Test condition	:	Gossypium was treated with a 1% lanolin paste of ECH. Seeds were treated with different light regimes after ECH treatment.

27.03.2002 (145)

Species	:	other terrestrial plant: pea and chick-pea seeds
Endpoint	:	other: cytogenic effect
Exposure period	:	
Unit	:	
Remark	:	Delayed disruption of chromosomal meiosis and accelerated aging of both plants were observed.
Test condition	:	Exposure period : 6 hour Concentration tested : 0.028 to 0.1 %.

27.03.2002 (145)

4.6.3 TOXICITY TO SOIL DWELLING ORGANISMS

4.6.4 TOX. TO OTHER NON MAMM. TERR. SPECIES

4.7 BIOLOGICAL EFFECTS MONITORING

4.8 BIOTRANSFORMATION AND KINETICS

4.9 ADDITIONAL REMARKS

5.0 TOXICOKINETICS, METABOLISM AND DISTRIBUTION

5.1.1 ACUTE ORAL TOXICITY

Type	:	LD50
Value	:	= 175 - 282 mg/kg bw
Species	:	rat
Strain	:	other: Fischer 344, Sprague-Dawley
Sex	:	male/female
Number of animals	:	5
Vehicle	:	other: undiluted
Doses	:	
Method	:	EPA OPP 81-1
Year	:	1970
GLP	:	no
Test substance	:	other TS

Result : MORTALITY:

Dose (mg/kg)	# Dead/# Treated Male	Female S-D	Male S-D	Female CDF	CDF
25	0/5	0/5	0/5	0/5	
50	0/5	0/5	0/5	0/5	
100	0/5	0/5	0/5	0/5	
200	1/5	2/5	0/5	0/5	
210	---	---	0/5	3/5	
225	---	---	5/5	5/5	
252	---	---	5/5	5/5	
398	4/5	5/5	5/5	5/5	
795	5/5	5/5	5/5	5/5	

---: not tested

Time to death not available.

CLINICAL SIGNS:

Dose (mg/kg)	Sign	# Affected/# Treated Male	Female S-D	Male S-D	Female CDF	CDF
25		0/5	0/5	0/5	0/5	
50		0/5	0/5	0/5	0/5	
100		0/5	0/5	0/5	0/5	
200	Slight Lethargy	5/5	5/5	5/5	0/5	
210	Slight Lethargy	---	---	5/5	5/5	
	Piloerection	---	---	5/5	5/5	
225	Lethargy	---	---	5/5	5/5	
	Piloerection	---	---	5/5	5/5	
252	Extreme Lethargy	---	---	5/5	5/5	
	Piloerection	---	---	5/5	0/5	
	Shallow Breathing	---	---	5/5	5/5	
	Darkened					

	Extremities	---	---	5/5	0/5
398	Lethargy	5/5	5/5	5/5	5/5
	Hyper-activity	1/5	0/5	0/5	0/5
	Watery eyes	0/5	0/5	0/5	5/5
	Diarrhea	0/5	0/5	0/5	5/5
795	Lethargy	5/5	5/5	5/5	5/5
	Severe Diarrhea	0/5	0/5	0/5	5/5

---: not tested

GROSS PATHOLOGY:
Roughening and thickening of the squamous epithelium of the non-glandular stomach was observed in rats given 100-210 mg/kg. Other findings were non-specific and not considered treatment-related.

POTENTIAL TARGET ORGANS: None identified.

SEX-SPECIFIC DIFFERENCES: No significant differences observed.

Test condition : TEST ORGANISM:
Source: Fischer 344 rats: Charles River Breeding Laboratories, Portage, MI; Sprague-Dawley rats: Spartan Research Animals, Inc., Haslett, MI

Age: 7-8 weeks

Mean Weight at Study Initiation: male Fischer 344 rats: 103-185 g female Fischer 344 rats: 80-132 g; male Sprague-Dawley rats: 262-325 g; female Sprague-Dawley rats: 192-208 g

Controls: None

ADMINISTRATION:

Doses: 25, 50, 100, 200, 210, 225, 252, 398, 795 mg/kg

Doses per time period: Single-dose oral gavage

Maximum volume administered: Fischer 344 rats: 2.8 ml; Sprague-Dawley rats: 4.7 ml

Post-Dose Observation Period: 2 weeks

Examinations: Clinical observations, gross pathological examination

Test substance : 99.8% epichlorohydrin
0.11% 2,3-dichloropropene
0.01% beta-chloroallyl alcohol

Reliability : (1) valid without restriction
Conducted prior to advent of GLP.

27.03.2002

(172)

Type : LD50
Value : = 246 mg/kg bw
Species : rat
Strain : other: Carworth-Wistar
Sex : male
Number of animals : 5

Vehicle : other: neat, undiluted
Doses :
Method : other
Year : 1963
GLP : no data
Test substance : no data

Method : Groups of five non-fasted male rats were given the undiluted chemical, then observed for signs of toxicity for 14 days.
Remark : Oral LD50 reported as 0.21 ml/kg; converted to 246 mg/kg.
Reliability : (2) valid with restrictions
27.03.2002 (190)

Type : LD50
Value : = 260 mg/kg bw
Species : rat
Strain : Sprague-Dawley
Sex : male
Number of animals :
Vehicle : other: cottonseed oil
Doses :
Method : other
Year : 1972
GLP : no data
Test substance : no data

Result : 95% Confidence Limits for LD50 value: 147 to 461 mg/kg.
Reliability : (2) valid with restrictions
27.03.2002 (97)

Type : LD50
Value : = 236 mg/kg bw
Species : mouse
Strain : ICR
Sex : male
Number of animals :
Vehicle : other: cottonseed oil
Doses :
Method : other
Year : 1972
GLP : no data
Test substance : no data

Result : 95% Confidence Limits for LD50 Value: 191 to 294 mg/kg.
Reliability : (2) valid with restrictions
27.03.2002 (97)

Type : LD50
Value : = 271 - 590 mg/kg bw
Species : mouse
Strain : other: white
Sex : no data
Number of animals : 30
Vehicle : other: 25% aqueous gum arabic solution
Doses :
Method : other
Year : 1941
GLP : no
Test substance : no data

Remark : LD50 value is between the two values cited; 100% lethality was observed at 0.5 ml/kg, while 0% lethality was observed

at 0.23 ml/kg.

Reliability : (2) valid with restrictions

27.03.2002 (64)

Type : LD50
Value : = 90 mg/kg bw
Species : rat
Strain : Wistar
Sex : male
Number of animals : 6
Vehicle : no data
Doses :
Method : other
Year : 1948
GLP : no
Test substance : no data

Test substance : Source and purity of test substance not indicated.
Reliability : (3) invalid
Vehicle unknown. Source and purity of test material not indicated.

27.03.2002 (151)

Type : LD50
Value : = 178 mg/kg bw
Species : guinea pig
Strain :
Sex :
Number of animals :
Vehicle :
Doses :
Method : other
Year :
GLP : no data
Test substance : no data

Reliability : (4) not assignable
Unable to obtain original reference.

27.03.2002 (75) (128)

5.1.2 ACUTE INHALATION TOXICITY

Type : LC50
Value : = 2165 - 3617 ppm
Species : rat
Strain : Fischer 344
Sex : male/female
Number of animals : 6
Vehicle : other: air
Doses :
Exposure time : 1 hour(s)
Method : other
Year : 1985
GLP : yes
Test substance : other TS

Result : MORTALITY:

	# Dead/# Treated		Time to Death	
Dose	Male	Female	Male	Female

(PPM)	CDF	CDF	CDF	CDF
552	0/6	0/6	---	---
1008	0/6	0/6	---	---
1970	0/6	2/6	---	1@2 days
		1@3 days		
2865	0/6	---	---	---
3275	0/6	---	---	---
3995	6/6	6/6	3@1 day	6@1 day
		1@2 days		
		1@3 days		
		1@4 days		

---: not tested

CLINICAL SIGNS:
Signs of toxicity were predominantly noted at exposure concentrations of 1970 ppm and above, although all rats exposed to 1008 or 552 ppm spent most of their exposure time huddled in their cages with eyes completely shut. Signs of eye and nasal irritation, respiratory difficulty, and secretion of a reddish, porphyrin-like material on the facial area were noted among rats exposed to levels greater than or equal to 1970 ppm. At concentrations of 3275 and 3995 ppm (males) and 3995 pom (females), hyperactivity during exposure was also observed. This was followed by post-exposure lethargy. At the top exposure level of 3995 ppm, all male and female rats were also cyanotic in appearance immediately prior to the end of exposure.

GROSS PATHOLOGY:
The most frequent observation noted at necropsy among male rats surviving the 2-week observation period was bilaterial corneal cloudiness at 1790 ppm (1/6), 2865 (5/6), or 3275 (6/6). No other observations noted were considered to be treatment-related.

POTENTIAL TARGET ORGANS: Eye.

SEX-SPECIFIC DIFFERENCES: None other than differing LC50's.

Test condition : TEST ORGANISMS:
Source: Charles River Breeding Laboratories, Kingston, NY
Age: 6-8 weeks
Weight at study initiation: males: 177-266 g; females: 126-148 g
Number of animals: 6/sex/exposure concentration
Contols: None

ADMINISTRATION:
Type of Exposure: whole-body vapor exposures
Concentrations:

Target	500	1000	2000	2800	3350	4000
Nominal	599	1133	2329	3306	3866	4609
Analyt.	552	1008	1970	2865	3275	3995

Exposures occurred in 2.6 cubic meter Rochester-type inhalation chambers. Atmospheres were generated by passing heated compressed air through a J-tube assembly. Chamber concentrations were monitored 7 times/hour using gas chromatography.

EXAMINATIONS:

Animals were observed for signs of toxicity during exposure and for 14 days post-exposure. Animlas were weighed at study initiation, and surviving rats were weighed on study days 2, 4, 8, 11, and 15. All animals were submitted for pathological examination of major organ systems either at death or at study termination. In addition, nasal cavities were split longitudinally for examination of the turbinate area.

STATISTICS
The LC50 for females was calculated as a function of the time-weighted average analytical exposure concentrations by the moving-average method (Thompson and Weil, 1952). The LC50 for males was estimated by calculating the geometric man between exposure levels that resulted in 0 and 100% mortality among males, as implemented in a computer program furnished by Dr. Charles E. Stephan, USEPA Environmental Research Laboratory, Duluth, MN.

Test substance : >99% purity
Reliability : (1) valid without restriction
27.03.2002 (171)

Type : LC50
Value : = 360 ppm
Species : rat
Strain : Sprague-Dawley
Sex : male
Number of animals : 120
Vehicle : other: air
Doses :
Exposure time : 6 hour(s)
Method : other
Year : 1980
GLP : no
Test substance : no data

Reliability : (2) valid with restrictions
27.03.2002 (96)

Type : LC50
Value : = 2370 - 8300 ppm
Species : mouse
Strain : no data
Sex : no data
Number of animals : 90
Vehicle : other: air
Doses :
Exposure time : 60 minute(s)
Method : other
Year : 1941
GLP : no
Test substance : no data

Remark : Exposure time varied from 30-60 minutes.
Reliability : (2) valid with restrictions
27.03.2002 (64)

Type : LC50
Value : = 635 - 1052 ppm
Species : mouse

Strain : no data
Sex : no data
Number of animals : 70
Vehicle : other: air
Doses :
Exposure time : 2 hour(s)
Method : other
Year : 1961
GLP : no
Test substance : no data

Reliability : (4) not assignable
Limited English translation from RTECS; original article is in Russian.

27.03.2002 (91)

Type : LC50
Value : = 445 ppm
Species : rabbit
Strain : no data
Sex : no data
Number of animals :
Vehicle : no data
Doses :
Exposure time : 4 hour(s)
Method : other
Year : 1958
GLP : no data
Test substance : no data

Reliability : (4) not assignable
Unable to ascertain original reference.

27.03.2002 (148)

Type : LC50
Value : = 561 ppm
Species : guinea pig
Strain : no data
Sex : no data
Number of animals :
Vehicle : no data
Doses :
Exposure time : 4 hour(s)
Method : other
Year : 1958
GLP : no data
Test substance : no data

Reliability : (4) not assignable
Unable to ascertain original reference.

27.03.2002 (148)

Type : other: acute vapor toxicity
Value : ca. 250 ppm
Species : rat
Strain : Sherman
Sex : male/female
Number of animals : 6
Vehicle : other: air
Doses :
Exposure time : 4 hour(s)
Method : other

Year : 1949
GLP : no
Test substance : no data

Reliability : (3) invalid
Unclear in text whether the value given represents an LC50 value. Upon investigation of original report, this value was found to represent the LC0 (Monthly Report, Carnegie-Mellon Institute, 12/31/46). However, the original report lacks sufficient detail (test material purity, procedures, etc.) to permit determination of the validity of the findings.

27.03.2002 (22)

Type : other: LC67
Value : = 250 ppm
Species : rat
Strain : Wistar
Sex : no data
Number of animals : 6
Vehicle : other: air
Doses :
Exposure time : 8 hour(s)
Method : other
Year : 1948
GLP : no data
Test substance : no data

Result : Exposure to 250 ppm for 8 hours killed 4/6 rats; exposure to 250 ppm for 4 hours killed 0/6 rats; exposure to 500 ppm for 2 hours killed 6/6 rats, with severe kidney injury. (Taken from Monthly Report, Carnegie-Mellon Institute, 12/31/46).

Reliability : (3) invalid
Non-standard LC50 protocol; purity of test material unknown. The original report lacks sufficient detail (test material purity, procedures, etc.) to permit determination of the validity of the findings.

27.03.2002 (151)

Type : LC50
Value : = 500 ppm
Species : rat
Strain :
Sex :
Number of animals :
Vehicle :
Doses :
Exposure time : 4 hour(s)
Method : other
Year :
GLP : no data
Test substance : no data

Reliability : (3) invalid
Original reference not cited, but data indicated to have come from Smyth and Pozzani, Carnegie-Mellon Institute. Upon investigation of original reference material (Monthly Report, Carnegie-Mellon Institute, 12/31/46), it is believed that this value was reported in error. The actual data in the report indicate 6/6 rats died after exposure to 500 ppm for 2 hours. However, the original report lacks sufficient detail (test material purity, procedures, etc.) to permit determination of the validity of the findings.

27.03.2002 (149)

Type	:	LC50
Value	:	= 789 ppm
Species	:	rat
Strain	:	
Sex	:	
Number of animals	:	
Vehicle	:	
Doses	:	
Exposure time	:	2 hour(s)
Method	:	other
Year	:	1981
GLP	:	no data
Test substance	:	no data

Reliability : (4) not assignable
27.03.2002 (98)

5.1.3 ACUTE DERMAL TOXICITY

Type	:	LD50
Value	:	= 515 mg/kg bw
Species	:	rabbit
Strain	:	New Zealand white
Sex	:	male/female
Number of animals	:	2
Vehicle	:	other: undiluted
Doses	:	
Method	:	other
Year	:	1976
GLP	:	no
Test substance	:	other TS

Method : Approximately 24 hours prior to dosing, the hair was removed from the trunk of 2 laboratory white rabbits/dose level with electric clippers. The test material was applied at 100, 200, 650, or 795 mg/kg body weight under an impervious cuff held in place with a cloth bandage taped to the hair. Following application the animals were returned to holding cages and allowed to eat and drink ad libitum. Following a 24-hour exposure period, the cuffs were removed and the skins washed with soap and water. The animals were observed during and after exposure and weighed at intervals up to two weeks post-application. The animals were then submitted for necropsy examination at death or at scheduled study termination.

Result : MORTALITY:

Dose (mg/kg)	# Dead/# Treated Male	Female	
100	0/2	0/2	
200	0/2	0/2	
465	1/2	0/2	Found dead 24 hours post-dosing
795	2/2	2/2	Found dead 24 hours post-dosing

Test condition : TEST ORGANISM:

Source, Age, Strain: Unknown

Weight at Study Initiation: 2.43-3.50 kg

Controls: None

ADMINISTRATION:

Area Covered: Unknown

Occlusion: Impervious cuff held in place with cloth bandage taped to hair

Doses: 100, 200, 465, 795 mg/kg; single 24-hour dose

Vehicle: None, administered undiluted

Removal of Test Material: Washing with soap and water 24 hours post-dosing

Maximum Volume Administered: 2.38 ml

Post-Dose Observation Period: 2 weeks

Examinations: Clinical observations, body weights

Test substance : >99% purity
Reliability : (2) valid with restrictions
Conducted prior to GLP requirements, does not meet guideline requirements for minimum number of animals/dose level.

27.03.2002 (171)

Type : LD50
Value : = 754 mg/kg bw
Species : rabbit
Strain : no data
Sex : no data
Number of animals :
Vehicle : other: undiluted
Doses :
Method : other
Year : 1972
GLP : no data
Test substance : no data

Reliability : (2) valid with restrictions
27.03.2002 (97)

Type : LD50
Value : = 1180 - 2360 mg/kg bw
Species : rat
Strain : other: white
Sex : no data
Number of animals : 10
Vehicle : other: undiluted
Doses :
Method : other
Year : 1941
GLP : no data
Test substance : no data

Remark : LD50 value lies between two values cited; 2/10 died at 1180 mg/kg, while 18/20 died at 2360 mg/kg.
Test condition : Number of animals/dose group:

Dose (mg/kg)	# Animals
590	10
1180	10
2360	20

Reliability : (2) valid with restrictions
27.03.2002 (64)

Type : LD50
Value : = 1534 mg/kg bw
Species : rabbit
Strain : New Zealand white
Sex : male
Number of animals : 4
Vehicle : no data
Doses :
Method : other
Year : 1963
GLP : no
Test substance : no data

Reliability : (2) valid with restrictions
27.03.2002 (189)

Type : LD50
Value : = 1534 mg/kg bw
Species : rabbit
Strain : no data
Sex : no data
Number of animals : 3
Vehicle : no data
Doses :
Method : other
Year : 1948
GLP : no
Test substance : no data

Reliability : (2) valid with restrictions
27.03.2002 (152)

Type : LD50
Value : = 1038 mg/kg bw
Species : rabbit
Strain :
Sex :
Number of animals :
Vehicle :
Doses :
Method : other
Year : 1960
GLP : no
Test substance :

Reliability : (4) not assignable
27.03.2002 (118)

Type : other: acute dermal toxicity study
Value :
Species : rabbit
Strain : no data
Sex : no data
Number of animals : 2

Vehicle	:	other: propylene glycol
Doses	:	
Method	:	other
Year	:	1953
GLP	:	no
Test substance	:	no data
Result	:	Dose (mg/kg) # Dead/# Dosed 63 1/2 126 0/2 252 1/2 500 2/2
Reliability	:	(3) invalid Results do not demonstrate dose response, propylene glycol as vehicle may have enhanced absorption, purity of epichlorohydrin unspecified.

27.03.2002 (171)

5.1.4 ACUTE TOXICITY, OTHER ROUTES

Type	:	LD50
Value	:	= 133 mg/kg bw
Species	:	rat
Strain	:	
Sex	:	
Number of animals	:	
Vehicle	:	
Doses	:	
Route of admin.	:	i.p.
Exposure time	:	
Method	:	other
Year	:	
GLP	:	no data
Test substance	:	no data
Reliability	:	(3) invalid Route of administration not relevant to potential industrial exposure.

27.03.2002 (116)

Type	:	LD50
Value	:	= 154 mg/kg bw
Species	:	mouse
Strain	:	
Sex	:	
Number of animals	:	
Vehicle	:	
Doses	:	
Route of admin.	:	i.p.
Exposure time	:	
Method	:	other
Year	:	
GLP	:	no data
Test substance	:	no data
Reliability	:	(3) invalid Route of administration not relevant to potential industrial exposure.

27.03.2002 (116)

Type	:	LD50
Value	:	= 118 mg/kg bw
Species	:	guinea pig
Strain	:	no data
Sex	:	no data
Number of animals	:	
Vehicle	:	other: cottonseed oil
Doses	:	
Route of admin.	:	i.p.
Exposure time	:	
Method	:	other
Year	:	
GLP	:	no data
Test substance	:	no data
Reliability	:	(3) invalid Route of administration irrelevant to potential industrial exposure.

27.03.2002 (97)

Type	:	LD50
Value	:	= 150 mg/kg bw
Species	:	rat
Strain	:	no data
Sex	:	male
Number of animals	:	57
Vehicle	:	other: propylene glycol
Doses	:	
Route of admin.	:	s.c.
Exposure time	:	
Method	:	other
Year	:	1967
GLP	:	no data
Test substance	:	no data
Reliability	:	(3) invalid Route of administration irrelevant to potential exposure scenarios.

27.03.2002 (122)

5.2.1 SKIN IRRITATION

Species	:	rabbit
Concentration	:	undiluted
Exposure	:	Occlusive
Exposure time	:	24 hour(s)
Number of animals	:	
Vehicle	:	
PDII	:	
Result	:	corrosive
Classification	:	corrosive (causes burns)
Method	:	other: 2-24 h application of undiluted epichlorohydrin
Year	:	1967
GLP	:	no data
Test substance	:	other TS
Result	:	RESULTS Epichlorohydrin applied on the skin in quantities of 0.5 ml

for 24 hours caused appearance of a lesion presenting as a central zone of coagulation necrosis surrounded by hard swelling also affecting the superficial layers of the dermis. At the periphery of the lesion was a zone of erythema of various intensities with numerous petechial hemorrhages covering the application area. The application of smaller quantities, 0.1 to 0.2 ml, for a shorter period, 2 hours, resulted in the appearance of a similar lesion but of less intensity and reduced dimensions. In all cases after two to three days the zones of necrosis and erythema were covered by eschar which healed slowly (after 30 days for the 0.5 ml application). Following recovery the macroscopic appearance of the skin was normal.

Test condition : TEST CONDITIONS
Test Animals: Rabbits, number tested, strain, sex, age, source and weight at study initiation, unknown
Administration/Exposure: Draize and Woodard, 1949; Preparation of Test Substance: undiluted; Area of Exposure: unknown; Occlusion: Yes; Total volume applied: 0.5 ml for 24 hours or 0.1 to 0.2 ml for 2 hours
Examinations : Draize and Woodard, 1949

Test substance : Purity not specified.

Reliability : (2) valid with restrictions
Study conducted prior to the advent of GLPs, detailed information on test conditions and results (i.e., individual animal scores for PDII) were not given in the publication.

27.03.2002 (122)

Species : rabbit
Concentration : undiluted
Exposure : Open
Exposure time : 24 hour(s)
Number of animals : 5
Vehicle :
PDII :
Result : slightly irritating
Classification :
Method : other
Year : 1963
GLP : no
Test substance : no data

Method : 0.01 ml applied to unoccluded rabbit skin for 24 hours.

Reliability : (2) valid with restrictions

27.03.2002 (189)

Species : rabbit
Concentration : 5 %
Exposure : Occlusive
Exposure time : 24 hour(s)
Number of animals :
Vehicle :
PDII :
Result : highly irritating
Classification : corrosive (causes burns)
Method : other: 24 h occlusive patch, 5 % ECH in cottonseed oil
Year : 1972
GLP : no data
Test substance : no data

Reliability : (3) invalid
Scale for irritancy grading not clearly defined. Action of

diluent on irritancy unclear.

27.03.2002 (97)

Species	:	rabbit
Concentration	:	.3 %
Exposure	:	Occlusive
Exposure time	:	24 hour(s)
Number of animals	:	
Vehicle	:	
PDII	:	
Result	:	not irritating
Classification	:	not irritating
Method	:	other: 0.3 % ECH in cottonseed oil, 24 h occlusive patch
Year	:	1972
GLP	:	no
Test substance	:	no data
Reliability	:	(3) invalid Reliability judged to be category 3 because material was applied in cottonseed oil, rather than neat.

27.03.2002 (97)

5.2.2 EYE IRRITATION

Species	:	rabbit
Concentration	:	undiluted
Dose	:	0 ml
Exposure time	:	24 hour(s)
Comment	:	
Number of animals	:	
Vehicle	:	
Result	:	corrosive
Classification	:	risk of serious damage to eyes
Method	:	other: instillation of 0.05 ml of undiluted ECH
Year	:	1963
GLP	:	no data
Test substance	:	no data
Remark	:	Severe corneal burns.
Result	:	RESULTS In the rabbit eye, 0.001 ml produced severe necrosis. An excess of 0.1% solution in water also caused necrosis, but a 0.01% aqueous solution did not (as documented in original study report 8-28). Individual and total scores were not available in original study report 8-28. No data given as to reversibility. Weil et al. (1946) published an injury grade of 4 out of a possible 10 (defined as: 0.02 ml undiluted gives injury of up to 5 points on a maximum scale of 20 points). This is inconsistent with the results cited in the original report.
Test condition	:	TEST CONDITIONS Test Animals: Rabbits, number tested, strain, sex, age, source and weight at study initiation, unknown Administration/Exposure: Preparation of Test Substance: undiluted; Amount of Substance Instilled: 0.001 ml; Post-Exposure Period: Scored at 24 hours post-dosing Examinations : Ophthalmoscopic examination: No; Scoring system: as cited in Carpenter and Smyth, 1946; Tool Used to Assess Score: fluorescein
Reliability	:	(2) valid with restrictions

27.03.2002 (188)

Species : rabbit
Concentration : 80 %
Dose : .1 ml
Exposure time : 3 hour(s)
Comment :
Number of animals :
Vehicle :
Result : highly irritating
Classification :
Method : other: instillation of 0.1 ml of 80% ECH in cottonseed oil
Year : 1972
GLP : no data
Test substance : no data

Remark : Corneal damage within 3 hours.
Reliability : (2) valid with restrictions
Study conducted prior to advent of GLP; cottonseed oil vehicle used rather than undiluted.

27.03.2002 (97)

Species : rabbit
Concentration : 20 %
Dose : .1 ml
Exposure time : 3 hour(s)
Comment :
Number of animals :
Vehicle :
Result : slightly irritating
Classification :
Method : other: instillation of 0.1 ml of 20% ECH in cottonseed oil
Year : 1972
GLP : no data
Test substance : no data

Remark : Conjunctival irritation and edema.
Reliability : (2) valid with restrictions
Study conducted prior to advent of GLP; cottonseed oil vehicle used rather than undiluted.

27.03.2002 (97)

Species : rabbit
Concentration : 5 %
Dose : .1 ml
Exposure time : 3 hour(s)
Comment :
Number of animals :
Vehicle :
Result : not irritating
Classification :
Method : other
Year : 1972
GLP : no
Test substance : no data

Reliability : (2) valid with restrictions
Study conducted prior to advent of GLP; cottonseed oil vehicle used rather than undiluted.

27.03.2002 (97)

5.3 SENSITIZATION

Type	:	Guinea pig maximization test
Species	:	guinea pig
Concentration	:	1st: Induction 5 % intracutaneous 2nd: Induction 5 % occlusive epicutaneous 3rd: Challenge 1 % occlusive epicutaneous
Number of animals	:	15
Vehicle	:	other: ethanol
Result	:	sensitizing
Classification	:	sensitizing
Method	:	OECD Guide-line 406 "Skin Sensitization"
Year	:	1977
GLP	:	no
Test substance	:	other TS
Result	:	9 of 15 guinea pigs showed a sensitizing effect.
Test substance	:	Purity not specified.
Reliability	:	(1) valid without restriction Study conducted prior to advent of GLP.

27.03.2002 (167)

Type	:	other: Maguire Test
Species	:	guinea pig
Concentration	:	1st: Induction 10 % occlusive epicutaneous 2nd: Challenge 10 % open epicutaneous 3rd:
Number of animals	:	10
Vehicle	:	other: dipropylene glycol methyl ether: Tween 80, 9:1
Result	:	sensitizing
Classification	:	
Method	:	other: Maguire method
Year	:	1986
GLP	:	no
Test substance	:	as prescribed by 1.1 - 1.4
Result	:	Five out of ten animals sensitized.
Reliability	:	(2) valid with restrictions Unknown whether study was conducted according to GLP. Does not totally comply with suggested guideline, but study is scientifically acceptable.

27.03.2002 (173)

Type	:	other: either Maguire or Landsteiner & Jacobs
Species	:	guinea pig
Concentration	:	1st: Induction .5 % open epicutaneous 2nd: Challenge .5 % open epicutaneous 3rd:
Number of animals	:	10
Vehicle	:	other: dipropylene glycol methyl ether: Tween 80 mixture, 9:1
Result	:	sensitizing
Classification	:	sensitizing
Method	:	other: unspecified (either Maguire or Landsteiner & Jacobs)
Year	:	1981
GLP	:	no
Test substance	:	no data
Remark	:	Positive reaction in all 10 experimental animals obtained. No concentration data given. Concentration data obtained from original unpublished report of The Dow Chemical Company.

Reliability	:	(2) valid with restrictions
27.03.2002		(134)
Type	:	Intracutaneus test
Species	:	guinea pig
Concentration	:	1st: Induction .1 other: ml diluted intracutaneous 2nd: Challenge 3rd:
Number of animals	:	18
Vehicle	:	no data
Result	:	not sensitizing
Classification	:	
Method	:	other
Year	:	1963
GLP	:	no
Test substance	:	no data
Reliability	:	(3) invalid Results inconsistent with later, better documented studies and human occupational experience.
27.03.2002		(189)

5.4 REPEATED DOSE TOXICITY

Type	:	
Species	:	other: mice, rats, rats
Sex	:	male/female
Strain	:	other: B6C3F1, Fischer 344, Sprague-Dawley
Route of admin.	:	inhalation
Exposure period	:	90 days
Frequency of treatm.	:	6 h/d, 5 d/week
Post exposure period	:	None
Doses	:	0, 5, 25, 50 ppm
Control group	:	yes
NOAEL	:	= 5 ppm
LOAEL	:	= 25 ppm
Method	:	other
Year	:	1979
GLP	:	no
Test substance	:	other TS

Method :

TEST ORGANISMS:
Fischer 344 rat: 9-11 weeks old, males 205-219 g, females 125-139 g.
Sprague-Dawley rat: 9-11 weeks old, males 357-376 g, females 236-245 g.
B6C3F1 mouse: 7-9 weeks old, males 20-27 g, females 20-22 g.

ADMINISTRATION/EXPOSURE:
Groups of 20 animals per sex per dose level were exposed to 0, 5, 25, or 50 ppm six hours daily, five days per week, for 12 weeks.

Whole-body vapor exposures were carried out in 14.5 cubic meter chambers. Atmospheres were generated by metering liquid through a pump into a warmed vaporization flask, then sweeping the vapors into the chamber with compressed air. Chamber air was assayed for vapor concentration at least 3 times during each 6-hour exposure period.

SATELLITE GROUPS: Groups of 5 male Fischer 344 rats and male B6C3F1 mice were added for pharmacokinetic/metabolism studies.

CLINICAL OBSERVATIONS AND FREQUENCY:
Animals were observed daily for signs of toxicity and morbidity/mortality. Body weights were collected twice weekly for the first two weeks of exposure, weekly for weeks three and four, and every two weeks thereafter.

One to two weeks prior to necropsy (rats) or at necropsy (mice), blood samples were collected for hematologic analysis. Parameters examined were packed cell volume, red blood cell count, hemoglobin concentration, and white blood cell count. Urinalysis samples from rats were collected when blood samples were collected; parameters examined were specific gravity, pH, sugar, protein, ketones, bilirubin, occult blood, urobilinogen.

Feed/water consumption were not monitored during the study. Ophthalmoscopic examinations were not performed during the study.

ORGANS EXAMINED AT NECROPSY:
At necropsy, blood samples were collected for analysis of clinical chemistry parameters: blood urea nitrogen, glutamic pyruvic transaminase activity, alkaline phosphatase activity, glutamic oxaloacetic transaminase activity, and glucose concentration.

A complete necropsy examination was conducted on each animal, during which organ weights for brain, heart, liver, kidneys, testes, spleen, and thymus were recorded. Approximately 40 organs/tissues (esophagus, stomach, small intestine, pancreas, mediastinal lymphoid tissue (thymus, mediastinal lymph nodes), urinary bladder, heart, testes, ovaries, uterus, gall bladder, pituitary gland, salivary glands, lungs, vertebral bone and bone marrow, spinal cord, spleen, kidneys, prostate, epididymides, skeletal tissue, oviducts, parathyroid gland, brain, skin, eyes, trachea, nasal turbinates, large intestine, liver, lymph nodes, seminal vesicles, aorta, adrenal gland, thyroid gland, mammary gland, adipose tissue, peripheral nerve) from each animal were examined histologically for the control and high dose groups; possible target organs were examined for low and
middle dose groups.

After thirty days on test, an interim sacrifice was conducted on 10 animals per sex per dose level. Parameters evaluated were hematology, urinalysis (rats only), clinical chemistry, gross pathology, organ weights, and histopathology. Histopathology was conducted on five animals per sex per dose level from the control and high dose groups.

STATISTICAL METHODS:
Body weights, hematology, urinalysis, clinical chemistries, and organ weights were analyzed via ANOVA with a Dunnett's Test.

Result : NOAEL, LOAEL:
The NOAEL was 5 ppm for all species and strains. The LOAEL

was 25 ppm for all species and strains.

Terminal white blood cell counts in male Fischer 344 rats were statistically decreased from controls only at 5 ppm. At 5 ppm, interim and terminal kill white blood cell counts in female Sprague Dawley rats were statistically identified as different from controls. Terminal SGOT values for male Fischer 344 rats at 5 ppm only were statistically lower than controls. Interim kill BUN values in male B6C3F1 mice and AP values in female B6C3F1 mice were statistically different from controls at 5 ppm, but were not different from controls at the terminal kill. Urine specific gravity was statistically decreased in female Fischer 344 rats at 5 ppm on test day 73, but not at study termination. Interim (day 30) absolute kidney and testes weights in male Fischer 344 rats at 5 ppm were statistically increased, but relative kidney and testes weights were unaffected. Terminal absolute kidney weights in male Sprague-Dawley rats at 5 ppm were statistically increased, but relative kidney weights were unaffected. Interim (day 30) absolute and relative liver weights in male and female B6C3F1 mice at 5 ppm were statistically decreased; this effect was not seen at study termination. Terminal spleen weights in female B6C3F1 mice at 5 ppm were statistically increased; this effect was not seen at higher exposure concentrations. Since neither dose-response nor temporal patterns were consistently present, all of the differences described above were not considered treatment-related.

ACTUAL DOSE RECEIVED:
Analysis of chamber air for epichlorohydrin found the concentrations (mean +/- SD) to be 5.01 +/- 0.42, 24.90 +/- 0.94, 50.10 +/- 1.60 ppm.
No treatment-related deaths were observed at any dose level.

TOXIC RESPONSE/EFFECTS:
Clinical Observations (Fischer 344 and Sprague-Dawley rats, B6C3F1 mice): During the hours of exposure, the rats appeared to show conjunctival redness and palpebral closure without subsequent evidence of ocular involvement. These effects appeared to be transient, with recovery occurring overnight. Slight decreases in cage movements were observed in rats exposed to 25 or 50 ppm primarily during the first ten days of exposure and intermittently thereafter. These effects were not observed in mice.

FISCHER 344 RATS
Body Weights: Female Fischer 344 rats exposed to 50 ppm showed statistically decreased body weights on day zero which tended to remain lower throughout the study. Female Fischer 344 rats exposed to 25 ppm occasionally showed decreased body weights during the first month of exposure, but not at study termination.
Clinical Chemistry: No treatment-related changes in clinical chemistries were found in Fischer 344 rats.
Hematology: No treatment-related changes in hematology were found in Fischer 344 rats.
Urinalysis: No treatment-related changes in urinalysis parameters were found in Fischer 344 rats.
Organ Weights: Absolute and/or relative kidney weights were increased in male and female Fischer 344 rats at 25 and 50 ppm at interim and terminal examinations. Various other

changes in organ weights were judged to be unrelated to treatment.
Gross Pathology: No lesions were observed which were considered treatment-related.

SPRAGUE-DAWLEY RATS
Body Weight: Male Sprague-Dawley rats exposed to 50 ppm showed statistically decreased body weights during the first month which tended to remain lower throughout the study. There were no treatment-related changes in body weights for female rats.
Clinical Chemistry: No treatment-related changes in clinical chemistries were found in Sprague-Dawley rats.
Hematology: No treatment-related changes in hematology were found in Sprague-Dawley rats.
Urinalysis: No treatment-related changes in urinalysis parameters were found in Sprague-Dawley rats.
Organ Weights: Absolute and/or relative kidney weights were increased in male and female Sprague-Dawley rats at either 25 or 50 ppm at interim and terminal examinations. Various other changes in organ weights were judged to be unrelated to treatment.
Gross Pathology: Kidneys in male Sprague-Dawley rats exposed to 25 or 50 ppm were slightly pale in color and increased in size at study termination. Livers in male Sprague-Dawley rats exposed to 50 ppm a slight accentuated lobular pattern with a pale color at study termination. No other lesions were observed which were considered treatment-related in either male or female Sprague-Dawley rats.

B6C3F1 MICE
Body Weight: Male and female B6C3F1 mice exposed to 50 ppm showed a trend toward decreased weight during the last few weeks of the study, occasionally identified as statistically significant.
Clinical Chemistry: No treatment-related changes in clinical chemistries were found in B6C3F1 mice.
Hematology: No treatment-related changes in hematology were found in B6C3F1 mice.
Organ Weights: Interim (day 30) absolute and relative liver weights in male mice at 5 and 50 ppm were statistically decreased; this effect was not seen at study termination. Male mice at 50 ppm had statistically significantly increased relative brain weights at study termination. Interim (day 30) absolute and/or relative liver weights in female mice at 5, 25, and 50 ppm were statistically decreased; this effect was not seen at study termination. Absolute heart weight was also decreased in female mice at 50 ppm; this effect was not seen at study termination.
Gross Pathology: At study termination, male mice (and one female mouse) at 50 ppm had decreased intraabdominal fat, consistent with decreased body weight. No other lesions were observed which were considered treatment-related in either male or female mice.

Histopathology (Fischer 344 and Sprague-Dawley rats, B6C3F1 mice): Histopathological examinations showed that the nose was the most sensitive organ to exposure. At the higher concentrations microscopic examination revealed hyperplasia, metaplasia and inflamed cell infiltration in the nasal turbinates. In addition, exposure at 25 or 50 ppm caused slight non-progressive kidney effects in rats but not mice,

as evidenced by increased kidney weights (relative and/or absolute). Slight non-degenerative liver effects were noted in rats of both strains as well as the mice exposed to 50 ppm. Male rats of both strains at 50 ppm had slight effects on the adrenal glands, possibly mediated by stress. In male Sprague-Dawley rats at 50 ppm, there were minimal changes in the contents of the epididymides.

Test substance : >99% purity
Reliability : (1) valid without restriction
Study conducted prior to advent of GLP.

27.03.2002 (132) (133)

Type :
Species : rat
Sex : male/female
Strain : Sprague-Dawley
Route of admin. : gavage
Exposure period : 90 day
Frequency of treatm. : Once daily
Post exposure period :
Doses : 1, 5, 25 mg/kg/day
Control group : yes, concurrent vehicle
NOAEL : = 1 mg/kg bw
LOAEL : = 5 mg/kg bw
Method : other
Year : 1996
GLP : no data
Test substance : other TS

Result : Epichlorohydrin did not adversely effect mortality, but toxicity, at the higher doses, was evident by: 1) losses in body weight gain and organ weights, 2) reductions in food and water consumption, and 3) in the hematological and microscopic examinations. Significant decreases in erythrocyte count, hemoglobin, and hematocrit levels were found in the high dose level in males after 90 days. Dose-related increases in kidney and liver weights were observed in both sexes at 25 mg/kg-day in the 90-day study. Histopathological examination identified the forestomach as the primary target organ for both sexes with significant dose-related increases in mucosal hyperplasia (acanthosis) and hyperkeratosis. Based on the data presented, for oral exposure of Sprague-Dawley rats to epichlorohydrin 1 mg/kg/day is suggested as the no observed adverse effect level (NOAEL) for a 90 day oral exposure. These conclusions were the same whether the lesions were analyzed for each sex individually or whether the data was pooled.

Test condition : Adult male and female Sprague-Dawley rats received epichlorohydrin via gavage in distilled water for 90 days at dose levels of 1, 5, and 25 mg/kg-day.
Test substance : Purity not specified.
Reliability : (1) valid without restriction
1B

27.03.2002 (27)

Type :
Species : rat
Sex : male
Strain : Sprague-Dawley
Route of admin. : i.p.
Exposure period : 12 weeks
Frequency of treatm. : 3 times a week

Post exposure period	:	none
Doses	:	11, 22, 56 mg/kg body weight
Control group	:	yes, concurrent vehicle
LOAEL	:	= 11 mg/kg bw
Method	:	other
Year	:	1972
GLP	:	no data
Test substance	:	no data
Result	:	A statistically significant, dose-dependent reduction in haemoglobin was found. In the two highest dosage groups the proportion of lymphocytes was significantly reduced, while the proportion of eosinophiles was increased in all of the dosage groups. In the highest dosage group a marked increase in organ weight of heart, liver and kidneys was observed.
Test substance	:	ECH in cottonseed oil as vehicle.
Reliability	:	(3) invalid Route irrelevant to potential industrial exposure.

27.03.2002 (97)

Type	:	
Species	:	rabbit
Sex	:	male
Strain	:	New Zealand white
Route of admin.	:	inhalation
Exposure period	:	20 d (35 ppm), 2 d (16 ppm) + 20 d (9 ppm)
Frequency of treatm.	:	daily
Post exposure period	:	
Doses	:	35, 16 and 9 ppm
Control group	:	no
NOAEL	:	= 9 ppm
LOAEL	:	= 16 ppm
Method	:	other
Year	:	1959
GLP	:	no data
Test substance	:	other TS
Remark	:	The atmospheres were prepared by atomizing solutions of ECH in propanol into a metered stream of air by means of controlled fluid-feed atomizer. A daily analytical check on the concentration of the ECH atmospheres was made.
Result	:	Two rabbits exposed to 35 ppm showed signs of nasal irritation although no gross or microscopic effects were observed in any tissues examined including the respiratory tract. Two more rabbits were exposed to 16 ppm also showed nasal irritation after 2 days; the concentration was decreased to 9 ppm and then continued for 20 days without producing effects on rabbits.
Test substance	:	Purity not specified.
Reliability	:	(3) invalid Study results confounded by presence of propanol used to generate atmospheres.

27.03.2002 (65)

Type	:	
Species	:	rat
Sex	:	male/female
Strain	:	Wistar
Route of admin.	:	inhalation

Exposure period : 11 (120 ppm), 18 (56, 27 ppm), 19 (17 ppm) and 18 (9 ppm) exposures
Frequency of treatm. : 6 h/d, 5 d/w
Post exposure period :
Doses : 9, 17, 27, 56 and 120 ppm
Control group :
NOAEL : = 17 ppm
LOAEL : = 27 ppm
Method : other
Year : 1959
GLP : no data
Test substance : other TS

Remark : The atmospheres were prepared by atomizing solutions of ECH in propanol into a metered stream of air by means of controlled fluid-feed atomizer.
A daily analytical check on the concentration of the ECH atmospheres was made.

Result : Groups of 4 males and 4 females rats exposed to ECH vapour :
120 ppm : The groups developped laboured breathing during
--------- the exposures and exhibited a nasal discharge from the 4th exposure onwards. After a total of 11 exposures, renal damage was evident in 4/8 rats, characterised histologically by atrophy of the peripheral cortical tubules. Necropsies performed at the end of the exposure period revealed lungs with patchy discolouration, congestion, oedema and areas of inflammation.
56 ppm : Rats demonstrated respiratory distress and nasal
--------- discharge after the 10th exposure. However, no abnormalities were noted at necropsy.
27 ppm : The exposures produced no specific toxic effects
--------- apart from generally poor condition of the rat compared to the colony.
17 ppm : Same remark.
---
9 ppm : No effects.

Test substance : Purity not specified.
Reliability : (3) invalid
Study results confounded by presence of propanol used to generate atmospheres.

27.03.2002 (65)

Type :
Species : rat
Sex :
Strain :
Route of admin. : inhalation
Exposure period : 4 w
Frequency of treatm. : 4 h/d
Post exposure period : 14 d
Doses : 8 ppm
Control group : yes, concurrent no treatment

Remark : Poorly reported East German study.
Result : Groups of 30 rats were exposed to ECH vapour.
Rats showed interstitial and desquamative pneumonia (extent and severity unspecified) both at the end of treatment and following the recovery period.
Oligourea was reported to have occured on day 10 of the exposure period (no data given) in the treated rats. The total amount of protein excreted in the urine was also decreased and this was probably due to the reduced volume of

urine collected. At day 10, histopathological evaluation revealed renal interstitial oedema. At day 30, 6/10 rats showed glomerulonephritis with some nephrosis. The extent and severity of all these changes were not stated. At day 14 after the end of treatment, glomeronephritis was observed in 5/10 animals.

Reliability : (3) invalid

27.03.2002 (71)

Type :
Species : rat
Sex :
Strain :
Route of admin. : inhalation
Exposure period : 98 d
Frequency of treatm. : continuous
Post exposure period :
Doses : 0.053, 0.53 and 5.3 ppm
Control group : yes

Remark : Brief Russian report with few experimental details.

Result : The only effects of toxicological significance were observed after exposure to 5.3 ppm.
In this group, necropsy at the end of the exposure period revealed emphysematic lungs with bronchopneumonia and small areas of oedema. "Cloudy swelling" of the epithelium of the kidney convoluted tubules was also observed. Microscopic foci of interstitial haemorrhage and venous congestion were observed in the heart. There were also reported to be severe lesions (unspecified) of the neurons in the medulla oblongata, hippocampus and cerebellum of the brain. From weekly observations made during the exposure period, it was claimed that rats exposed to 5.3 ppm exhibited an increase, compared to controls, in the "latent reaction period" of the "motor-defence response to stimulation with electric current". No changes were observed in haematological parameters (eg RBC, WBC) in any of the groups. Neurological lesions induced by ECH have not been reported in any other studies.

Reliability : (3) invalid
Study detail insufficient to ascertain validity.

27.03.2002 (63)

5.5 GENETIC TOXICITY 'IN VITRO'

Type : other: review
System of testing : Various
Test concentration :
Cycotoxic concentr. :
Metabolic activation :
Result :
Method :
Year : 1997
GLP :
Test substance :

Conclusion : From the results of the bacterial mutagenicity assays and DNA damage induced by ECH it appears that it is a direct-acting mutagen. Results of the cytogenetic assays clearly reflect its behaviour as a direct-acting mutagen.

All the reports of in vitro cytogenetic assay are in concordance with those of in vitro mutagenicity assays in microorganisms. Thus, the overall appraisal of the reports on bacterial mutagenicity and cytogenetic assays indicates that ECH is a mutagen as well as a clastogen both in vitro and in vivo.

Reliability : (1) valid without restriction
1d

27.03.2002 (69)

Type : other: review
System of testing :
Test concentration :
Cycotoxic concentr. :
Metabolic activation :
Result :
Method :
Year : 1981
GLP :
Test substance :

Conclusion : The available data provide good evidence of gene and chromosomal mutagenicity of ECH in several experimental systems both in vitro and in laboratory animals. Cytogenetic studies of workers exposed to ECH have yielded equivocal evidence for a clastogenic effect on lymphocytes.

Reliability : (1) valid without restriction
1d

27.03.2002 (161)

Type : other: Bacterial host-mediated assay
System of testing : S. typhimurium (G48, TA100, TA1950)
Test concentration :
Cycotoxic concentr. :
Metabolic activation :
Result : positive
Method :
Year :
GLP :
Test substance :

Remark : Strains of S. typhimurium sensitive to base-pair substitution were inoculated into the peritoneal cavities of mice, wich were subsequently exposed either i.m. or s.c. to ECH. In the same experiment, no increase in revertants was observed in strains (TA1957 and TA1952) sensitive to frameshift mutations.

Reliability : (3) invalid

27.03.2002 (158)

Type : other: Yeast host-mediated assay
System of testing : S. pombe (P1)
Test concentration :
Cycotoxic concentr. :
Metabolic activation :
Result : negative
Method :
Year :
GLP :
Test substance :

Remark : No increase was observed in forward mutation frequency in

the P1 strain of the yeast S. pombe isolated from the peritoneal cavity of mice which had been treated orally with ECH.

Reliability : (3) invalid
27.03.2002 (141)

Type : Ames test
System of testing : Salmonella typhimurium TA 98,100,1535,1537,1538
Test concentration :
Cycotoxic concentr. :
Metabolic activation : with and without
Result : positive
Method : OECD Guide-line 471
Year :
GLP : no data
Test substance :

Remark : In standard assays, ECH has been shown to increase the yield of revertant in strains of Salmonella typhimurium (TA 100, TA 1535) and E. Coli (WP3uvrA), Klebsiella pneumoniae. Other S. typhimurium strains were negative or marginally positive (TA 98, TA 1537, TA 1538).

In the presence of metabolic activation, reduction of the genotoxic potential was seen.

Exposure of bacteria in vapour phase or sealed systems also resulted in a positive response.

Reliability : (2) valid with restrictions
27.03.2002 (3) (10) (29) (33) (45) (46) (107) (108) (119) (130) (162) (185)

Type : Ames test
System of testing : Salmonella typhimurium TA 100, 1535; G 46
Test concentration :
Cycotoxic concentr. :
Metabolic activation : no data
Result : positive
Method : OECD Guide-line 471
Year :
GLP : no
Test substance :

Reliability : (2) valid with restrictions
27.03.2002 (158)

Type : Sister chromatid exchange assay
System of testing : human lymphocytes
Test concentration :
Cycotoxic concentr. :
Metabolic activation : with and without
Result : positive
Method :
Year :
GLP :
Test substance :

Remark : Human lymphocytes were cultivated for 73 h in the presence of 5-bromo-2-deoxyuridine and exposed to ECH with/without S-9 Mix. At an ECH concentration of 0.0004 M, without activation a 3-fold increase in the SCE rate was observed compared to the control, while with activation through S-9 Mix the same increase was effected by an ECH concentration

of 0.001 M.
Reliability : (2) valid with restrictions
27.03.2002 (193)

Type : Unscheduled DNA synthesis
System of testing : human fibroblasts (WI-38)
Test concentration : 0.005-0.8 microl/ml
Cycotoxic concentr. :
Metabolic activation :
Result : positive
Method :
Year :
GLP : no data
Test substance :

Remark : Other tests have failed to demonstrate the same effect (primary rat hepatocytes, human lymphocytes, human cervical carcinoma (HeLa) cells)
Reliability : (3) invalid
27.03.2002 (123) (130) (140)

Type : Cytogenetic assay
System of testing : Chinese hamster ovary cells
Test concentration : 0.017-0.1 microl/ml
Cycotoxic concentr. :
Metabolic activation :
Result : positive
Method :
Year :
GLP :
Test substance :

Remark : Sister chromatid exchange and chromosome aberration test
Reliability : (2) valid with restrictions
27.03.2002 (114)

Type : Cytogenetic assay
System of testing : human lymphocytes
Test concentration :
Cycotoxic concentr. :
Metabolic activation :
Result : positive
Method :
Year :
GLP :
Test substance :

Remark : Increased in chromosome breaks and exchanges in PHA-stimulated human peripheral lymphocytes. No effect when ECH was used before stimulation.
Reliability : (3) invalid
27.03.2002 (93) (117) (158)

Type : Yeast gene mutation assay
System of testing :
Test concentration :
Cycotoxic concentr. :
Metabolic activation : with and without
Result : positive
Method :
Year :
GLP :

Test substance :

Remark : The induction of both forward and reverse mutations by epichlorohydrin in strains of Neurospora crassa, Schizosaccharomyces pombe and cerevisiae have been reported. Also inter and intra chromosomal recombination, gene conversion, mitotic cross-overs and mitotic aneuploidy in S. cerevisiae as well as reduced survival in repair-deficient strains was observed.
The addition of metabolic activation results in a reduction of the genotoxic activity.

Reliability : (2) valid with restrictions
27.03.2002 (33) (34) (88) (109) (110) (142) (143) (146) (181)

Type : Mammalian cell gene mutation assay
System of testing :
Test concentration :
Cycotoxic concentr. :
Metabolic activation :
Result :
Method :
Year :
GLP :
Test substance :

Remark : In various mammalian cell lines including mouse lymphoma and human embryonic, ECH in the liquid phase induce an increase in the frequency of forward mutation (e.g. at the HGPRT and TK loci).

Reliability : (2) valid with restrictions
27.03.2002 (2) (33) (87) (123)

5.6 GENETIC TOXICITY 'IN VIVO'

Type : other: review
Species :
Sex :
Strain :
Route of admin. :
Exposure period :
Doses :
Result :
Method :
Year : 1997
GLP :
Test substance :

Conclusion : From the results of the bacterial mutagenicity assays and DNA damage induced by ECH it appears that it is a direct-acting mutagen. Results of the cytogenetic assays clearly reflect its behaviour as a direct-acting mutagen.
All the reports of in vitro cytogenetic assay are in concordance with those of in vitro mutagenicity assays in microorganisms. Thus, the overall appraisal of the reports on bacterial mutagenicity and cytogenetic assays indicates that ECH is a mutagen as well as a clastogen both in vitro and in vivo.

Reliability : (1) valid without restriction
1d
27.03.2002 (69)

Type	:	other: review
Species	:	
Sex	:	
Strain	:	
Route of admin.	:	
Exposure period	:	
Doses	:	
Result	:	
Method	:	
Year	:	1981
GLP	:	
Test substance	:	
Conclusion	:	The available data provide good evidence of gene and chromosomal mutagenicity of ECH in several experimental systems both in vitro and in laboratory animals. Cytogenetic studies of workers exposed to ECH have yielded equivocal evidence for a clastogenic effect on lymphocytes.
Reliability	:	(1) valid without restriction 1d

27.03.2002 (161)

Type	:	Cytogenetic assay
Species	:	mouse
Sex	:	male
Strain	:	CD-1
Route of admin.	:	other: oral administration in water
Exposure period	:	single treatment
Doses	:	50, 200 mg ECH/kg b.w.
Result	:	negative
Method	:	other
Year	:	1983
GLP	:	no data
Test substance	:	as prescribed by 1.1 - 1.4
Remark	:	At intervals of 6, 24, 48 h following treatment, samples of bone marrow were taken from the animals' femur for chromosome aberration examination.
Result	:	For neither of the two dose levels was an increased chromosome aberration rate found. No toxic effects are reported.
Reliability	:	(2) valid with restrictions

27.03.2002 (142)

Type	:	Cytogenetic assay
Species	:	rat
Sex	:	male/female
Strain	:	Fischer 344
Route of admin.	:	inhalation
Exposure period	:	4 weeks
Doses	:	0, 5, 25, 50 ppm 6 h/d, 5 d a week
Result	:	
Method	:	
Year	:	
GLP	:	
Test substance	:	
Remark	:	The authors estimated that the amount of absorbable ECH at the 3 administered concentrations was 0.6, 12, 24 mg/animal/day.
Result	:	Although not all of the administered ECH was absorbed and a

part of that which was absorbed was metabolized before reaching the bone marrow, no significant increase in the number of chromosome aberrations was observed.

Reliability : (2) valid with restrictions
27.03.2002 (26)

Type : Cytogenetic assay
Species : rat
Sex :
Strain :
Route of admin. : inhalation
Exposure period : 120 hours
Doses : 1.3 - 33 ppm
Result :
Method :
Year :
GLP :
Test substance :

Result : analysis of bone marrow and peripheral lymphocytes indicates no increase in the frequency of chromosome aberrations.
Reliability : (2) valid with restrictions
27.03.2002 (157)

Type : Cytogenetic assay
Species : mouse
Sex :
Strain :
Route of admin. : gavage
Exposure period : single or multiple exposure
Doses : 1 x 100 mg/kg or 5 x 20 mg/kg
Result :
Method :
Year :
GLP :
Test substance :

Remark : Bone marrow was examined at 6, 24, 48 hour post treatment.
Result : Dose-dependant increase in frequency of chromosome breaks as compared to DMSO-treated controls.
Reliability : (2) valid with restrictions
27.03.2002 (158)

Type : Cytogenetic assay
Species : mouse
Sex :
Strain :
Route of admin. : i.p.
Exposure period : single or multiple
Doses : 1 x 100 mg/kg or 5 x 20 mg/kg
Result :
Method :
Year :
GLP :
Test substance :

Remark : Bone marrow was examined at 6, 24, 48 hour post treatment.
Result : Dose-dependant increase in frequency of chromosome breaks as compared to DMSO-treated controls.
Effects more pronounced than with oral administration.
Reliability : (3) invalid
27.03.2002 (158)

Type : Dominant lethal assay
Species : mouse
Sex : male/female
Strain :
Route of admin. : i.p.
Exposure period : single treatment
Doses : 150 mg ECH/kg b.w.
Result :
Method :
Year :
GLP :
Test substance :

Result : During the 8-week mating period the male animals showed no effects from the treatment.
Reliability : (3) invalid
27.03.2002 (57)

Type : Dominant lethal assay
Species : mouse
Sex : male/female
Strain :
Route of admin. : i.p.
Exposure period : single treatment
Doses : 5, 10, 20 mg ECH/kg b.w.
Result :
Method :
Year :
GLP :
Test substance :

Result : No induction of dominant lethal mutations.
Reliability : (3) invalid
27.03.2002 (158)

Type : Dominant lethal assay
Species : mouse
Sex : male/female
Strain :
Route of admin. : oral unspecified
Exposure period : single administration
Doses : 20, 40 mg ECH/kg b.w.
Result :
Method :
Year :
GLP :
Test substance :

Result : No induction of dominant lethal mutations were observed.
Reliability : (2) valid with restrictions
27.03.2002 (158)

Type : Mammalian germ cell cytogenetic assay
Species : mouse
Sex : male/female
Strain :
Route of admin. : inhalation
Exposure period : 8 weeks
Doses : atmosphere containing 125 mg ECH/m3
Result :
Method :

Year :
GLP :
Test substance :

Remark : 20 males were mated once a week with 40 females.
Result : A significant increase in resorption in the 3rd week following exposure for 120 h. An increased number of chromosome aberrations in the spermatogonia, as well as morphologically abnormal sperm were observed.
Reliability : (2) valid with restrictions
27.03.2002 (160)

Type : Micronucleus assay
Species : mouse
Sex : male
Strain : Swiss Webster
Route of admin. : other: oral, ECH in corn oil
Exposure period : 16 days, 19 days post-treatment
Doses : 12 doses of 10 mg ECH/kg b.w.
Result :
Method :
Year :
GLP :
Test substance :

Remark : During the 19-day post-treatment observation period, from the 8th day following treatment the number of micronuclei observed in normochromatic erythrocytes of the animals' peripheral blood increased continually.
Reliability : (2) valid with restrictions
27.03.2002 (186)

Type : Unscheduled DNA synthesis
Species : other: rat mucous membrane
Sex : no data
Strain :
Route of admin. : oral unspecified
Exposure period : single dose
Doses : 50 , 100 mg ECH/kg b.w.
Result :
Method :
Year :
GLP :
Test substance :

Result : 14-16 hours after treatment there was a significant 2-3-fold increase in the rate of 3-H-thymidine incorporation.
Reliability : (3) invalid
27.03.2002 (21)

Type : other: sperm head morphology
Species : mouse
Sex :
Strain :
Route of admin. : i.p.
Exposure period : 5 days
Doses : up to 0.2 mg/kg
Result :
Method :
Year :
GLP :
Test substance :

Result : No effect on sperm-head morphology.
Reliability : (3) invalid
27.03.2002 (168)

5.7 CARCINOGENICITY

Species : rat
Sex : male/female
Strain : Wistar
Route of admin. : gavage
Exposure period : 2 years
Frequency of treatm. : 5 days/week
Post exposure period : Not applicable
Doses : 0, 2 and 10 mg/kg.d
Result : positive
Control group : yes, concurrent vehicle
Method : other
Year : 1985
GLP : no data
Test substance : other TS

Result : MORTALITY/TIME TO DEATH:
During the initial 4 months of the study, intercurrent mortality occured due to intestinal obstruction by trichobezors (hair-balls). This condition was relieved by a change of diet. Survival after 1 year was 80% and 98% (control), 62% and 94% (low dose), and 62% and 90% (high dose), for males and females, respectively; after 2 years these percentages were 62 and 76, 40 and 62, and 44 and 58, respectively.

CLINICAL SIGNS:
None reported.

BODY WEIGHTS/GAINS:
Male rats showed a significant dose-related reduction in body weight after 100 weeks. A tendency for reduced body weight gain was present in females.

FOOD/WATER CONSUMPTION:
None reported.

EYE EXAMINATION:
None reported.

HEMATOLOGY:
There were no differences either in red blood cell parameters or differential leukocyte counts.

CLINICAL CHEMISTRY/URINALYSIS/ORGAN WEIGHTS:
None reported.

GROSS PATHOLOGY/HISTOPATHOLOGY/TIME TO TUMOR(S):

Tumor Incidence Chronology

Tumor incidence (rats with tumors/rats examined)
during the periods (months)

	0-12	12-14	14-16	16-18	18-20	20-22	22-24	Terminal
Females								
Control	0/10	0/0	0/0	0/0	2/2	2/3	2/4	27/31
10 mg	2/19	1/2	0/2	1/2	0/0	0/0	2/2	22/22
Males								
Control	0/1	0/0	0/0	0/0	1/1	2/3	5/7	38/38
10 mg	0/5	0/1	0/0	1/1	1/2	7/7	6/6	29/29

High dose group animals (all but 1) necropsied after 20 months showed proliferative alterations of the forestomach mucosa. At earlier time points and in the low dose group, lower incidence and severity of proliferative changes of the mucosa were observed. Other tumors observed at gross inspection were not uncommon for the strain of rats with respect to site and incidence.

At histologic examination, lesions of the forestomach appeared to be composed principally of hyperplasia of basal cells of the squamous epithelium. The lesions ranged from slight local hyperplasia at low dose level to a very high incidence of carcinomas at high dose level (100% in females, 81% in males at risk (>18 months)). The first carcinoma in the high dose females occurred after 22 months and in males 20 months. In these carcinomas, both differentiated and undifferentiated components were present, and the mitotic index was generally low. Invasion was often accompanied by proliferative inflammatory reaction but in the vicinity of epithelial defects inflammation was more exudative in character.

Test condition : TEST ORGANISMS:
Male and female Wistar rats: age at study initiation unknown, initial body weight ~60 g (male) and ~50 g (female), 50 per sex per dose group

ADMINISTRATION/EXPOSURE:
Groups of animals were dosed via gavage at 0 (distilled water), 2, or 10 mg/kg/day five days per week, for lifetime. Experiment was terminated after 2 years.

ECH in water solutions was given at a rate of 0.5 ml/100 g body weight.

CLINICAL OBSERVATIONS AND FREQUENCY:
Animals were observed weekly for the first year and daily thereafter for health, behavior, and mortality. Body weights were collected weekly during the first 12 weeks and every 4 weeks thereafter.

Feed/water consumption were not monitored during the study. Ophthalmoscopic examinations were not performed during the study.

Hematology was conducted on 10 animals per sex per dose group. The following parameters were evaluated: hemoglobin concentration, hematocrit value, erythrocyte and total and differential leukocyte counts, mean corpuscular volume, mean corpuscular hemoglobin, and mean corpuscular hemoglobin concentration (calculated).

Clinical chemistry and urinalysis evaluations were not performed.

ORGANS EXAMINED AT NECROPSY:
A complete necropsy examination was conducted on each animal, including: brain, heart, lungs (inflated with fixative), liver, spleen, kidneys, pituitary, thyroid, thymus, pancreas, adrenals, ovaries, testes, uterus, prostate, mesenteric lymph nodes, submandibular salivary glands, esophagus, stomach, small and large intestine, urinary bladder (inflated with fixative), nasal cavity with turbinates. In addition, tumors and lesions suspected of being tumors were collected and examined. Histopathologic examination was conducted on all tissues from all animals.

STATISTICAL METHODS:
Except for pathology, experimental data were analyzed by the Student's t-test. Pathology data were analyzed by the prevalence method described by Peto et al.

Test substance : Purity: 99.5%
Reliability : (1) valid without restriction
Although no data are available as to guideline or GLP compliance, this study was carried out in a manner which can be subsumed under valid testing guidelines.

27.03.2002 (192)

Species : rat
Sex : male
Strain : Sprague-Dawley
Route of admin. : inhalation
Exposure period : lifetime
Frequency of treatm. : 6 hours/day, 5 days/week
Post exposure period : Not applicable
Doses : 30 ppm (113 mg/m3) and 10 ppm (38 mg/m3)
Result : positive
Control group : yes, concurrent vehicle
Method : other
Year : 1980
GLP : no data
Test substance : other TS

Remark : Groups of 40 and 100 rats were exposed to ECH vapour and observed for their remaining lives.
Control groups consisted of 100 each of a (sham)-treated and unexposed rats. The rates of mortality abd weight gain were combined for the 2 treated groups because there was no significant difference between these parameters.

Result : In the lifetime exposure study, both ECH-exposedgroups showed no significant mortality up to 16 weeks after the start of exposure. By week 48 at 10 ppm and week 60 at 30 ppm, the mortality rate was 45/100 rats for both exposure conditions. The 2-year survival was about 5-10% in all groups including controls. No nasal tumors were observed at 10 ppm. After 30 ppm, 2 animals developped tumours, 1 a nasal papilloma (detected at 402 days after the start of exposure) and 1 a nasal squamous cell carcinoma (detected at 752 days from the start of exposure). Again, no nasal tumours were found in controls. In both of these studies, no difference was noted in the incidence of other types of tumour compared to controls.
MORTALITY/TIME TO DEATH:
Both epichlorohydrin-exposed groups showed no significant mortality up to 16 weeks after the start of exposure. By week 48 at 10 ppm and week 60 at 30 ppm, the mortality rate

was 45/100 rats for both exposure conditions. In all cases severe lung congestion and pneumonia were observed. The 2-year survival was about 5-10% in all groups including controls. By 136 weeks from the first exposure, mortality reached 100%.

CLINICAL SIGNS:
None reported

BODY WEIGHT GAINS:
Weight gain for animals exposed to 10 ppm paralleled that of controls, but the group exposed to 30 ppm began to show significant weight loss after 40 weeks.

FOOD/WATER CONSUMPTION:
None reported.

EYE EXAMINATION:
None reported.

CLINICAL CHEMISTRY/HEMATOLOGY/URINALYSIS/ORGAN WEIGHTS:
None reported.

GROSS PATHOLOGY/HISTOPATHOLOGY/TIME TO TUMOR(S):
Both the 10 and 30 ppm group showed pulmonary congestion, bronchiolectisis, and pneumonia without neoplastic changes in the lungs. Tumors in non-respiratory organs were also reported, but no treatment-related increases in incidence of tumors was noted.

No nasal tumors were observed at 10 ppm. At 30 ppm, 2 animals developed tumors, 1 a nasal papilloma (detected at 402 days after the start of exposure) and 1 a nasal squamous cell carcinoma (detected at 752 days from the start of exposure). No nasal tumors were found in controls.

Test condition : TEST ORGANISMS:
Male Sprague-Dawley rats: 8 weeks old, initial body weight unknown, 100 per dose group

ADMINISTRATION/EXPOSURE:
Groups of 100 animals were exposed to 10 or 30 ppm six hours daily, five days per week, for lifetime. Groups of 100 animals, either sham-exposed or untreated, were used as controls.

Whole-body vapor exposures were carried out in 1.3 cubic meter chambers. Atmospheres were generated by passing an air stream over the liquid in a generating flask, then diluting the effluent vapor with a second air stream prior to introduction to the exposure chambers. Chamber air was assayed for vapor concentration every half-hour during each 6-hour exposure period.

CLINICAL OBSERVATIONS AND FREQUENCY:
Animals were observed daily for signs of toxicity and morbidity/mortality. Body weights were collected monthly.

Feed/water consumption were not monitored during the study. Ophthalmoscopic examinations were not performed during the study. Hematology, clinical chemistry, and urinalysis evaluations were not performed.

ORGANS EXAMINED AT NECROPSY:
A complete necropsy examination was conducted on each animal, with particular attention given to the respiratory tract. Histologic sections were prepared from each pulmonary lobe, the larynx, trachea, stem bronchi, liver, bladder, kidneys, spleen and other organs with gross pathologic alterations.

STATISTICAL METHODS:
Statistical analysis of the data was not carried out.

Test substance : Purity: 99%
Reliability : (2) valid with restrictions
Study not performed according to GLP, but animal numbers, exposure duration and histopathology sufficiently documented and scientifically acceptable.

27.03.2002 (96)

Species : rat
Sex : male
Strain : Sprague-Dawley
Route of admin. : inhalation
Exposure period : 30 days
Frequency of treatm. : 6 hours/day, 5 days/week
Post exposure period : Exposures followed by lifetime observation.
Doses : 100 ppm (378 mg/m3)
Result : positive
Control group : yes, concurrent vehicle
Method : other
Year : 1980
GLP : no data
Test substance : other TS

Remark : Groups of 40 and 100 male rats were exposed to epichlorohydrin vapour and observed for their remaining lives.
Control groups consisted of 100 each of a (sham)-treated and unexposed rats. The rates of mortality and weight gain were combined for the 2 treated groups because there was no significant difference between these parameters.

Result : A mortality rate of 9% was seen among the treated animals within the first 8 weeks of the initial exposure, compared to 0% in the controls. Between 330 and 933 days after the onset of exposure, 13% of the treated rats developed nasal tumours, of which 83% were squamous cell carcinomas. All of the carcinomas and 1 papilloma appeared to have developed from the mucosa of the anterior half of the nasal cavity. No such tumors were observed in either sham-exposed or untreated controls over the same time period.

Test substance : Purity: 99%
Reliability : (2) valid with restrictions
Study not performed according to GLP nor does it comply with a specific testing guideline. Only one sex and one dose level tested. However, sufficient number of animals was used and study length was sufficient to detect a carcinogenic effect.

27.03.2002 (96)

Species : rat
Sex : male
Strain : Wistar
Route of admin. : drinking water

Exposure period	:	81 weeks
Frequency of treatm.	:	daily
Post exposure period	:	none
Doses	:	0, 375, 750, 1500 mg/l
Result	:	positive
Control group	:	yes, concurrent vehicle
Method	:	other
Year	:	1981
GLP	:	no
Test substance	:	other TS

Result : At the end of the study, the final body weights showed a dose-dependent reduction (7-45%) compared to controls.
A dose-dependent increase was observed in the incidence of squamous epithelial-cell hyperplasia of the forestomach of the treated rats. At the 2 higher doses, there was also a dose-related increase in the incidence of forestomach papillomas and carcinomas.
No such changes were observed in the control rats.

Test condition : In a briefly reported study, groups of 18 rats received ECH in drinking water continuously for up to 81 weeks. After week 60, ECH administration had to be stopped intermittently due to the poor condition of the rats.
ECH intake was determined by daily measurements of water consumption.

Test substance : ECH (Nakarai Chem. Ltd., Kyoto) was dissolved in drinking water freshly every day and placed in a bottle covered with black tape to protect it from the light.

Reliability : (2) valid with restrictions
Although this study was not performed under GLP and only 1 sex was tested, test parameters documented were sufficient to accept the data. (2e)

27.03.2002 (83) (90)

Species	:	mouse
Sex	:	female
Strain	:	other: ICR/HA
Route of admin.	:	dermal
Exposure period	:	83 w
Frequency of treatm.	:	3 d/w
Post exposure period	:	
Doses	:	2 mg
Result	:	negative
Control group	:	yes, concurrent vehicle
Method	:	other: skin painting (with and without promotor PMA)
Year	:	1974
GLP	:	no
Test substance	:	other TS: ECH and PMA solutions in acetone

Remark : There were together 2 different skin-painting studies with and without promotor on a group of 50 mice :
- Without PMA : see conditions hereup.
- With PMA : single 2 mg application of ECH followed 2 weeks later by applications 3 d/w of the tumour promotor PMA.

Result : 9/30 mice treated with promotor developed skin papillomas, and in 1 case carcinoma. This result compared to 3/30 mice developing papillomas in the PMA-only treated group indicates that ECH may act as a tumour initiator in mice.
ECH applied as "one brushful" without promotor failed to induce skin tumours.
No tumours were observed in the control animals treated with

acetone.

Test substance : Solutions in acetone :
- ECH : 20 g/l
- PMA : 25 mg/l (Phorbol Myristate Acetate).

Reliability : (3) invalid
Dose inadequately documented as "1 brushful", positive result only obtained after coadministration of PMA as a promoter.

27.03.2002 (175)

Species : mouse
Sex : female
Strain : ICR
Route of admin. : i.p.
Exposure period : 450 days
Frequency of treatm. : once a week
Post exposure period : none
Doses : 1 mg in 0.05 ml tricaprylin
Result : ambiguous
Control group : no data specified
Method : other
Year : 1974
GLP : no
Test substance : no data

Remark : Pulmonary papilloma in 11 of 30 animals.
Reliability : (3) invalid
Route of administration not relevant for potential human exposure.

27.03.2002 (176)

Species : mouse
Sex : male/female
Strain : other: Strain A/J
Route of admin. : other: oral and i.p.
Exposure period : 8 weeks
Frequency of treatm. : 3 days/week
Post exposure period : 24 weeks
Doses : 0 (vehicle), 20 (i.p. only), 50 (i.p. only), 100 mg/kg/day
Result : positive
Control group : yes, concurrent vehicle
Method : other
Year : 1986
GLP : no data
Test substance : other TS

Remark : Groups of 16 (m) and 16 (f) were observed.
Result : No significant increase in the incidence of tumours per lung after 24 weeks post-treatment for oral route of administration. At a total i.p. dose of 2400 mg/kg administered over 8 weeks, 67% of male mice developed lung tumors, which was statistically greater than controls treated with the same vehicle.
Test substance : Reagent grade purchased from Sigma Chemical Co., St. Louis, MO.
Reliability : (3) invalid
Inadequate number of animals for guideline oncogenicity study, treatment period of 3 times per week for 8 weeks insufficient for determination of oncogenicity, only partial gross examination of internal organs, histology of lung and liver only.

28.03.2002 (163)

Species	:	mouse
Sex	:	female
Strain	:	ICR
Route of admin.	:	s.c.
Exposure period	:	580 days
Frequency of treatm.	:	once a week
Post exposure period	:	None
Doses	:	1 mg in 0.05 ml tricaprylin
Result	:	positive
Control group	:	yes, concurrent vehicle
Method	:	other
Year	:	1974
GLP	:	no
Test substance	:	other TS
Remark	:	Local sarcomas and in one case an adenocarcinoma.
Test substance	:	Test material purified by distillation; purity confirmed by boiling point, IR and NMR spectroscopy.
Reliability	:	(3) invalid Route of administration irrelevant to potential routes of human exposure.

28.03.2002 (176)

5.8.1 TOXICITY TO FERTILITY

Type	:	Fertility
Species	:	rat
Sex	:	male/female
Strain	:	Sprague-Dawley
Route of admin.	:	inhalation
Exposure period	:	10 weeks
Frequency of treatm.	:	6 hours/day
Premating exposure period		
Male	:	10 weeks
Female	:	10 weeks
Duration of test	:	20 weeks
No. of generation studies	:	
Doses	:	0, 5, 25, 50 ppm
Control group	:	yes, concurrent vehicle
NOAEL parental	:	= 5 ppm
other: fertility NOAEL	:	= 5 ppm
Method	:	other
Year	:	1979
GLP	:	no
Test substance	:	other TS
Result	:	NOAEL/LOAEL P, FERTILITY

In the 50 ppm group, the fertility index for male rats was significantly reduced. Males from the 25 ppm group were able to fertilize untreated female animals, but there was a reduced number of implantations compared with the controls. This effect disappeared 2 weeks following termination of treatment. The NOAEL for reproduction/fertility in males was 5 ppm.

The reproductive capacity of female rats was not adversely affected. The females showed normal estrus patterns during

the 2-week mating period following termination of exposures and were able to become pregnant and deliver viable young. There were no adverse effects on the percentage of pregnant females, length of gestation period, litter size, pr pup survival through 2 days postpartum in any exposure group. The NOAEL for reproduction/fertility in females was 50 ppm.

In male and female rats there were treatment-related histopathologic changes in the nasal turbinates at the 25 and 50 ppm exposure levels. The microscopic changes were degenerative in nature and characterized by inflammation, focal erosions, hyperplasia, and metaplasia with a squamous appearance to the turbinate mucosa. The kidneys o males and females from the interim sacrifice showed dilated tubules in the 50 ppm group. In addition, males in the 25 and 50 ppm groups showed a slightly increased incidence of focal tubular change. These changes occurred in the control rat kidneys; however, they were observed with a greater frequency in the 25 and 50 ppm groups only. There were no other treatment-related changes detected in any other tissues examined. The NOAEL for all other effects in both sexes was 5 ppm.

Reproductive Parameters - Fertility Index of Male Rats Exposed to Epichlorohydrin by Inhalation

	Exposure Level, ppm a			
Week of Study	0	5	25	50
2	100(25/25)b	100(25/25)	100(25/25)	16(4/25)c
4	100(25/25)	96(24/25)	88(22/25)	8(2/25)c
7	100(25/25)	100(25/25)	92(23/25)	8(2/25)c
10	100(25/25)	100(25/25)	96(24/25)	12(3/25)c
12	100(25/25)	100(25/25)	100(25/25)	96(24/25)
15	100(25/25)	100(25/25)	100(25/25)	100(25/25)
20	100(25/25)	100(25/25)	100(25/25)	100(25/25)

a Male rats were exposed to 0, 5, 25, or 50 ppm of epichlorohydrin vapor for 6 hrs/day; 5 days/week for 10 weeks. During the 2nd, 4th, 7th, and 10th weeks of exposure, 25 male rats per exposure level were housed with 2 unexposed female rats each during the period between exposures for 7 days. Matings were also conducted during weeks 12, 15, and 20 of the recovery period.

b Male fertility index = # fertile males/# males housed with females x 100

c Significantly different from the control value by the Fisher's exact probability test, $p<0.05$.

Reproductive Parameters - Average Number of Implantations, Corpora Lutea, and Resorptions in Unexposed Female Rats Bred to Male Rats Exposed to Epichlorohydin by Inhalation

Exposure Level, ppm (a)

Week of Study	0	5	25	50
Week 2 -				
Average # implantations	13.7+/- 1.8b	14.0+/- 1.5	7.8+/- 3.3c	1.0+/- 0.0 c
Average # corpora lutea	14.4+/- 1.9	14.6+/- 1.6	12.4+/- 2.4d	8.8+/- 3.3 d
Average # resorptions	0.8+/- 1.0	0.8+/- 0.9	0.4+/- 0.5	0.5+/- 0.6
Week 4 -				
Average # implantations	13.1+/- 1.7	13.7+/- 1.6	8.4+/- 3.6 c	2.0+/- 1.4 c
Average # corpora lutea	13.6+/- 1.4	13.8+/- 1.3	13.4+/- 2.0	8.5+/- 4.9 d
Average # resorptions	0.7+/- 0.8	1.1+/- 1.8	0.9+/- 0.9	0.5+/- 0.7
Week 7 -				
Average # implantations	13.0+/- 1.5	13.6+/- 2.3	7.1+/- 3.8 c	1.0+/- 0.0 c
Average # corpora lutea	13.9+/- 1.0	14.5+/- 1.7	13.2+/- 1.5	10.5+/- 0.7 d
Average # resorptions	0.6+/- 0.5	0.9+/- 1.9	0.5+/- 0.6	0.5+/- 0.7
Week 10 -				
Average # implantations	14.2+/- 1.1	13.8+/- 1.8	9.1+/- 4.7c	4.0+/- 4.4 c
Average # corpora lutea	14.4+/- 1.4	15.0+/- 1.7	13.4+/- 2.3	11.7+/- 0.6 d
Average # resorptions	0.9+/- 0.8	1.0+/- 1.0	0.6+/- 0.7	2.0+/- 1.0
Week 12 -				
Average # implantations	13.7+/- 2.6	13.3+/- 1.7	12.6+/- 3.1	13.8+/- 1.2
Average # corpora lutea	14.2+/- 1.4	13.9+/- 1.5	14.0+/- 1.2	14.3+/- 1.6 e
Average # resorptions	1.0+/- 1.2	0.9+/- 1.8	1.1+/- 1.0	0.4+/- 0.5
Week 15 -				
Average # implantations	14.2+/- 1.9	14.1+/- 1.5	14.5+/- 1.2	13.7+/- 2.2
Average # corpora lutea	14.0+/- 1.5	14.3+/- 1.0	14.5+/- 1.3	14.5+/- 1.5
Average # resorptions	0.7+/- 0.7	1.2+/- 1.7	0.9+/- 0.8	1.2+/- 1.0
Week 20 -				
Average # implantations	14.2+/- 2.0	14.4+/- 1.6	13.9+/- 1.6	15.2+/- 1.4 d
Average # corpora lutea	13.1+/- 2.2	14.1+/- 1.6	13.6+/- 2.1	14.5+/- 1.1
Average # resorptions	0.8+/- 1.0	0.9+/- 0.9	0.7+/- 1.2	0.5+/- 0.4

a Male rats were exposed to 0, 5, 25, or 50 ppm of epichlorohydrin vapor for 6 hrs/day; 5 days/week for 10

weeks. During the 2nd, 4th, 7th, and 10th weeks of exposure, 25 male rats per exposure level were housed during the period between exposures with 2 unexposed female rats each. Matings were also conducted during weeks 12, 15, and 20 of the recovery period.

b Mean 1 S.D. The average number of implantations, corpora lutea, or resorptions for the two female rats bred to each male was calculated. Group means were then calculated from these averaged values.

c Significantly different from the control value by a non-parametric analysis of variance by ranks, using Wilcoxon's test.

d Significantly different from the control value by an analysis of variance and Dunnett's test, $p<0.05$.

e Significantly different from the control value by a modified Wilcoxon test, $p<0.05$.

Reproductive Parameters - Average Preimplantation Loss and Average Resorption Rate in Unexposed Female Rats Bred to Male Rats Exposed to Epichlorohydrin by Inhalation

	Week on Study	Exposure Level, ppm (a) 0	5	25	50
Average preimplantation loss, percent b	2nd	8	5	42 c	84 c
	4th	6	4	38	78
	7th	6	8	48 c	90 c
	10th	4	9 c	36 c	66 c
	12th	7	6	12	5
	15th	5	4	3	8 c
	20th	9	4 c	6 c	6 d
Average resorption rate, percent e	2nd	6	6	4	50 f
	4th	5	8	13	50 g
	7th	4	7	6	50 g
	10th	6	9	14	78 c,h
	12th	8	8	10	3 c
	15th	7	8	6	11
	20th	8	7	5	4

a Male rats were exposed to 0, 5, 25, or 50 ppm of epichlorohydrin vapor for 6 hrs/day, 5 days/week for 10 weeks. During the 2nd, 4th, 7th, and 10th weeks of exposure, 25 male rats per exposure level were housed during the period between exposures with 2 unexposed female rats each. Matings were also conducted during weeks 12, 15, and 20 of the recovery period.

b Pre-implantation loss = # corpora lutea minus # implantations / # corpora lutea X 100
The average pre-implantation loss for the 2 females bred to each male rat was calculated. Group means were then calculated from these averaged values.

c Significantly different from the control value by a modified Wilcoxon test, $p<0.05$.

d $p = 0.053$, modified Wilcoxon test.

e Resorption rate # resorptions / # implantations x 100
The average resorption rate for the 2 females bred to each male rat was calculated. Group means were then calculated from these averaged values.

f Only 4 of the female rats bred to exposed males were pregnant. Two females each had only one implantation site which was resorbed.

g Only 2 of the female rats bred to exposed males were pregnant. One female had only one implantation site which was resorbed.

h Only 3 of the female rats bred to exposed males were pregnant. One female had only one implantation site which was resorbed; one female had two implantation sites which were both resorbed.

Reproductive Parameters - Fertility Index Survival Indices in Female Rats Exposed to Epichlorohydrin by Inhalation

	Exposure Level, ppm a			
	0	5	25	50
No. Females	25	25	25	25
No. maternal deaths during delivery	0	1	0	1
Fertility index b	84%(21/25)	92%(23/25)	92%(23/25)	92%(23/25)
Gestation period, days c	22+/-0.6	22+/-0.6	23+/-2.0	22+/-1.0
Litter size at birth c	12+/-4	12+/-5	12+/-4	12+/-3
Gestation survival index	97% (243/250)	97% (261/269)	96% (268/278)	98% (265/270)
24-Hr survival index e	99% (240/243)	100% (261/261)	99% (265/268)	98% (259/265)
2-Day survival index f	98% (238/243)	100% (261/261)g	98% (262/268)	97% (258/265)
Sex ratio on day 1, M:F	52:48	55:45	49:51	49:51

a Female rats were exposed to 0, 5, 25, or 50 ppm of epichlorohydrin vapor for 6 hrs/day, 5 days/week for 10 weeks. Directly following termination of the exposures 25 female rats per exposure level were housed with two different unexposed male rats for a 5-day period with each male.

b No. of females delivering a litter/no. of females placed with males.

c Mean 1 S.D.

d No. of liveborn neonates/total no. of pups.

e Percentage of liveborn neonates which survived for 24 hrs.

f Percentage of liveborn neonates which survived for 2 days.

g Significantly different from the control value by the Fisher's exact probability test, $p<0.05$.

Test condition : TEST ORGANISMS/EXPOSURE
Groups of 30 rats per sex per dose level were exposed (whole-body) to 0 (chambered control), 5, 25, or 50 ppm epichlorohydrin vapor six hours daily, five days per week, for 10 weeks, then held for a 10-week recovery period. Means of daily analytical concentrations were 5.2+/-0.4, 24.7+/-1.4, 50.0+/-1.8 ppm for the 50 days of exposure.

Exposures were carried out in 14.5 cubic meter chambers. Atmospheres were generated by metering liquid through a pump into a warmed vaporization flask, then sweeping the vapors into the chamber with compressed air. Chamber air was assayed for vapor concentration 3-4 times during each 6-hour exposure period.

MATING PROCEDURES/PARAMETERS ASSESSED DURING STUDY (P AND
F1)
Groups of 25 exposed female rats were mated to unexposed male rats at the end of the 10-week exposure period. The females were cohoused with the males for 2 consecutive 5-day periods, until the presence of sperm was detected in a vaginal smear. These females were then allowed to carry and deliver their litters in nesting boxes. The day of delivery was noted, and the number of live and dead pups recorded on day 0 (delivery) and days 1 and 2 post-delivery. The pups were examined on day 1 for morphologic alterations and presence of milk in the stomach as an indication of nursing.

Groups of 25 exposed male rats were mated to unexposed female rats during the 2nd, 4th, 7th, and 10th weeks of exposure. Males were cohoused for 7 days with 2 females each during the time when exposure was not in progress. All of the males used for the experiment were able to sire at least one litter in a pre-exposure mating. The area beneath each male's cage was examined for evidence of copulatory plugs as evidence of mating. Twelve days after the last day of cohabitation, the females were sacrificed and their uterine contents examined for number of corpora lutea, implantation sites, and resorption sites.

Animals were observed daily for signs of toxicity. Body weights were collected weekly.

One week prior to exposure and one week after the last exposure, blood samples were collected for hematologic

analysis from 5 rats/sex/dose. Parameters examined were packed cell volume, red blood cell count, hemoglobin concentration, and white blood cell count, and clinical chemistry parameters: blood urea nitrogen, glutamic pyruvic transaminase activity, alkaline phosphatase activity, glutamic oxaloacetic transaminase activity, and glucose concentration. Urinalysis samples from rats were collected when blood samples were collected; parameters examined were specific gravity, pH, sugar, protein, ketones, bilirubin, occult blood, urobilinogen. The animals on whom these determinations were made were sacrificed at the end of the exposure period.

A complete necropsy examination was conducted on each remaining animal at the end of the 10-week recovery period, during which organ weights for brain, heart, liver, kidneys, testes, and epididymides were recorded. Approximately 40 organs/tissues from five rats/sex/dose level were examined histologically.

Test substance : Production grade, 98.8% purity
Reliability : (1) valid without restriction
1d

28.03.2002 (79)

Type : Fertility
Species : rabbit
Sex : male
Strain : New Zealand white
Route of admin. : inhalation
Exposure period : 10 weeks
Frequency of treatm. : 6 hours/day, 5 days/week
Premating exposure period
Male : 10 weeks
Female : none
Duration of test : 20 weeks
No. of generation studies :
Doses : 0, 5, 25 and 50 ppm
Control group : yes, concurrent vehicle
NOAEL parental : = 5 ppm
other: NOAEL fertility : = 50 ppm
Method : other
Year : 1979
GLP : no
Test substance : other TS

Result : NOAEL/LOAEL P

Rabbits exposed to 50 ppm showed a statistically significant decrease in body weight as compared to controls. The majority of rabbits exposed to 25 or 50 ppm showed evidence of nasal turbinate inflammation at gross necropsy. Rabbits exposed to 25 or 50 ppm showed a greater incidence of bilateral suppurative rhinitis, sinusitis, focal erosion, or metaplasia of the nasal epithelium. There were no histopathological changes at 5 ppm considered treatment-related. Therefore, the NOAEL for parental toxicity was 5 ppm.

Measurements of semen samples made after 10 weeks of exposure indicated no adverse effects on sperm morphology,

motility, viability or concentration.

No significant effects on the average number of implantations, corpora lutea, or resorptions were observed among females bred to exposed males. The fertility index of males was not affected by exposure; all males were able to impregnate an unexposed female. The unexposed females bred to exposed males showed a higher incidence of preimplantation loss than the control group, 22% for the 5 ppm group and 27% for the 50 ppm group. However, both of these values were within the range of pre-implantation loss percentage observed historically among rabbits within the testing laboratory, a range of 9-27%. The average preimplantation loss at 25 ppm was only 12%. Therefore, the NOAEL for reproduction/fertility effects was 50 ppm.

Test condition : TEST ORGANISMS/EXPOSURE
Groups of 10 male rabbits per dose level were exposed (whole-body) to 0 (chambered control), 5, 25, or 50 ppm epichlorohydrin vapor six hours daily, five days per week, for 10 weeks, then held for a 10-week recovery period. Means of daily analytical concentrations were 5.2+/-0.4, 24.7+/-1.4, 50.0+/-1.8 ppm for the 50 days of exposure.

Exposures were carried out in 14.5 cubic meter chambers. Atmospheres were generated by metering liquid through a pump into a warmed vaporization flask, then sweeping the vapors into the chamber with compressed air. Chamber air was assayed for vapor concentration 3-4 times during each 6-hour exposure period.

MATING PROCEDURES/PARAMETERS ASSESSED DURING STUDY (P AND
F1)

Semen evaluation was conducted on all males on a weekly basis during the 10-week exposure period, which included sperm count, motility, morphology, and ratio of live to dead sperm.

Groups of 10 exposed male rabbits were allowed to mate with unexposed female rabbits during the 10th week of exposure. Females were injected with human chorionic gonadotropin to induce ovulation. On day 28 of gestation, the females were sacrificed and their uterine contents examined for number of corpora lutea, implantation sites, and resorption sites.

Animals were observed daily for signs of toxicity. Body weights were collected weekly.

One week prior to exposure and one week after the last exposure, blood samples were collected for hematologic analysis from 4 rabbits/dose. Parameters examined were packed cell volume, red blood cell count, hemoglobin concentration, and white blood cell count, and clinical chemistry parameters: blood urea nitrogen, glutamic pyruvic transaminase activity, alkaline phosphatase activity, glutamic oxaloacetic transaminase activity, and glucose concentration.

A complete necropsy examination was conducted on each remaining animal at the end of the 10-week recovery period, during which organ weights for brain, heart, liver, kidneys,

testes, and epididymides were recorded. Approximately 40 organs/tissues from 4 rabbits/dose level were examined histologically.

Test substance : Production grade, 98.8% purity
Reliability : (1) valid without restriction
1d

28.03.2002 (79)

Type : Fertility
Species : rat
Sex : male
Strain : Long-Evans
Route of admin. : gavage
Exposure period : 21 days
Frequency of treatm. : once a day, 5 days/week
Premating exposure period
Male : 21 days
Female : not applicable
Duration of test : 21 days
No. of generation studies :
Doses : 0, 12.5, 25, 50 mg/kg/day.
Control group : yes, concurrent vehicle
NOAEL parental : = 25 mg/kg bw
other: LOAEL sperm motion parameters : = 12.5 mg/kg bw
Method : other
Year : 1989
GLP : no data
Test substance : other TS

Remark : In a well-conducted and well-reported study, groups of 20 (m) and 10 (f) rats received ECH by oral gavage.
Males received ECH daily prior to mating to evaluate effects on late-stage spermatids and epididymal spermatozoa only. At the end of the treatment, ejaculatory sperm was assessed by mating each (m) with hormonally primed untreated (f). Two days later, (m) in the 0 and 50 mg/kg groups only were allowed to mate for up to 5 days with a different prooestrus (f) each day until each (m) had copulated successfully with one female.
The (f) were sacrified on day 15 of pregnancy and corpora lutea, implantations and resorptions were counted. (m) were sacrified 48 h. after successful mating to access testicular and epididymal sperm.
For the measurement of cauda epididymal motion, an additional group of animals was used at each dose level and treated with ECH using an identical protocol to the one described above. These groups were mated 2 days after the last day of dosing (day 23) corresponding to the matings used for ejaculatory sperm assessment described above.

Result : Complete sterility in the highest dose group in the mating trials but no effect om mating performance, sperm count, motility and morphology immediately after the end of treatment. Mean curvilinear velocity, straight-line velocity, amplitude of lateral head displacement of cauda epididymal sperm, beat/cross frequency were significantly different from control at 12.5 mg/kg/day and above, and showed dose-dependent trends.

Test substance : 99+% purity, Aldritch Chemical
ECH diluted in corn oil
Reliability : (1) valid without restriction

1d

28.03.2002 (169)

Type	:	Fertility
Species	:	rat
Sex	:	female
Strain	:	Long-Evans
Route of admin.	:	gavage
Exposure period	:	5 weeks
Frequency of treatm.	:	once a day, 5 days/week
Premating exposure period		
Male	:	not applicable
Female	:	2 weeks
Duration of test	:	8 weeks
No. of generation studies	:	
Doses	:	0, 25, 50, 100 mg/kg b.w.
Control group	:	yes, concurrent vehicle
NOAEL parental	:	= 50 mg/kg bw
NOAEL F1 offspring	:	= 50 mg/kg bw
other: NOEL fertility	:	= 50 mg/kg bw
Method	:	other
Year	:	1989
GLP	:	no data
Test substance	:	other TS
Remark	:	In a well-conducted and well-reported study, groups of 20 (m) and 10 (f) rats received ECH by oral gavage. Females received ECH prior to mating with an untreated (m) and then treatment continued through pregnancy until parturition. If delivery of a litter had not occured by day 23 of pregnancy, (f) were killed and examined for signs of pregnancy. Litters were sexed on day one culled to eight pups [4 (m) + 4 (f)] on post-natal day 8 followed through until day 42.
Result	:	Within the first week of treatment, all rats in the 100 mg/kg/day group died or were so moribund as to warrant sacrifice. On autopsy, findings included hemorrhagic stomachs and kidneys with pale cortices and hemorrhagic medullae. The remaining animals showed no significant treatment-related effects. No effect was seen on female fertility or on mean number and survival of the offspring or weanling weight.
Test substance	:	99+% purity, Aldritch Chemical ECH diluted in corn oil
Reliability	:	(1) valid without restriction 1d

28.03.2002 (169)

Type	:	Fertility
Species	:	rat
Sex	:	male
Strain	:	Wistar
Route of admin.	:	gavage
Exposure period	:	5 days (20 or 50 mg/kg/day) or 1 day (100 mg/kg)
Frequency of treatm.	:	daily
Premating exposure period		
Male	:	5 days or 1 day
Female	:	untreated
Duration of test	:	10 weeks or 20 weeks

No. of generation studies	:	
Doses	:	20, 50, or 100 mg/kg
Control group	:	yes
LOEL parental	:	= 20 mg/kg bw
Method	:	other
Year	:	1974
GLP	:	no
Test substance	:	other TS
Result	:	Multiple treatments with ECH resulted in male infertility as assessed by mating with untreated female. Fertility studies following a single dose resulted in a reduction in the weekly average numbers of offspring per litter compared to historical controls. Histopathological studies on males receiving a single dose of ECH indicated no apparent effects up to 8 weeks post-treatment, but by week 12 large cysts of retained sperm were observed in the ductuli efferentes of the testis and the proximal caput epididymis in 4/5 rats.
Test condition	:	Groups of 5 male rats were treated either for 5 consecutive days with 20 or 50 mg/kg or given a single dose of 100 mg/kg of ECH by oral gavage and then mated with untreated females during a 10 week period post-exposure. Other groups (size unspecified) of males were treated with a single oral dose of 100 mg/kg and sacrificed up to 20 weeks post-treatment. Reproductive tissues for these animals were examined histologically.
Test substance	:	ECH obtained from Aldritch Chemical Company and purified by distillation.
Reliability	:	(2) valid with restrictions 2e

28.03.2002 (24)

Type	:	other: testicular toxicity
Species	:	rat
Sex	:	male
Strain	:	
Route of admin.	:	oral unspecified
Exposure period	:	single treatment
Frequency of treatm.	:	once
Premating exposure period		
Male	:	
Female	:	
Duration of test	:	
No. of generation studies	:	
Doses	:	25, 50 mg ECH/kg b.w.
Control group	:	
Result	:	The number of morphologically abnormal sperm was significantly increased in the 50 mg/kg group, while a significant reduction in the total number of sperm was only observed in the 25 mg/kg group. No further interpretation offered. The animals were sacrificed 11 days after treatment. There was no significant decrease in weight of the testes.
Reliability	:	(2) valid with restrictions

28.03.2002 (23)

Type	:	other: Dominant Lethal Study
Species	:	mouse
Sex	:	male/female
Strain	:	ICR
Route of admin.	:	other: i.p.; oral
Exposure period	:	single i.p/oral; 5 days i.p./oral
Frequency of treatm.	:	once/5-times
Premating exposure period		
Male	:	5 days
Female	:	untreated
Duration of test	:	1 day/5 days
No. of generation studies	:	
Doses	:	single i.p.: 5, 10, 20 mg/kg b.w.; single oral: 20, 40 mg/kg b.w.; 5 daily i.p.: 1, 5 mg/kg b.w., 5 daily oral. 20, 40 mg/kg b.w.
Control group	:	yes
other: NOEL Fertility	:	= 16 mg/kg bw
Method	:	other
Year	:	1976
GLP	:	no
Test substance	:	other TS
Result	:	I.p. or oral administration caused a reduction in fertility, but not sterility. No dose-effect relationship was found.
Test substance	:	Manufactured in Czechoslovakia.
Reliability	:	(4) not assignable 4e Route of administration not relevant to potential human exposure for i.p. study; documentation of methods insufficient for assessment.

28.03.2002 (158)

Type	:	Fertility
Species	:	rat
Sex	:	male
Strain	:	Sprague-Dawley
Route of admin.	:	oral unspecified
Exposure period	:	12 days
Frequency of treatm.	:	one daily administration
Premating exposure period		
Male	:	
Female	:	
Duration of test	:	19 days
No. of generation studies	:	
Doses	:	15 mg/kg/day
Control group	:	yes, concurrent no treatment
Method	:	other
Year	:	1970
GLP	:	no
Test substance	:	other TS
Result	:	Sterility within 7 days, which was reversible within one week after ending treatment. Histological examination on the last day of treatment apparently revealed no effects on the testes, epididymis, prostate or seminal vesicles, and no effects on either libido or ejaculatory ability.
Test substance	:	Schuchard Catalog Number EP051
Reliability	:	(3) invalid 3A Insufficient methodological details shown or data given.

28.03.2002 (73)

Type	:	other: testicular toxicity
Species	:	rat
Sex	:	male
Strain	:	Fischer 344
Route of admin.	:	s.c.
Exposure period	:	1 day
Frequency of treatm.	:	once
Premating exposure period		
Male	:	not applicable
Female	:	not applicable
Duration of test	:	75 days
No. of generation studies	:	
Doses	:	75 mg/kg
Control group	:	yes, concurrent vehicle
Method	:	other
Year	:	1983
GLP	:	no data
Test substance	:	other TS
Remark	:	Groups of 40 males were treated once and then serially sacrificed (8 each time) up to 75 days after treatment.
Result	:	Sperm concentration was reduced in the treated group and the percent of abnormal sperm in the cauda epididymis increased at 25 and 75 days after treatment. Histological examination revealed progressive degeneration leading to atrophy of the seminiferous tubules in 90 % of the tested rats by day 75. Formation of sperm granuloma (3/8 rats) and spermatocoeles (2/8 rats) were also found in the caput region of the epididymis.
Test substance	:	>99% purity
Reliability	:	(2) valid with restrictions 3c Route of administration not relevant to potential human exposure.

28.03.2002 (86)

5.8.2 DEVELOPMENTAL TOXICITY/TERATOGENICITY

Species	:	rat
Sex	:	female
Strain	:	Sprague-Dawley
Route of admin.	:	inhalation
Exposure period	:	day 6-15
Frequency of treatm.	:	7 h/d
Duration of test	:	21 d
Doses	:	2.5, 25 ppm
Control group	:	yes
NOAEL maternal tox.	:	= 2.5 ppm
NOAEL teratogen.	:	> 25 ppm
LOAEL Maternal Toxicity	:	= 25 ppm
Method	:	other
Year	:	1979
GLP	:	no
Test substance	:	other TS
Result	:	NOAEL/LOAEL

At the maternal LOAEL, effects including reduced body weight

and food intake for the dams were observed at the 25 ppm exposure level. The NOEL for maternal toxicity was 2.5 ppm.

No adverse effects related to treatment were observed in the embryos or fetuses at any exposure level. Therefore, the fetal NOEL was 25 ppm.

BODY AND LIVER WEIGHTS OF PREGNANT RATS EXPOSED TO EPICHLOROHYDRIN BY INHALATION

	ppm Epichlorohydrin (a)		
	0	2.5	25
Number of Dams(b)	36	33	32
Maternal body weight (g) on gestation day			
6	277+/-26(c)	263+/-27(d)	262+/-20(d)
8	284+/-26	272+/-23	263+/-20(d)
10	294+/-27	280+/-24(d)	271+/-20(d)
12	305+/-28	294+/-23	283+/-21(d)
16	334+/-31	324+/-23	311+/-2l(d)
21	413+/-41	402+/-43	394+/-31
Maternal body weight gain (g) on gestation days			
6-7	6+/-3	8+/-6	1+/-7(d)
8-9	10+/-5	8+/-9	8+/-9
10-11	1+/-5	14+/-8	12+/-8
12-15	30+/-9	31+/-7	29+/-9
16-20	79+/-17	77+/-21	82+/-19
Total 6-21	136+/-27	138+/-34	131+/-28
Maternal Liver weight on day 21			
Absolute(e)	15.97+/-1.77	16.12+/-1.72	15.83+/-1.76
Relative(f)	38.82+/-3.87	40.25+/-2.90	40.30+/-4.08
Gravid Uterus Weight on day 21			
Absolute(d)	97+/-29	89+/-34	93+/-24
Adjusted body weight (g)	316+/-25	313+/-22	297+/-22(d)

(a) Bred rats were exposed to 0, 2.5, or 25 ppm epichlorohydrin by inhalation for 7 hrs/day on days 6 through 15 of gestation.

(b) Data from non-pregnant rats were not included in these analyses.

(c) Mean +/- S.D.

(d) Significantly different frcm controls by Dunnett's test $P<0.05$.

(e) g, Mean +/- S.D.

(f) g, liver/kg body weight, mean +/- S.D.

(g) Maternal body weight minus the gravid uterus weight (g), mean +/- S.D.

FOOD AND WATER CONSUMPTION OF PREGNANT RATS EXPOSED TO
EPICHLOROHYDRIN BY INHALATION

	ppm Epichlorohydrin(a)		
	0	2.5	25
Number of Dams(b)	36	33	32
Food consumption on gestation days(c)			
6-8	23+/-3(d)	24+/-4	20+/-3(e)
9-11	24+/-3	24+/-3	22+/-3(e)
12-14	25+/-2	26+/-3	24+/-3(e)
15-17	31+/-4	30+/-4	30+/-3
18-20	30+/-3	29+/-3	31+/-3
Water consumption on gestation days(e)			
6-8	47+/-8	47+/-8	49+/-11
9-11	52+/-9	55+/-10	58+/-11(e)
12-14	57+/-7	59+/-9	65+/-11(e)
15-17	68+/-9	70+/-10	74+/-9(e)
18-20	63+/-8	65+/-9	69+/-9(e)

(a) Bred rats were exposed to 0, 2.5, or 25 ppm epichlorohydrin by inhalation for 7 hrs/day on days 6 through 15 of gestation.

(b) Data from non-pregnant rats were not included in these analyses.

(c) Expressed as grams/rat/day.

(d) Mean +/- S.D.

(e) Significantly different from control values by Dunnett's test P<0.05.

OBSERVATIONS AT CESAREAN SECTION OF RATS EXPOSED TO EPICHLOROHYDRIN BY INHALATION

	ppm Epichlorobydrin(a)		
	0	2.5	25
Number of bred females	46	44	43
Number of maternal deaths/number bred	0/46	0/44	0/43
Apparent pregnancy rate, %(b)	85(39/46)	86(38/44)	77(33/43)
Pregnant with stain only, %(c)	29(2/7)	0(0/6)	10(1/10)

Percent pregnant,

total(d)	89(41/46)	86(38/44)	79(34/43)
Number of Litters	36	33	32
Corpora lutea/dam(e)	14+/-2	14+/-3	15+/-2
Implantation sites/ dam(e)	13+/-3	12+/-4	13+/-3
Preimplantatian Loss(e)	2+/-2	3+/-0	2+/-0
Fetuses/Litter(e)	12+/-4	11+/-4	12+/-3
Resorptions/Litter (e,f)	1+/-1	1+/-1	1+/-2
Percent Implantations resorbed(f)	5(25/460)	4(17/386)	7(30/408)
Percent litters with resorptions(f)	44(16/36)	36(12/33)	44(14/32)
Litters totally resorbed(f)	0	0	0
Resorptions/litters with resorptions(f)	1.6(25/16)	1.4(17/12)	2.1(30/14)
Percent dead fetuses	0.2(1/435)	0(0/369)	0(0/378)
Sex ratio, M:F, %	47:53	47:53	52:48
Fetal body weight, (grams)g	5.60+/-0.36	5.59+/-0.44	5.49+/-0.45
Fetal crown-rump length, (mm)g	42.7+/-1.8	42.3+/-1.4	42.4+/-1.5

(a) Bred rats were exposed to 0, 2.5 or 25 ppm epichlorobydrin by inhalation for 7 hrs/day on days 6 through 15 of gestation.

(b) Number of females with visible implantations at the time of C-section or necropsy/total bred. Among rats exposed to 2.5 ppm epichlorohydrin, 5 animals delivered a litter prior to day 21 of gestation. At the 25 ppm level, a single female delivered early, and 3 control rats delivered prior to gestation day 21.

(c) Number of females detected as being pregnant only after staining uterus with sodium sulfide stain/total stained.

(d) Number of females pregnant by visual inspection of the uterus or by sodium sulfide stain/total bred.

(e) Mean +/- S.D.

(f) Resorptions detected by sodium sulfide staining were not included in these calculations.

(g) Mean of litter means +/- S.D.

No values were significantly different from the control values by the appropriate statistical test, p<O.05.

INCIDENCE OF FETAL ALTERATIONS AMONG LITTERS OF RATS EXPOSED TO EPICHLOROHYDRIN BY INHALATION(a)

	ppm Epichlorohydrin 0	2.5	25
	Number Fetuses (Number Litters)		
EXTERNAL EXAMINATION	435(36)	369(33)	378(32)
SOFT TISSUE EXAMINATION	147(36)	127(33)	130(32
SKELETAL EXAMINATION	435(36)	369(33)	378(32)
BONES OF THE SKULL(b)	288(33)	242(29)	248(31)

		Percent Affected (Number Affected)		
Total Major Malformations	F(e)	1(5)	1(3)	1(3)
	L	11(4)	9(3)	9(3)
External Examination				
Short Trunk, Hypoplastic Tail*	F	0.5(2)	0.3(l)	0(0)
	L	6(2)	3(l)	0(0)
Acaudia*	F	0(0)	0(0)	0.3(l)
	L	0(0)	0(0)	3(l)
Multiple Facial Anomalies(d)*	F	0.2(l)	0(0)	0(0)
	L	3(l)	0(0)	0(0)
Inward rotation of right hind paw*	F	0(0)	O.3(l)	0(0)
	L	0(0)	3(l)	0(0)
Inward rotation of both hind limbs*	F	0(0)	0(0)	0.3(l)
	L	0(0)	0(0)	3(l)
Subcutaneous Edema	F	0.2(l)	0(0)	0(0)
	L	3(l)	0(0)	0(0)
Soft Tissue Examination				
Dilated Ureter (Unilateral or Bilateral)	F	3(4)	2(3)	1(1)
	L	6(2)	6(2)	3(l)
Dilated Renal Pelvis (Unilateral or Bilateral)	F	l(l)	0(0)	2(2)
	L	3(l)	0(0)	6(2)
Encephalomenin-gocele*	F	l(l)	0(0)	l(l)
	L	3(l)	0(0)	3(l)
Unilateral External Hydrocephalus*	F	0(0)	l(l)	0(0)
	L	0(0)	3(l)	0(0)
Slightly Dilated Ventricle (brain)	F	0(0)	l(l)	0(0)
	L	0(0)	3(l)	0(0)
Shortened Left Lateral Ventricle (brain)*	F	0(0)	0(0)	l(l)
	L	0(0)	0(0)	3(l)
Subcutaneous	F	0(0)	0(0)	l(l)

Hemorrhage (head-nasal area)	L	0(0)	0(0)	3(1)

Skeletal Examination

Skull - delayed ossification	F	15(44)	14(35)	12(30)
	L	48(16)	41(12)	58(18)
- bone island	F	1(2)	2(4)	1(2)
	L	6(2)	14(4)	7(2)
- extra site of ossification	F	3(9)	2(6)	1(3)
	L	15(5)	14(4)	6(2)
- occipital unfused and misshapen*	F	0(0)	0.4(l)	0(0)
	L	0(0)	3(l)	0(0)
Sternebrae - Delayed ossification	F	4(18)	5(18)	6(24)
	L	31(11)	39(13)	34(11)
- unfused	F	0.2(l)	0.3(l)	0.3(l)
	L	3(l)	3(l)	3(l)
Ribs - Extra ribs	F	1(4)	0.3(l)	0.5(2)
	L	11(4)	3(l)	6(2)
- missing*	F	0.2(l)	0(0)	0.3(l)
	L	3(l)	0(0)	3(l)
- wavy ribs	F	1(4)	0.3(l)	0.3(l)
	L	11(4)	3(l)	3(l)
Vertebrae - Missing*	F	1(3)	0.3(l)	0.3(l)
	L	8(3)	3(l)	3(l)
- misshapen*	F	0.2(l)	0(0)	0(0)
	L	3(l)	0(0)	0(0)
- delay in ossification cervical centra	F	25(107)	23(84)	28(105)
	L	72(26)	76(25)	78(25)
- bilobed thoracic centra	F	5(22)	7(25)	5(18)
	L	39(14)	52(17)	28(9)
- unfused thoracic centra	F	0.2(l)	1(3)	1(4)
	L	3(l)	6(2)	13(4)
- Spurs	F	18(76)	14(50)	13(48)
	L	75(27)	70(23)	59(19)
Other				
- Asymmetric pelvis	F	0(0)	0(0)	0.3(l)
	L	0(0)	O(0)	3(l)
Multiple Skeletal Defects(e)*	F	0.2(1)	0(0)	0(0)
	L	3(l)	0(0)	0(0)

(a) Bred rats were exposed to 0, 2.5 or 25 ppm of epichlorohydrin by inhalation for 7 hrs/day on days 6

through 15 of gestation.

(b) In litters containing less than 4 fetuses, all fetuses were decapitated during the soft tissue examination and were therefore not available for examination of bones of the skull.

(c) F = Fetuses L = Litters

(d) One fetus in the control group exhibited multiple facial anomalies including the formation of a nasal proboscis, micrognathia of both upper and lower jaws, a small head and facial area, pinnae attached posterior to the normal position, and micropthalmia.

(e) One control fetus exhibited multiple skeletal defects, including misshapen tibias and fibulas; misshapen right femur; misshapen radii and ulnas; unossified centra and delayed ossification of all skull bones.

* Considered to be a major malformation.

No value differed significantly from the control value by a modified Wilcoxon Test, P<0.05.

Test condition : TEST ORGANISMS:
Groups of 43-46 pregnant Sprague-Dawley rats (~250 g) per dose level were exposed to 0, 2.5, or 25 ppm seven hours per day on days 6 through 15 of gestation.

ADMINISTRATION/EXPOSURE
Whole-body exposures were carried out in 4.3 cubic meter Rochester-type chambers. Atmospheres were generated by metering liquid through a pump into a warmed vaporization flask, then sweeping the vapors into the chamber with compressed air. Chamber air was assayed for vapor concentration 2-7 times during each 7-hour exposure period.

Chamber Concentrations (ppm):

Target	0	2.5	25
Nominal	0	2.43+/-0.32	24.4+/-1.1
Analytical	0	2.46+/-0.32	24.6+/-1.0

PARAMETERS ASSESSED DURING STUDY
Animals were observed daily during the exposure period for signs of toxicity. Body weights were recorded on gestation days 6-10, 12, and 16. Food and water consumption were also recorded at 3-day intervals beginning on gestation day 6.

Cesarean-sections were performed on all animals on gestation day 21. Liver weights were recorded at that time, and samples of nasal turbinates, trachea, and lungs were preserved for possible histologic examination. Examination of these tissues was not deemed necessary.

At cesarean-section, developmental parameters were recorded: the number and position of live, dead, and resorbed fetuses, the number of corpora lutea, and the weight of the gravid uterus with ovaries attached. After being weighed and measured for crown-rump length, all fetuses were examined for external alterations and cleft palate. One-third of each litter, randomly selected, was examined for evidence of soft-tissue alterations by fresh dissection. Heads of

fetuses undergoing soft-tissue examination were preserved in Bouin's fixative and examined by free-hand serial sectioning. All fetuses were then eviscerated and processed for skeletal examination.

Test substance : Purity = 99.8%
Reliability : (1) valid without restriction
1B

28.03.2002 (78) (125)

Species : rabbit
Sex : female
Strain : New Zealand white
Route of admin. : inhalation
Exposure period : days 6-18
Frequency of treatm. : 7 hours/day
Duration of test : 29 days
Doses : 2.5, 25 ppm
Control group : yes
NOAEL maternal tox. : > 25 ppm
NOAEL teratogen. : > 25 ppm
Method : other
Year : 1979
GLP : no
Test substance : other TS

Result : NOAEL/LOAEL

No evidence of maternal toxicity was evident in body weights, organ weights, or clinical observations at any exposure level. Therefore, the NOEL for maternal toxicity was 25 ppm.

No adverse effects related to treatment were observed in the embryos or fetuses at any exposure level. Therefore, the fetal NOEL was 25 ppm.

BODY AND LIVER WEIGHTS OF PREGNANT RABBITS EXPOSED TO EPICHLOROHYDRIN BY INHALATION

ppm Epichlorohydrin (a)

	0	2.5	25
Number of Dams(b)	23	18	16
Maternal body weight (kg) on gestation day			
6	3.94+/-0.50(c)	3.96+/-0.38	3.87+/-0.26
8	3.95+/-0.44	3.93+/-0.36	3.83+/-0.25
10	3.97+/-O.43	3.96+/-0.34	3.82+/-0.23
12	3.99+/-0.45	3.96+/-0.36	3.84+/-0.26
16	4.06+/-0.44	4.05+/-0.36	3.91+/-0.28
19	4.04+/-0.46	4.07+/-0.36	3.91+/-0.29
29	4.I0+/-0.42	4.18+/-0.34	4.00+/-0.23
Maternal body weight gain (kg) on gestation days			
6-7	-0.01+/-0.15	-0.03+/-0.08	-0.04+/-0.04
8-9	0.02+/-0.06	0.03+/-0-12	

-0.01+/-0.07
10-11 0.02+/-0.06 0.00+/-0.12
0.02+/-0.05
12-15 0.07+/-0.09 0.08+/-0.07
0.07+/-0.05
16-18 -0.02+/-0.11 0.03+/-0.08
0.00+/-0.09
19-28 0.06+/-0.19 0.II+/-0.14
0.09+/-0.18

Total 6-29 0.14+/-0.31 0.22+/-0.21
0.13+/-0.20

Maternal Liver weight on day 29
Absolute(d) 111+/-21 II2+/-14 117+/-21
Relative(e) 27.2+/-4.3 26.7+/-2.8 29.3+/-5.1

Gravid Uterus Weight on day 29
Absolute(d) 366+/-103 390+/-139 360+/-I00
Adjusted
body weight (f) 3.73+/-0.39 3.79+/-0.30
3.64+/-0.25

(a) Bred rabbits were exposed to 0, 2.5 or 25 ppm of epichlorohydrin by inhalation for 7 brs/day on days 6 through 18 of gestation.

(b) Data from non-pregnant rabbits were not included in these analyses.

(c) Mean +/- S.D.

(d) g, Mean +/- S.D.

(e) g, liver/kg body weight, mean +/- S.D.

(f) Maternal body weight minus the gravid uterus weight (g), mean +/- S.D.

No values were significantly different from the control values by Dunnett's test, P<0.05.

OBSERVATIONS AT CESAREAN SECTION OF RABBITS EXPOSED TO EPICHLOROHYDRIN BY INHALATION

	ppm Epichlorobydrin(a)		
	0	2.5	25
Number of bred females	25	20	20
Number of maternal deaths/number bred	0/25	0/20	1/20
Apparent pregnancy rate, %(b)	92(23/25)	95(19/20)	80(16/20)
Pregnant with stain only, %(c)	50(1/2)	0(0/1)	33(1/3)
Percent pregnant, total(d)	96(24/25)	95(19/20)	85(17/20)
Number of Litters	23	18	16

Corpora lutea/dam(e)	9+/-3	10+/-3	9+/-2
Implantation sites/ dam(e)	7+/-2	8+/-3	7+/-2
Preimplantatian Loss(e)	2+/-2	2+/-3	2+/-2
Fetuses/Litter(e)	7+/-2	7+/-3	7+/-2
Resorptions/Litter (e,f)	0+/-1	1+/-1	0+/-1
Percent Implantations resorbed(f)	6(9/165)	9(13/140)	4(4/110)
Percent litters with resorptions(f)	26(6/23)	33(6/18)	19(3/16)
Litters totally resorbed(f)	0	0	0
Resorptions/litters with resorptions(f)	1.5(9/6)	2.2(13/6)	1.3(4/3)
Percent dead fetuses	1(1/156)	0(0/127)	0(0/106)
Sex ratio, M:F, %	54:46	57:43	58:42
Fetal body weight, (grams)g	37.0+/-6.6	36.3+/-4.6	37.9+/-5.3
Fetal crown-rump length, (mm)g	92.4+/-5.6	92.2+/-4.3	93.9+/-5.9

(a) Bred rabbits were exposed to 0, 2.5 or 25 ppm epichlorobydrin by inhalation for 7 hrs/day on days 6 through 18 of gestation.

(b) Number of females with visible implantations at the time of C-section or necropsy/total bred. One female from the 2.5 ppm exposure level delivered a litter prior to day 29 of gestation.

(c) Number of females detected as being pregnant only after staining uterus with sodium sulfide stain/total stained.

(d) Number of females pregnant by visual inspection of the uterus or by sodium sulfide stain/total bred.

(e) Mean +/- S.D.

(f) Resorptions detected by sodium sulfide staining were not included in these calculations.

(g) Mean of litter means +/- S.D.

No values were significantly different from the control values by the appropriate statistical test, p<O.05.

INCIDENCE OF FETAL ALTERATIONS AMONG LITTERS OF RABBITS EXPOSED TO EPICHLOROHYDRIN BY INHALATION(a)

	ppm Epichlorohydrin		
	0	2.5	25
	Number Fetuses (Number Litters)		
EXTERNAL EXAMINATION	156(23)	127(18)	106(16)
SOFT TISSUE EXAMINATION	67(23)	53(18)	47(16)
SKELETAL EXAMINATION	156(23)	127(18)	106(16)

Percent Affected (Number Affected)

Total Major Malformations	F(e)	l(l)	5(6)	l(l)
	L	4(1)	17(3)	6(1)

External Examination

No external alterations observed.

Soft Tissue Examination

Fused Innaminate and Left Carotid Arteries	F	79(53)	72(38)	72(34)
	L	100(23)	94(17)	94(15)
Satellite Vessels Off of Major Arteries	F	33(22)	36(19)	30(14)
	L	70(16)	67(12)	63(10)
Extra Vessels Off of Major Arteries	F	6(4)	8(4)	4(2)
	L	17(4)	22(4)	13(2)
Multiple Heart Defects(c)*	F	1(1)	0(0)	0(0)
	L	4(l)	0(0)	0(0)
Dilated Renal Pelvis*	F	0(0)	0(0)	2(l)
	L	0(0)	0(0)	6(l)

Skeletal Examination

Skull				
- foramen in skull	F	5(8)	2(3)	l(l)(d)
	L	22(5)	11(2)	6(l)
- bone island	F	5(7)	2(2)	l(l)
	L	22(5)	11(2)	6(1)
Sternebrae				
- delayed ossification	F	83(130)	87(110)	86(91)
	L	100(23)	100(18)	100(16)
- fused	F	1(1)	1(1)	0(0)
	L	4(1)	6(1)	0(0)
Ribs				
- extra ribs	F	63(98)	52(66)	39(41)(e)
	L	96(22)	94(17)	75(12)
- lumbar spurs	F	6(9)	9(11)	4(4)
	L	3O(7)	44(8)	19(3)
Vertebrae				
- unfused centrum	F	0(0)	2(2)	0(0)
	L	0(0)	11(2)	0(0)
- hemivertebrae*	F	0(0)	3(4)	0(0)
	L	0(0)	17(3)	0(0)

- misshapen*	F	0(0)	2(3)	0(O)
	L	0(0)	11(2)	0(0)

Other

Multiple Skeletal Defects(f)*	F	0(0)	1(1)	0(0)
	L	0(0)	6(1)	0(0)

(a)Bred rabbits were exposed to 0, 2.5, or 25 ppm of epichlorohydrin by inhalation 7 hrs/day on days 6 through 18 of gestation.

(b) F = fetuses; L = litters.

(c)One fetus at 0 ppm exhibited multiple defects, including fused pulmonary artery and aorta, missing valves of the heart and an opening in the interventricular septum.

(d) p = .059

(e)Significantly different from control value by a modified Wilcoxon test, p<O.05.

(f)One fetus at 2.5 ppm of epichlorohydrin exhibited multiple skeletal defects, including a forked rib, an unfused centrum, a misshapen and an unfused vertebrae, a missing rib, scoliosis and a hemivertebra.

*Considered to be a major malformation.

Test condition : TEST ORGANISMS:
Groups of 16-23 pregnant New Zealand White rabbits (~4 kg) per dose level were exposed to 0, 2.5, or 25 ppm seven hours per day on days 6 through 18 of gestation.

ADMINISTRATION/EXPOSURE
Whole-body exposures were carried out in 4.3 cubic meter Rochester-type chambers. Atmospheres were generated by metering liquid through a pump into a warmed vaporization flask, then sweeping the vapors into the chamber with compressed air. Chamber air was assayed for vapor concentration 2-7 times during each 7-hour exposure period.

Chamber Concentrations (ppm):

Target	0	2.5	25
Nominal	0	2.43+/-0.32	24.4+/-1.1
Analytical	0	2.46+/-0.32	24.6+/-1.0

PARAMETERS ASSESSED DURING STUDY
Animals were observed daily during the exposure period for signs of toxicity. Body weights were recorded on gestation days 6-10, 12, 16, and 19. No food and water consumption data were recorded.

Cesarean-sections were performed on all animals on gestation day 29. Liver weights were recorded at that time, and samples of nasal turbinates, trachea, and lungs were preserved for possible histologic examination. Examination of these tissues was not deemed necessary.

At cesarean-section, developmental parameters were recorded: the number and position of live, dead, and resorbed fetuses,

the number of corpora lutea, and the weight of the gravid uterus with ovaries attached. After being weighed and measured for crown-rump length, all fetuses were examined for external alterations and cleft palate. One-third of each litter, randomly selected, was examined for evidence of soft-tissue alterations by fresh dissection. All fetuses were then eviscerated and processed for skeletal examination.

Test substance : Purity = 99.8%

Reliability : (2) valid with restrictions
2C Study did not produce evidence of maternal toxicity, but was robust in the examination of fetal parameters.

28.03.2002 (77) (125)

Species : rat
Sex : female
Strain : other: CD
Route of admin. : gavage
Exposure period : 6th - 15th day of pregnancy
Frequency of treatm. : once a day
Duration of test : 21 days
Doses : 40, 80, 160 mg/kg
Control group : yes, concurrent vehicle
NOAEL maternal tox. : = 40 mg/kg bw
NOAEL teratogen. : > 160 mg/kg bw
Method : other
Year : 1982
GLP : no
Test substance : other TS

Result : No teratogenic or fetotoxic effects on the developing embryos were observed.
Lethal effects in dams (3/27) at 160 mg/kg/day. Greater than 10% reduction in average body weight gain during pregnancy at 80 mg/kg/day.

Test substance : Reagent grade material from Fisher Scientific, Fair Lawn, NJ.

Reliability : (1) valid without restriction
1B

28.03.2002 (102)

Species : mouse
Sex : female
Strain : CD-1
Route of admin. : gavage
Exposure period : Days 6-15
Frequency of treatm. : once a day
Duration of test : 18 d
Doses : 80, 120, 160 mg/kg
Control group : yes, concurrent vehicle
NOAEL maternal tox. : = 120 mg/kg bw
NOAEL teratogen. : = 160 mg/kg bw
Method : other
Year : 1982
GLP : no
Test substance : other TS

Result : No increase in the average percent of fetal malformations. There were statistically significant decreases in mean fetal weight at 120 mg/kg (93 % of control value) and 160 mg/kg (91 % of control value). However, rodents dosed with 18 or 46 mg/kg/day via oral gavage for 10 days (Daniel, 1996)

exhibited dose-related increases in liver and kidney weights. Hence, the observed effects on fetal body weight may have been secondary to toxic effects on maternal organs which were not examined.

Test substance : Reagent grade material from Fisher Scientific, Fair Lawn, NJ.

Reliability : (1) valid without restriction
28.03.2002

(102)

5.8.3 TOXICITY TO REPRODUCTION, OTHER STUDIES

5.9 SPECIFIC INVESTIGATIONS

5.10 EXPOSURE EXPERIENCE

Remark : Sensitization:

Work-related contact dermatitis is known to occur among employees at plants producing or processing epoxy resins (Jolanki et al., 1987; Prens et al., 1986; van Joost, 1988; van Joost et al., 1990).
There was an evaluation between 1974 and 1984 of 26 cases of contact dermatitis among the 228 workers of a Dutch epoxy resin production plant. All of the workers had contact with process chemicals as a result of their particular jobs. 19 of 26 employees with contact dermatitis submitted themselves to a voluntary, epicutaneous patch test. In 8 cases there was a positive reaction to epichlorohydrin. The bisphenol A/epichlorohydrin oligomer (mean molecular weight 385) elicited a positive reaction in 10 cases, liquid resin in 8 cases, hardened resin in 7 cases and bisphenol A in none of the cases. In the opinion of the authors, residues of free epichlorohydrin in the resins and, due to its volatility, unavoidable concentrations in the air were responsible for the observed cases of sensitization (Prens et al., 1986)
There was in Finland 74/542 (13 %) cases of occupational dermatitis registered between 1974 and 1983 which were caused by epoxy resins (paints, varnishes, adhesives, electrical insulation materials etc.). On these patients epicutaneous tests were carried out with standard series of epoxy resins and the component materials epichlorohydrin and bisphenol A. In all instances the results for the standard were positive, while those for the component materials were negative. All of the resin preparations which led to positive effects were found to contain an epichlorohydrin-Bisphenol A oligomer with a molecular weight of 340 at concentrations of 0.2-15 %. This oligomer is known to be a strong allergen. The authors conclude that this allergen was responsible for causing the investigated cases of dermatitis, whereby the solvent in which the resins were dissolved favourably influenced skin penetration (Jolanki et al., 1987).
Van Joost reports a total of 11 cases of contact dermatitis among the 228 workers of the epoxy resin producing plant mentioned in Prens et al. (1986). In the patch test all of the cases reacted positively towards epichlorohydrin. 6 of

the 11 cases were tested against other resin components. All 6 reacted negatively towards bisphenol A, while in 4 cases liquid resin and the epichlorohydrin/ bisphenol A oligomer (molecular weight 385) elicited a positive reaction. Two cases, which showed the most marked sensitization reaction towards epichlorohydrin, reacted negatively towards the epoxy resins and the epichlorohydrin/bisphenol A oligomer.

28.03.2002 (80) (129) (177) (178)

Remark : Genotoxicity:

Effects of ECH on the lymphocytes of peripheral blood
In 3 studies of workers at a factory in Czechoslovakia, 5 examinations of chromosome aberrations in peripheral lymphocytes were carried out. The examinations were conducted by Kucerova et al. (1977) before exposure began (control) and repeated after one and two years. After 4 and 8 years exposure, examinations were conducted by Sram et al. (1981, 1983). The majority of the 23 to 35 workers were exposed during the whole course of the 3 studies. In the later studies, the peripheral lymphocytes of additional control persons, of suitable age and sex and with similar smoking and drinking habits, were also examined and used as an additional control. The concentration of epichlorohydrin in the air to which the workers were exposed dropped from study to study. In the first study it was 0.5-5 mg/m3, in the second study, in the region of the stipulated threshold value of 1 mg/m3 and in the final study, a mean ECH concentration of 0.4 mg/m3 was measured. In the first 2 studies a significant increase in the number of chromosome aberrations was found compared both to the internal control, before exposure began, and to the external controls included in the 2nd study.
In the 3rd study a slight increase in the number of chromosome aberrations was found, which, however, did not prove to be statistically significant.
Picciano (1977) examined the lymphocytes of 93 workers in the epoxy resin industry. Details of duration or level of exposure are not given; however, the author assumes exposure to be within the limits set down by the then valid American standards of max. 5 ppm (19 mg/m3). A significant increase in chromosome aberrations was found in these workers compared to a group 75 control persons who were examined in the course of taking up employment.
Van Sittert & De Jong (1985) investigated 2 groups of workers at a plant processing ECH. One group of 50 workers as directly involved with ECH-containing solutions and exposed to < 0.3-2.7 ppm (< 1.1-10 mg/m3) ECH over a period of about 7 years, while the other group of 45 workers was engaged in processing the ECH products (< 0.3.-0.8 ppm = < 1.1-3 mg/m3; duration of exposure about 6.5 years). In the group exposed to ECH the number of chromosome aberrations in the peripheral lymphocytes compared to a control group of other factory workers was not statistically different.
Workers employed in various plants at a Dutch chemical complex were evaluated by De Jong et al (1988) for the period 1976-1981. They were exposed to, among other substances, epichlorohydrin. At one plant the workplace concentration of ECH was generally below the stipulated limits; for example, a mean weekly concentration (8-h

time-weighted average) of 0.1-1.6 mg ECH/m3 was found. While in another plant, ECH concentrations of up to 25 mg/m3 were detected. At such high concentrations the employees wore breathing devices for protection, so that the actual concentration to which they were exposed remained unknown. Chromosome aberrations in lymphocytes or peripheral blood were used as measure of any cytogenetic effects. A biologically significant increase in the numbers of chromosome aberrations was not found, since those of the various control groups were more or less just as high. From these results the authors conclude that the employed method of monitoring was not sensitive enough to register the cytogenetic effects caused by low concentrations of genotoxic substances.

11.12.2001 (31) (94) (124) (156) (159) (180)

Remark : Fertility

Milby & Whorton (1980; 1981) carried out studies on 2 cohorts of male workers involved with the manufacture of ECH. The average level of ECH exposure ranged from 0.1-<1 ppm (0.38-3.8 mg/m3). The general state of health and the blood data of the workers were found to be normal. The 2 groups consisted of 44 and 84 men, respectively, and were compared in respect to testicular function with a control group of 90 men from another chemical factory. The fertility of the men was deduced from their general state of health, their hormonal status (FSH, LH, testosterone) and analyses of their sperm (sperm count). No adverse effects were found.

Venable et al (1980) studied workers exposed to various mixture of ECH, allyl chloride and 1,3 dichloropropane, all at estimated conc of < 1 ppm (8 hour TWA) during the 5 years preceeding the study. Measurement of testicular size, semen volume and sperm count, viability, motility and morphology all indicated no differnece between the exposed and control groups. Also no difference was noted concerning serum hormones

11.12.2001 (111) (112) (182)

Remark : Carcinogenicity

In a succession of retrospective studies carried out by Enterline (1977, 1978, 1981, 1982, 1990), mortality and tumour rate were investigated in 863 male workers who had been involved, in some cases for more than 20 years (1948-1983), with work-related use of ECH. The men investigated were employed at one of 2 different ECH production plants and were assigned, depending on the degree of exposure (low, moderate, high), to one of 3 groups. As a rule, the workers were not questioned about their life-style or habits (e.g. smoking). The local mortality rate served as a control. A particularly high incidence of deaths involving cancer of the respiratory organs in the years 1969-1977 (9 of 52 deaths, versus an expected value of 6.8) was at first thought to be due to a carcinogenic effect of ECH. However, subsequent studies, as well as a re-evaluation of the above by Brown & Rinsky (1979) (in which the failure to include such factors as life-style and habits of workers, e.g. heavy smoking, the imprecise data on actual exposure and the lack

of pathological data were emphasised) have cast doubt on the validity of its conclusions. A later publication revealed that of the 10 cases of death due to lung cancer observed up until 1979, 7 were smokers, some of them heavy, while only one was a confirmed nonsmoker and of the other 2 the smoking habits were unknown. In addition, in the course of these studies, 3 cases of leukaemia also occurred, which was significantly above the statistically expected value of 0.5. However, since the 3 cases involved 3 different forms of leukaemia, the authors did not rule out the possibility of them having different causes. Another 22 deaths were due to diseases of the heart. Among workers subjected to no or low ECH exposure only 5 such deaths were registered, compared to an expected number 12.75. For this unexpectedly low number of deaths through heart disease a "healthy worker effect" is possibly responsible. Among workers subjected to medium to high ECH exposure the number of heart-related deaths (17) was close to the expected number of 16.13. Thus, there is the possibility of exposure to ECH being associated with death due to heart disease. However, this is questioned by other authors, since factors such as life situation and smoking were not taken into consideration (de Voogd, 1990).

In another study at the same ECH plants, workers were studied not in respect to mortality but in respect to their illnesses. In this study too the workers were classified into 3 groups (low, medium, high) acc. to the level of ECH they were exposed to. Unlike in the Enterline studies, the classification was based on ECH concentrations measured in the workplace air. Concentrations of 0.5-1 ppm were reported as representing average levels of exposure. One group consisted of 280 workers investigated in the previous Enterline studies and for whom health histories were available for the years 1981-1988. The 2nd group consisted of workers who had taken up employment at the plant later than those involved in the Enterline studies. Between 1981 and 1988 the authors of this study collected data on the health history and habits of these 2 groups and compared them with the corresponding data for the local population. Unlike the Enterline studies, in this later study neither of the 2 groups provided any indication of there being a correlation between ECH exposure and heart disease, lung disease or leukaemia. On the other hand the study did reveal a significant increase, depending on the level of ECH exposure, which the authors, however, on account of the kinds of complaint observed, considered to be due to other working conditions rather than to exposure to ECH (Tsai et al., 1990). A follow up of this study demonstrated no increased mortality or illnesses related to ECH exposure (including cancer) (TSAI, 1994, in press)

11.12.2001 (35) (47) (48) (49) (50) (51) (170)

Remark : Industrial hygiene

Analyses of workplace air at a German manufacturer of epoxy resins in 1989 failed to detect epichlorohydrin at a detection limit of 1 mg/m3.

11.12.2001 (144)

Remark : Industrial hygiene

The workplace concentration of epichlorohydrin of the 2 German manufacturers (Dow Deutschland, Inc. and Solvay Deutschland) is well < 1 ppm (= 3.78 mg/m3). At the Dow plant, 90 % of the measurements produced results below the determination limit of 0.1 ppm.

11.12.2001 (184)

Remark : Industrial hygiene

According to the German Chemicals Trade Association, 61 individual results are available for the period of 1982-1991 (mean values for a shift; sampling period 1 hour; duration of exposure 6 hours) obtained from 21 firms: 98.4 % of the determinations were below the TRK concentration of 12 mg/m3 and half of these are less than half of the TRK concentration (< 6 mg/m3).

11.12.2001 (7)

Remark : Carcinogenicity

Delzel et al reported on an epidemiology study on 2548 workers (New Jersey, USA) exposed for at least 6 months between 1952 and 1985. In a subgroup of 44 men potentially exposed to ECH during 4 years a significantly higher number of observed (4) then expected (0.9) cases of lung cancer was noted. However lack of details on smoking habit, exposure data preclude any firm conclusion. The authors indicate that this result may be a chance observation. The study draws no conclusion.

In a follow-up study by Barbone et al (1992), taking into account smoking habits, an elevated odds ratio for lung cancer was found for men who worked in the anthraquinone dye and epichlorohydrin manufacturing area of the plant corresponding to a 40 % increased risk (non significant).

11.12.2001 (5) (36)

Remark : Carcinogenicity

Hagmar et al (1986) performed an epidemiology study on 664 workers in a Swedish chemical plant for at least 1 month between 1942 and 1979. Matched, case-referent studies were performed on 32 men who had cancer diagnosed between 1958 and 1984 (time of the follow-up). Analysis of the data reveal no association between the incidence of any type of cancer and potential exposure to ECH.

11.12.2001 (72)

Remark : Carcinogenicity

Bond et al. (1986) performed a nested case-control study on workers in Texas. From 19608 workers employed between 1940 and 1980, 308 cases of lung cancer were observed. Five cases of lung cancer were observed in ECH potentially exposed workers whereas 24 potentially exposed workers had no lung cancer. These results indicate no increased risk of developing lung cancer after ECH exposure.

11.12.2001 (9)

Remark : Carcinogenicity

Tassignon et al (1983) reported on a European-wide epidemiology study where workers were exposed to levels up to 1 ppm (8 h TWA) for at least 1 year. Only 4 cancers were observed in the whole cohort and the SMR for malignant neoplasms was 80.

11.12.2001 (166)

Remark : Carcinogenicity and mortality study

Olsen et al (1994) examined workers exposed for at least 1 month between 1957 and 1986 in the production of ECH and allyl chloride for lung cancer and heart disease mortality. There were no significant elevated SMRs for all malignant neoplasms, lung cancer, circulatory system disease or arteriosclerotic heart disease when compared to external (US) or internal (Texas operation) populations. The study results are limited by the cohort size (1064 workers), duration of follow-up, few numbers of observed and expected deaths, level of potential exposure experience.

11.12.2001 (120)

Remark : Irritation

Skin, eye and respiratory irritation have been reported in man exposed accidentally.

28.03.2002 (56) (76) (147)

5.11 ADDITIONAL REMARKS

Type : Biochemical or cellular interactions

Remark : Prodi et al. (1986) investigated the binding of ECH to nucleic acids and proteins from various organs of rats and mice. 4 male Wistar rats and 12 male adult BALB/c mice were administered i.p. doses of 127 microcuries [2-14C]-ECH/kg b.w. in 0.9 % NaCl solution. 22 h following administration, the fasted animals were sacrificed and their livers, lungs, kidneys and stomachs examined in respect to ECH covalently bound to DNA. On the basis of the covalent binding index (CBI) for carcinogens (classification after Lutz), ECH should be considered as a weak initiator.

28.03.2002 (131)

Type : Biochemical or cellular interactions

Remark : Covalent binding to macromolecules was measured in vitro in various tissue homogenate of the rat and man. Results showed that covalent binding in human was either similar to or lower than that in rat tissues. Invivo binding after exposure of rats to 2 ppm for 6 hours demonstrated the highest binding in the nasal epithelium (unlike in vitro results)

13.12.2001 (165)

Type : Excretion

Remark : In anesthetized rats exposed nose-only to 100 ppm ECH for up to 2 hours, about 50 % of the total amount of ECH inhaled was removed by the respiratory tract. Analysis of the upper and lower respiratory tracts independently indicated that removal of ECH occurred equally well in both regions, but that excretion via the respiratory tract of the unmetabolised substance did not occur.

13.12.2001 (164)

Type : Metabolism

Remark : After Fakhouri & Jones (1979) and Gingell et al. (1985) the metabolic transformation of ECH proceeds via 2 main routes:

1. Conjugation with glutathione (GSH), forming GSH- and mercapturic acid derivatives which are eliminated in the urine.

2. Hydrolysis of ECH to alpha-chlorohydrin (either mediated by epoxy hydrolase or occurring spontaneously in acidic milieu) which, following further transformation, is either expired as carbon dioxide or excreted in the urine as GSH conjugate. The transformation of alpha-chlorohydrin is possibly accompanied by the formation of oxalic acid.
However, the study by Fakhouri & Jones (1979) did not involve the use of radio-labelled ECH. And the use of propylene glycol, which has a certain structural similarity with ECH, as vehicle may also have had an effect on metabolism.

13.12.2001 (60) (68)

Type : Toxicokinetics

Remark : Independent of the mode of administration and of the amount administered, in rats ECH is rapidly and completely, i. e. to over 90 %, absorbed and within 2-4 h is distributed throughout the whole body (Weigel et al. (1978); Smith et al. (1979)). The highest concentrations of radioactivity were found in the kidneys, gut, liver, lachrymal glands, pancreas and spleen. Oral and inhalative exposure differed in as immediately following oral administration the highest concentration of radioactivity was measured in the stomach, while following inhalative administration the highest level of radioactivity was found in the nasal turbinate. In a number of organs (liver, kidneys, spleen) ECH-induced pathological alterations were observed. Lower levels of radioactivity were found in blood, lungs, brain and gonads.

13.12.2001 (150) (187)

Type : Toxicokinetics

Remark : Half-life values of ECH and its metabolite, alpha-chlorohydrin, in the blood of Swiss-Albino mice, which had been administered 200 mg/kg b.w. doses of the substances (oral or i.p.), were found to be 3.6-5.3 and 65 minutes.

13.12.2001 (142)

Type : other: Respiratory irritation study (RD50)

Remark : Rats were exposed for 15 minutes to ECH concentrations from 101 to 1963 ppm. A clear decrease in respiratory rate was seen at 363 ppm and above. The RD50 was calculated at 1342 ppm. At 1963 ppm clear nasal discharge was observed. Similar studies in mice using head-only exposures for 10 minutes yielded an RD50 value of 687 ppm

28.03.2002 (66) (82)

6.1 ANALYTICAL METHODS

6.2 DETECTION AND IDENTIFICATION

7.1 FUNCTION

7.2 EFFECTS ON ORGANISMS TO BE CONTROLLED

7.3 ORGANISMS TO BE PROTECTED

7.4 USER

7.5 RESISTANCE

8.1 METHODS HANDLING AND STORING

Remark : Handling

ECH is stable under normal conditions;

Conditions to avoid:
- Heating the product above boiling point
- Open flames, sparks
- Heat/heat sources
- Direct sunlight

Materials to avoid:
- Alcohols, phenols, amines, organic acids
- Oxidizing agents
- Concentrated sulfuric acid, alkalines
- Anhydrous metallic chlorides

Hazardous decomposition products:
- HCl, CO

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8.2 FIRE GUIDANCE

8.3 EMERGENCY MEASURES

8.4 POSSIB. OF RENDERING SUBST. HARMLESS

8.5 WASTE MANAGEMENT

Remark : DISPOSAL (WASTE OR PRODUCT)

Recover or recycle when possible. Otherwise, incinerate (residence time of 2 secs above 1200 degrees C) in a system with wet scrubbing facilities (as hydrogen chloride will be produced), or dispose to licensed contractor. Contaminated water should be routed to and treated at an approved facility. Biotreatment and chemical conversion may also be options; check with local authorities and obey regulations.

CONTAINER DISPOSAL

Drain container thoroughly. After draining, vent in a safe place away from sparks and fire. Removal of trace quantities should be attempted through use of low - or medium-pressure steam. Solvent may also be used; rinse three times with suitable solvent and treat rinsings as for product disposal.

Send to drum recoverer or metal reclaimer. Residues may cause an explosion hazard; do not puncture, cut or weld uncleaned drums.

15.03.2002 (153)

8.6 SIDE-EFFECTS DETECTION

8.7 SUBSTANCE REGISTERED AS DANGEROUS FOR GROUND WATER

8.8 REACTIVITY TOWARDS CONTAINER MATERIAL

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10.1 END POINT SUMMARY

10.2 HAZARD SUMMARY

10.3 RISK ASSESSMENT