FOREWORD

INTRODUCTION

1,2-EPOXYBUTANE
CAS N°.: 106-88-7
**SIDS Initial Assessment Report**

for

**11th SIAM**

(Orlando, USA, 23-26 January 2001)

**Chemical Name:** 1,2-epoxybutane

**CAS No:** 106-88-7

**Sponsor Country:** Germany

National SIDS Contact Point in Sponsor Country

Lead Organization:

Name of lead organization: BMU (Bundesministerium für Umwelt, Naturschutz und Reaktorsicherheit)

Contact person: Prof. Dr. Ulrich Schlottmann

Address: Postfach 12 06 29
D - 53048 Bonn- Bad Godesberg

**History:** see next page;

**Testing:**

No new SIDS testing ( X )

New SIDS testing ( )

**Date of Circulation:** 10. November 2000
OECD/ICCA - The BUA* Peer Review Process

Qualified BUA personnel (toxicologists, ecotoxicologists) perform a quality control on the full SIDS dossier submitted by industry. This quality control process follows internal BUA guidelines/instructions for the OECD/ICCA peer review process and includes:

- a full (or update) literature search to verify completeness of data provided by industry in the IUCLID/HEDSET

- Review of data and assessment of the quality of data

- Review of data evaluation

- Check of adequacy of selection process for key studies for OECD endpoints, and, where relevant, for non-OECD endpoints by checking original reports/publications

- Review of key study description according robust summaries requirements; completeness and correctness is checked against original reports/publications
  (if original reports are missing: reliability (4) not assignable)

- Review of validity of structure-activity relationships

- Review of full SIDS dossier (including SIAR, SIAP and proposal for conclusion and recommendation for further work)

- In case of data gaps, review of testing plan or rationale for not testing.

* BUA (GDCh-Beratergremium für Altstoffe): Advisory Committee on Existing Chemicals of the Association of German Chemists (GDCh)
SID S INITIAL ASSESSMENT PROFILE

<table>
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<tr>
<th>CAS No.</th>
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<tbody>
<tr>
<td>Chemical Name</td>
<td>1,2-epoxybutane</td>
</tr>
<tr>
<td>Structural Formula</td>
<td>$\text{C}_4\text{H}_8\text{O}$</td>
</tr>
</tbody>
</table>

RECOMMENDATIONS

For use in closed systems the substance is currently of low priority for further work.

For other uses the substance is a candidate for further work.

SUMMARY CONCLUSIONS OF THE SIAR

Human Health

1,2-Epoxybutane caused acute toxic effects in mammals: LD$_{50}$ rat (oral) 900 mg/kg body weight, LC$_{50}$ rat (inhalative, 4 h) $> 6,300 < 20,000$ mg/m$^3$, LD$_{50}$ rabbit (dermal) 1,757 (1,255 - 2,546) mg/kg body weight.

It was irritating to the eyes. Irritating effects to the skin were severe (corrosion) if evaporation was minimised due to occlusive application, but there was no effect by semi-occlusive application. 1,2-Epoxybutane was not sensitising in a guinea pig maximisation test. In 90-day inhalation studies with rats and mice 1,2-epoxybutane mainly caused nasal lesions (NOAEC 600 and 150 mg/m$^3$, respectively). Systemic effects occurred at higher concentrations (rat 2400 mg/m$^3$: decreased mean body weight gain; mice 2400 mg/m$^3$: e.g. renal tubular necrosis).

1,2-Epoxybutane was genotoxic in vitro. However, it caused neither chromosomal aberrations in bone marrow nor dominant-lethal mutations in germ cells of rats.

There is clear evidence for 1,2-epoxybutane being a locally acting carcinogen in male rats (inhalation of 600 mg/m$^3$ caused no tumours and 1,200 mg/m$^3$ caused neoplasms of the nasal cavity and the lung of male rats) and there is equivocal evidence for a carcinogenic activity in female rats. There was no evidence for carcinogenic activity in male or female mice. However, the mortality of females was increased in this study due to an infection and this raises difficulties in the interpretation of the result. Regarding the overall database on genotoxicity and structural relationship to epoxyethane and -propane, epoxybutane seems to be a genotoxic compound, showing a carcinogenic activity at the site of application only at high concentrations. However, irritating properties of the compound may cause cell proliferation and contribute thereby to tumor induction.

With respect to reproductive toxicity the 90 day studies with rat and mice did not reveal adverse effects on the reproductive organs up to 2400 mg/kg body weight. Additionally, the lack of an effect from pre-gestational exposure in the developmental toxicity study and a negative dominant-lethal test may indicate that 1,2-epoxybutane does not reach male and female germ cells in effective concentrations.

No developmental toxicity or teratogenicity was detected in rats after inhalation of up to 3,000 mg/m$^3$ throughout gestation. From the rabbit study no conclusions can be drawn due to high mortality in the high dose group.
1,2-Epoxybutane has a water solubility of 59 g/l, a vapor pressure of 227 hPa and a log Kow of 0.68. According to Mackay I air is the main target compartment for 1,2-epoxybutane (89 %), while 11 % partitions to water. The substance has no considerable potential for bio- and geoaccumulation (log P ow = 0.68). The half-life for photochemical degradation in air is calculated to 7.6 days. 1,2-Epoxybutane is classified as readily biodegradable, failing the 10d-window criterion. In sewage treatment plants the substance will be eliminated by stripping and biodegradation. Hydrolysis and photolysis are slowly under environmental conditions.

The following aquatic effects concentrations are available:

Leuciscus idus: LC50 (96 h) = 100 - 215 mg/l, Daphnia magna: EC50 (48h) = 69.8 mg/l, Scenedesmus subspicatus: ErC50 (72 h) > 500 mg/l, Pseudomonas putida: EC50 (17 h) = 4,840 mg/l. All values are related to nominal concentrations. Due to the volatility of the substance the real effect values may be lower. QSAR estimations give effect values of 20 mg/l for fish and 32 mg/l for daphnia and show that the effect values are indeed lower than those found in the test but not by orders of magnitude. Based on the measured and predicted effect data the substance can be classified as moderately toxic. A PNEC of 20 µg/l can be derived based on the predicted effect value for fish using an assessment factor of 1000. No data are available on terrestrial organisms.

Exposure

In the European Union there is only one known producer of 1,2-epoxybutane. The production volume of this chemical in BASF Aktiengesellschaft Ludwigshafen was 5,000-10,000 t in 1999. The total production volume is mainly used at the production site as an intermediate (non-disperse use) for synthesis in closed systems of fuel additives, non-ionic surfactants, defoamers and various other products. Monitoring data showed no emission into the air during production and processing. There is no information on emission of 1,2-epoxybutane into the hydrosphere. In the USA the substance is used as a stabilizer in hydrocarbon solvents. Therefore emissions into the environment cannot be excluded during formulation and use of the solvents.

NATURE OF FURTHER WORK RECOMMENDED

For use in closed systems no further work is recommended.

For other uses there is a need for an exposure assessment.
### PHYSICAL-CHEMICAL

<table>
<thead>
<tr>
<th>CAS NO: 106-88-7</th>
<th>SPECIES</th>
<th>PROTOCOL</th>
<th>RESULTS</th>
</tr>
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<tbody>
<tr>
<td>2.1 Melting Point</td>
<td>-</td>
<td></td>
<td>129.5 °C</td>
</tr>
<tr>
<td>2.2 Boiling Point</td>
<td>-</td>
<td></td>
<td>63.4 °C (at 1013 hPa)</td>
</tr>
<tr>
<td>2.3 Density</td>
<td>-</td>
<td></td>
<td>0.83 g/cm³</td>
</tr>
<tr>
<td>2.4 Vapour Pressure</td>
<td>-</td>
<td></td>
<td>227 hPa (at 24 °C)</td>
</tr>
<tr>
<td>2.5 Partition Coefficient (Log P&lt;sub&gt;ow&lt;/sub&gt;) OECD 107</td>
<td>-</td>
<td>OECD 107</td>
<td>0.68 (at 25 °C)</td>
</tr>
<tr>
<td>2.6 Water Solubility pH</td>
<td>-</td>
<td></td>
<td>59 g/l at 20 °C ca. 7 at 50 g/l 20°C</td>
</tr>
</tbody>
</table>

### ENVIRONMENTAL FATE AND PATHWAY

<table>
<thead>
<tr>
<th>3.1.1 Photodegradation</th>
<th>Calculated</th>
<th>in air t₁/₂ = 7.6 days</th>
</tr>
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<tbody>
<tr>
<td>3.1.2 Stability in Water</td>
<td>Measured</td>
<td>t₁/₂ = 156 hours</td>
</tr>
<tr>
<td>3.2 Monitoring Data</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>3.3 Transport and Distribution</td>
<td>Henry-constant Calculated acc. to Mackay</td>
<td>22.977 Pa*m³/mol</td>
</tr>
<tr>
<td></td>
<td>In Air</td>
<td>88.98 %</td>
</tr>
<tr>
<td></td>
<td>In Water</td>
<td>11.01 %</td>
</tr>
<tr>
<td></td>
<td>In Sediment</td>
<td>0 %</td>
</tr>
<tr>
<td></td>
<td>In Soil</td>
<td>0 %</td>
</tr>
<tr>
<td></td>
<td>In Biota</td>
<td>0 %</td>
</tr>
<tr>
<td>3.5 Biodegradation</td>
<td>ISO 14593 OECD 301 D OECD 301 A</td>
<td>80 - 90 % after 28 days 17 % after 29 days 90 % after 28 days</td>
</tr>
</tbody>
</table>

### ECOTOXICOLOGY

<table>
<thead>
<tr>
<th>4.1 Acute/Prolonged Toxicity to Fish</th>
<th>Leuciscus idus</th>
<th>DIN 38 412</th>
<th>LC₅₀ (96 hours) = 100 - 215 mg/l</th>
</tr>
</thead>
<tbody>
<tr>
<td>4.2 Acute Toxicity to Aquatic Invertebrates</td>
<td>Daphnia magna</td>
<td>Directive 84/449/EEC, C.2 comparable to OECD 202</td>
<td>EC₅₀ (24 hours) = 159.7 mg/l EC₅₀ (48 hours) = 69.8 mg/l</td>
</tr>
<tr>
<td>4.3 Toxicity to Aquatic Plants e.g. Algae</td>
<td>Scenedesmus subspicatus</td>
<td>DIN 38412, Part 9 comparable to OECD 201</td>
<td>EC₅₀ (72 hours) = &gt; 500 mg/l</td>
</tr>
<tr>
<td>4.4 Toxicity to bacteria</td>
<td>Pseudomonas putida</td>
<td>DIN 38412, Part 8</td>
<td>EC₅₀ (17 hours) = 4,840 mg/l</td>
</tr>
<tr>
<td>(4.6.3) Toxicity to Other Non-Mammalian Terrestrial Species (Including Birds)</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>CASE NO: 106-88-7</td>
<td>SPECIES</td>
<td>PROTOCOL</td>
<td>RESULTS</td>
</tr>
<tr>
<td>------------------</td>
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<td>----------</td>
<td>---------</td>
</tr>
<tr>
<td><strong>5.1.1 Acute Oral Toxicity</strong></td>
<td>Rat</td>
<td>BASF Test</td>
<td>LD₅₀ = 900 mg/kg b.m.</td>
</tr>
<tr>
<td><strong>5.1.2 Acute Inhalation Toxicity</strong></td>
<td>Rat</td>
<td>BASF Test</td>
<td>LC₅₀ &gt; 6,300 mg/m³</td>
</tr>
<tr>
<td><strong>5.1.3 Acute Dermal Toxicity</strong></td>
<td>Rabbit</td>
<td>According to Smyth 1962</td>
<td>LD₅₀ = 1,757 (1,255-2,546) mg/kg bm</td>
</tr>
</tbody>
</table>

| **5.2 Acute Dermal Toxicity** | Mouse | 90 day inhalation study | NOAEC = 1200 mg/m³ (nasal lesions) |
| **5.3 Acute Dermal Toxicity** | Mouse | 90 day inhalation study | NOAEC = 150 mg/m³ (nasal lesions) |

| **5.4 Repeated Dose Toxicity** | Rat, Mouse | 90 day inhalation study | NOAEC = 1200 mg/m³ (nasal lesions) |
| **5.5 Genetic Toxicity In Vitro** | | | |
| **A. Bacterial Test** | Salmonella typhimurium | OECD 471 + (With external metabolic activation) + (Without external metabolic activation) |
| **B. Non-Bacterial In Vitro Test** | CHO cells | Cytogenetic study +/- (With metabolic activation) + (Without metabolic activation) |

| **5.6 Genetic Toxicity In Vivo** | Rat | Cytogenetic study, inhalative exposure | |
| **5.7 Genetic Toxicity In Vivo** | Rat | Dominant lethal-test, inhalative exposure | |

| **5.8 Toxicity to Reproduction** | Rat | Inhalative exposure, pregestational and throughout gestation | NOAEC > 3000 mg/m³ (General toxicity) |
| **5.9 Developmental Toxicity/Teratogenicity** | Rabbit | Inhalative exposure, pregestational and throughout gestation | NOAEC > 3000 mg/m³ (Foetal data) |

| **Further Data** | Rabbit | Draize Test 1959, semi-occlusive | Not irritating |
| **Corrosiveness/Irritation Skin** | Rabbit | BASF-Test occlusive | Corrosive |
| **Corrosiveness/Irritation Eye** | Rabbit | Draize Test 1959 | Irritating |
| **Sensitisation** | Guinea Pig | Maximisation Test | Not sensitising |
| **Carcinogenicity** | Rat | 2 Years inhalation up to 1,200 mg/m³ | Clear evidence in males (respiratory system) |
| | Mouse | 2 Years inhalation up to 300 mg/m³ | Equivocal evidence in females |

| **5.11 Experience with Human Exposure** | | | |

| **Corrosiveness/Irritation Skin** | Rabbit | Draize Test 1959, semi-occlusive | Not irritating |
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1. IDENTITY
Chemical Name: 1,2-epoxybutane
Synonyms: 1,2-butene oxide
1,2-butylene epoxide
1,2-butylene oxide
1,2-epoxybutane
2-ethyloxirane
ethylethylene oxide
n-butylenoxid-1,2
n-Butene 1,2-oxide
oxiran, ethyl-

CAS Number: 106-88-7
Empirical Formula: C₄H₈O
Structure:

General Substance Information
Substance type: organic
Physical status: colourless liquid
Purity: 99.9 % w/w

Physical and chemical properties
The solubility of 1,2-Epoxybutane in water is 59 g/l at 20°C¹ and the vapour pressure is 227 hPa at 24°C ². A Henry’s law constant of 22.977 Pa*m³*mol⁻¹ can be calculated with the values of mol mass, vapour pressure and solubility. The partition coefficient log P_{OW} is measured to 0.68 ³. Since the density of 1,2-Epoxybutan (0.83 g/cm³ at 20°C) is slightly lower than that of water ⁴, flotation or stratification in surface waters in case of accidental losses cannot be excluded.
2. GENERAL INFORMATION ON EXPOSURE

In the European Union, BASF AG, Ludwigshafen, is the only known producer of 1,2-epoxybutane. The production volume in 1999 was 5,000 – 10,000 tons. There is no information on imported volumes. It has been reported, that 3600 tons of 1,2-epoxybutane were produced in the U.S.A. in 1978.32

The total production of the substance takes place in closed system. 1,2-Epoxybutane is then pumped to the processing plants through closed pipelines. Therefore both production and processing of 1,2-Epoxybutane at BASF AG, Ludwigshafen, are carried out in a closed system of units connected to each other. The substance is mainly used in the chemical industry as an intermediate for synthesis in closed systems (non-disperse use) in Germany (BASF AG). Approx. 70 % of the total production volume are used for synthesis of fuel additives. Approx. 30 % of the total production volume are used for synthesis of non-ionic surfactants, defoamers and various other products. Only a small part of the produced volume is isolated and transported to external users.

The Swedish product register (1999) includes products that contain 1,2-epoxybutane, however, no further information is available.

In the USA the substance is widely used as stabilizer for chlorinated hydrocarbon solvents. It is also used as a chemical intermediate for the production of butylenes glycols and their derivatives (polybutylene glycols, mixed poly glycols and glycol ethers and esters)32.

2.1 Environmental Exposure and Fate

Environmental Exposure

The production and processing of 1,2-epoxybutane at BASF are connected to closed systems.

Thus during normal operating between 1979 to 2000 monitoring data showed no emission of 1,2-epoxybutane to air. There is no information on emission of 1,2-epoxybutane into the hydrosphere.

Emissions into the environment during formulation and use of hydrocarbon solvents that contain 1,2-epoxybutane as stabilizer as well as during use of other products that contain the substance cannot be excluded.

Environmental Fate

The distribution modelling using Mackay, Level I, which is calculated with the values of mol mass, vapour pressure, solubility and partition coefficient, indicates air to be the main target compartment as 89% partitions to the air and 11% goes into the water. Slow degradation in air is to be expected according to the calculated photodegradation value of \( t_{1/2} = 7.6 \) days. Long range distribution via the atmosphere is therefore possible. The substance hydrolyses slowly (\( t_{1/2} = 156 \) h). For 1,2-epoxybutane there are equivocal results from biodegradation tests available. While the substance was not readily biodegradable in a closed bottle test according to OECD 301 D (17% after 29 days), in a CO2-Headspace test according to ISO 14593 80-90% degradation was reached within 28 days. Both tests are appropriate for testing volatile substance. In addition to these two tests there is a DOC die-away test according to OECD 301 A available. Deviating from the guideline the test was performed in closed bottles. It was shown that the substance remained in the water phase during the test. After 28 days
90 % biodegradation measured as DOC was found. However, the 10d-window-criterion was not fulfilled.

As conclusion from the available test results it can be summarized that 1,2-epoxybutane is readily biodegradable, failing the 10d-window-criterion. According to the model SIMPLETEAT 74 % of 1,2-epoxybutane will be eliminated in sewage treatment plants, both by stripping and biodegradation.

No experimental data on bioaccumulation are available. The log Kow of 0.68 indicates a low potential for bioaccumulation.

### 2.2 Human Exposure

At the workplace at BASF AG the measured concentration were 1.89 mg/m$^3$ (95 % percentile) during 1979 to 2000 and can occur in the following activities: sampling, cleaning/maintenance, filling, dispersive use in laboratories, pilot plants and workshops.
3. HUMAN HEALTH

3.1 Hazard Assessment Experience with Human Exposure

3.1.1 Experience with human exposure

No data available.

3.2 Effects on Human Health

3.2.1 Acute Toxicity

\[ \text{LD}_{50} \text{ rat (oral): 900 mg/kg body mass}^{12} \]

\[ \text{LC}_{50} \text{ rat (inhalative): } > 6,300 \text{ mg/m}^3^{13} \]

In a range-finding study all rats died after the inhalation of 20,000 mg/m\(^3\) for 4h but no deaths occurred at 6,000 mg/m\(^3\).\(^{14}\) Thus the LC\(_{50}\) should be between 6,300 and 20,000 mg/m\(^3\).

\[ \text{LD}_{50} \text{ rabbit (dermal): 1,757 (1,255 - 2,546) mg/kg body mass.}^{15} \]

IRT (Inhalation Risk Test): The inhalation of a highly saturated vapour-air mixture (atmosphere saturated with 1,2-epoxybutane at 20°C) represents a severe acute risk: 2 of 12 rats died within 3 minutes and 6 of 6 rats died within 10 minutes.\(^{12}\)

3.2.2 Corrosiveness and Irritation

1,2-Epoxybutane is corrosive when evaporation was minimised due to occlusive application: The occlusive exposure of 0.5 ml for 1 hour resulted in full-thickness necrosis of the skin of 2/4 rabbits\(^ {17}\). However, 1,2-Epoxybutane was not irritating to the rabbit skin by semi-occlusive application: The application of 0.5 ml for 4 hours did not cause any edema or erythema 24 hours, 48 hours and 8 days post application.\(^ {16}\) In conclusion 1,2-epoxybutane has a potential for skin irritation. The intensity of the irritating effect depends on the application and the possibility of evaporating.

1,2-Epoxybutane was irritating to the eyes of rabbits: 0.05 ml were administered to the eyes of rabbits; 1 hour post application mild redding and edema were observed and 23 hours later additionally clouding was observed. However, all effects disappeared within eight days.

3.2.3 Sensitisation

1,2-Epoxybutane was not sensitising (0/10 animals) in a guinea pig maximisation test with open epicutaneous application\(^ {19}\).

3.2.4 Repeated Dose Toxicity

In a 14-day Inhalation study rats and mice were exposed to 0, 400, 800, 1600, 3200, or 6400 ppm (0, 1200, 2400; 4800, 9600, 19000 mg/m\(^3\)) 1,2-Epoxybutane (5 males and 5 females of each species). All rats at 9600 and 19000 mg/m\(^3\) and 2/5 female rats at 4800 mg/m\(^3\) died, all mice at 4800, 9600, 19000 mg/m\(^3\) and 1/5 male mice at 2400 mg/m\(^3\) died. Erratic movements and piloerection were compound-related effects in rats exposed at 4800 mg/m\(^3\). Clinical signs observed in mice at 2400 mg/m\(^3\) included dyspnea and listlessness on the first exposure day. Final mean body mass of surviving rats exposed at 2400 or 4800 mg/m\(^3\) were 12%-33% lower than those of the controls; final mean body weights of surviving mice at 2400 mg/m\(^3\) were 10%-12% lower than those of the
controls. Necropsy was performed on all animals, tissues for the following animals examined histologically for rats: 1 male at 9600 mg/m³, 2 males and 2 females at 4800 mg/m³, 1 male at 2400 mg/m³ and for mice: 2 males at 4800 mg/m³, 2 males and 1 female at 2400 mg/m³, 1 male at 1200 mg/m³. Compound-related lesions included pulmonary hemorrhage and rhinitis in rats at 4800 mg/m³ and nephrosis in mice at 2400 and 4800 mg/m³.

In 90-days inhalation studies 10 rats or mice per concentration and gender inhaled 0, 150, 300, 600, 1200 or 2400 mg/m³ 1,2-epoxybutane (6 hours per day and 5 days per week). In rats, no compound related deaths occurred. Rats in the high-dose group showed a decreased body weight gain. No other clinical signs of toxicity were observed. In the high dose group, there was inflammation of the nasal cavities (primarily the mucosa of the turbinates and the septum including olfactory and respiratory epithelium) of all males and females.

All mice of the high-dose (2400 mg/m³) group and 2 male mice in the 150 mg/m³ group died within 10 weeks. There were no dose-dependent changes in the body weight. Mice exposed to the high dose were listless and had inflammations with necrosis of renal tubuli and inflammations of nasal turbinates. At lower exposure levels of 300 mg/m³ to 1200 mg/m³ only the nasal inflammation was observed. This effect was dose-dependent and was not observed in the lowest dose group (150 mg/m³). 14, 18

Rat LOAEC = 2400 mg/m³ NOAEC = 1200 mg/m³
Mouse LOAEC = 300 mg/m³ NOAEC = 150 mg/m³

In additional 90-days inhalation studies rats and mice were exposed to lower concentrations of 1,2-butylene oxide (0, 75, 150 or 600 ppm; 0, 225, 450, 1800 mg/m³). No treatment-related mortalities occurred. Slight growth retardation was apparent for female rats and female mice in the 1800 mg/m³ group only. Exposure to 1800 mg/m³ resulted in histopathologic changes in the nasal mucosa in rats and mice after 13 weeks. Other than non-specific microscopic changes in the nasal mucosa, no definite target organs could be identified. Hematologic analyses of rats and mice sacrificed after 4 weeks revealed no changes of toxicologic significance. After 13 weeks, there were no statistically significant differences and no apparent effects on the hematologic parameters of male rats. The mean hemoglobin values of female rats in the 150 ppm group, and the mean red blood cell count of female rats in the 150 ppm group were statistically significantly higher than for controls; these values were within the range of normal for female rats of the same strain and age, and were considered to be sporadic occurrence with no toxicologic significance. Hematologic analyses for female mice in the 450 and 1800 mg/m³ groups after 13 weeks revealed some statistically significant differences which were thought to be of minimal toxicologic significance in view of the lack of a dose-response relationship and the absence of microscopic evidence of bone marrow toxicity. 27

NOAEC (rats and mice) 450 mg/m³
LOAEC (rats and mice) 1800 mg/m³

Conclusion:
1,2-Epoxybutane mainly caused nasal lesions (inflammation of nasal cavity) in the 90-day inhalation studies with rats and mice. Higher concentrations additionally affected kidneys of mice. The overall NOAEC was 1200 and 150 mg/m³ for rats and mice and the LOAECs were 1800 and 300 mg/m³ for rats and mice, respectively.

3.2.5 Genetic Toxicity

1,2-Epoxybutane is a directly acting mutagen in vitro. It induced gene mutations in bacteria (Ames tests with and without external metabolic activation, standard plate assay and pre-incubation assay14, 20). In mammalian cells (mouse lymphoma assay 3 and HPRT-assay with human lymphoblastoid cells 29) and chromosome aberrations in mammalian cells (equivocal with but
positive without external metabolic activation in CHO cells\textsuperscript{24}). The use of S9-mix decreased the mutagenic activity. Several tests with \textit{Drosophila melanogaster} were inconclusive\textsuperscript{22, 28}. In mammals, 1,2-epoxybutane caused no chromosomal aberrations in bone marrow. Sprague-Dawley rats (10 animals per dose, gender and time) were exposed to 1,2-butyleneoxide at doses of 750 or 3000 mg/m\textsuperscript{3} (7 hours single exposure or 5 consecutive days). Animals were killed and slides were prepared 6, 24 and 48 hours after exposure. The exposure groups did not show any increase in the frequency of aberrant cells except in the 6 h sample time males exposed to 3000 mg/m\textsuperscript{3} 1,2-epoxybutane. If cells only containing gaps were excluded from the analysis, then the statistical significance of the difference from the air control group was reduced. This result is probably insufficient evidence on which to base a conclusion for the clastogenic potential of this compound \textit{in vivo} since the effect was small and was not observed in female rats. 1,2-Epoxybutane caused no dominant-lethal mutations in germ cells of rats (7 hours inhalation of 750 or 3000 mg/m\textsuperscript{3}, five times)\textsuperscript{22}. This may indicate that the chemical does not reach these organs in sufficient concentrations (spontaneous reactions with cellular nucleophiles and enzymatic detoxification e.g. by glutathiontransferases have been described, \textit{cf.} 3.2.9, Toxicokinetics).

\textbf{Conclusion}

1,2-Epoxybutane is clearly mutagenic \textit{in vitro}. Yet, mammals are able to detoxify 1,2-epoxybutane efficiently. Thus no mutagenic effects were detected in bone marrow and germ cells of rats. At the most, mutations might occur in tissues where the concentration is high due to direct contact with 1,2-epoxybutane (e.g. epithelia of the respiratory tract).

3.2.6 Toxicity to reproduction

There are no specific studies on toxicity to reproduction. Derogation Statement: However, the subchronic and chronic studies with rats and mice did not reveal adverse effects on the reproductive organs. In the subchronic studies necropsy was performed on all animals; all controls and the two highest dose groups were examined histologically. Reproductive tissues examined: prostate or uterus/ovaries, mammary gland. In the chronic studies necropsy and histologic examination was performed on all animals. Reproductive tissues examined: clitoral or preputial gland, mammary gland, prostate/testes/epididymis or ovaries/uterus in the chronic study. There are additional subchronic inhalation studies with mice and rats in which all reproductive organs were examined.\textsuperscript{23} Representative sections of reproductive tissues in the control and high exposure groups were prepared by conventional histologic techniques: gonads, mammary gland, prostate, seminal vesicles, uterus. Weights of testes were recorded for each animal. Again, even at the highest concentration (1800 mg/m\textsuperscript{3}) no effects on the reproductive organs were observed.

Additionally, the lack of an effect from pre-gestational exposure in the developmental toxicity study (\textit{cf.} 3.2.7) and a negative dominant-lethal test (\textit{cf.} 3.2.5) may indicate that 1,2-epoxybutane does not reach male and female germ cells in effective concentrations.

3.2.7 Developmental Toxicity / Teratogenicity

Rabbits inhaled 750 or 3,000 mg/m\textsuperscript{3} of 1,2-epoxybutane on days 1 through 24 of gestation (7 hours/day, 5 days/week), and foetuses were examined on the 30\textsuperscript{th} day. Because of the low fertility in the original butylene oxide experiment with rabbits (Replicate I), the low level exposure was subsequently repeated (Replicate II). One of 23 rabbits (Replicate I) and 5/25 rabbits (Replicate II) died in the low, 14 of 24 rabbits died in the high dose group. There was no significant change in the gender ratios of the offspring. The 8 foetuses of the litters of the 2 surviving high dose litters were markedly smaller than were those of the control or low dose groups. In these two litters, there
was a trend of decreased numbers of live foetuses per litter and an increase in the frequency of resorptions (statistical analysis could not be performed). One of the 8 foetuses of the high dose group was stunted (in comparison: 4 foetuses/4 litters in the low dose group and 1 foetus in the control group) and had additional lesions. Incidences of an extra rib were higher in this and the low dose group than in the control group. Due to the maternal toxicity, the authors of the study concluded, that alterations of the nature or incidence of morphologic changes related to exposure were not noted in rabbits.  

An analogous study was performed with rats. They were treated on days 1 through 19 of gestation, and foetuses were examined on the 21st day. One animal in the high-dose group died, but there were no other signs of maternal toxicity. There was neither foetal toxicity nor teratogenicity. A satellite group was additionally treated 21 days prior to conception. In this group a slightly reduced percentage of sperm-positive rats were pregnant although no clear dose relationship was seen.  

Rat: NOAEC maternal = 3,000 mg/m³  NOAEC foetal = 3,000 mg/m³

### Conclusion

1,2-Epoxybutane does not show a foetotoxicity or teratogenicity potential in rats, whereas a study in rabbits is inconclusive because of a high mortality rate in high-dose dams.

#### 3.2.8 Carcinogenicity

50 Rats per dose and gender inhaled 600 or 1,200 mg/m³ of 1,2-epoxybutane for two years (6 hours/day, 5 days/week). Necropsy and histologic examination was performed on all animals; the following tissues were examined: adrenal glands, brain, clitoral or preputial gland, colon, esophagus, gross lesions and tissue masses, heart, kidneys, lungs and mainstem bronchi, mammary gland, mandibular lymph nodes, nasal cavity and nasal turbinates, pancreas, parathyroids, pituitary gland, prostate/testes/epididymis or ovaries/uterus, rectum, regional lymph nodes, salivary glands, skin, small intestine, spleen, sternebrae including marrow, stomach, thymus, thyroid gland, trachea, tracheobronchial lymph nodes, and urinary bladder.

30, 18, and 23 of the males and 32, 21 and 22 of the females survived until the termination of the study in the control, low-dose and high-dose groups, respectively. Papillary adenomas of the nasal cavity were found in 7 males and 2 females of the high-dose group. No such tumours occurred in controls or in the low-dose group. Alveolar and bronchiolar carcinomas were found in one female of the control group, one male of the low-dose group and 4 males of the high dose group. The incidence of alveolar and bronchiolar adenomas and carcinomas in the males of the high-dose group was significantly increased compared to controls. There were treatment-related, non-neoplastic changes in the nose (inflammation, epithelial hyperplasia and squamous metaplasia of the nasal epithelium and atrophy of the olfactory epithelium) of males and females in the low and high-dose group. The authors conclude: "Under the conditions of this 2-year inhalation study, there was clear evidence of carcinogenic activity of 1,2-epoxybutane for male F344/N rats and equivocal evidence of carcinogenic activity for female F344/N rats."  

An analogous study was performed in which mice were exposed to 150 or 300 mg/m³ of 1,2-epoxybutane (Necropsy and histological examinations were the same as for rats; the gallbladder was additionally examined). 41, 45 and 33 males and 29, 25 and 9 females survived until the termination of the study in the control, low-dose and high-dose groups, respectively. After week 69, the survival of female animals of the high dose group was significantly lower than the survival of the female animals of the control group. The decreased survival was associated with suppurative inflammation of ovary and uterus; Klebsiella oxytoca was isolated from the ovarian/uterine lesions. A single squamous-cell papilloma was found in the nasal cavity of a male of the high-dose group. This finding was not statistically significant and could not clearly be related to the exposure. There were treatment-related, non-neoplastic nasal changes at both dose levels (inflammation, emphysema, erosion, regeneration, hyperplasia and squamous metaplasia of the nasal epithelium and atrophy of the olfactory epithelium) and inflammation and hyperplasia of the nasolacrimal duct. The authors
conclude: "Under the conditions of this 2-year inhalation study, there was no evidence of carcinogenic activity of 1,2-epoxybutane for male or female B6C3F1 mice exposed at 150 or 300 mg/m³." \(^{14}\)

In summary, the inhalation of 1,200 mg/m³ 1,2-epoxybutane caused a significant increase of benign neoplasms of the nasal cavity and of benign and malignant neoplasms of the lungs of male rats, but 600 mg/m³ caused no tumours. In female rats two tumours of the nasal cavity were seen at this dose level. No treatment related tumours were found in male and female mice by inhalation of 150 and 300 mg/m³. However, the mortality of females was increased in this study due to an infection and this raises difficulties in the interpretation of the result.

In an 18-months gavage study with mice (1800 and 2400 mg/kg body mass for males and females, respectively) merely squamous cell carcinoma of the forestomachs of male mice were observed\(^{30}\).

In vitro-cell transformation assays with various rodent embryo cells gave positive as well as negative results\(^{31}\).

There is clear evidence for 1,2-epoxybutane being a locally acting carcinogen in male rats, equivocal evidence for a carcinogenic activity in female rats and no evidence in male or female mice under the conditions of these tests.

**Conclusion**

1,2-Epoxybutane showed carcinogenic activity in male rats only at 1200 mg/m³. Regarding the overall database on genotoxicity and structural relationship to epoxyethane and -propane, 1,2-epoxybutane seems to be a genotoxic compound, showing a carcinogenic activity at the site of application only at relatively high concentrations. There are no mechanistic studies available. However, irritating properties of the compound may cause cell proliferation and contribute, thereby, to tumour generation.

**3.2.9 Toxicokinetics**

Rabbits and rats were given 137 and 180 mg/kg b.m. respectively by stomach intubation. The major sulphur-containing metabolite in the urine was (2-hydroxybutyl)mercapturic acid. Butylmercapturic acid could not be detected. Urine was collected and assayed every 24 hours until no metabolites were detected. The excretion of (2-hydroxybutyl)mercapturic acid in the urine was 4% (rabbits) and 11% (rats) of the administered 1,2-epoxybutane, respectively.\(^{25}\)

1,2-Epoxybutane is extensively metabolised and rapidly eliminated in F344 male rats following either inhalation or gavage. It appears that physical and biological processes involved in absorption, metabolism and elimination of 1,2-epoxybutane are essentially linear throughout the exposure range (300 to 6000 mg/m³). Conjugation with glutathione is an important detoxification mechanism and is less likely overwhelmed by exposure with 1,2-epoxybutane than exposure to epoxyethane or epoxypropane. The results suggest, that 1,2-epoxybutane would not seriously deplete glutathione in rats.\(^{26}\)
4. Hazards to the Environment

The following acute toxicity tests with aquatic organisms are available:

- **Leuciscus idus**: \( LC_{50} \) (96 h) = 100 - 215 mg/l
- **Daphnia magna**: \( EC_{50} \) (48h) = 69.8 mg/l
- **Scenedesmus subspicatus**: \( EC_{50} \) (72 h) > 500 mg/l; \( EC_{20} \) (72 h) = 130 mg/l
- **Pseudomonas putida**: \( EC_{50} \) (17 h) = 4,840 mg/l

All values are related to nominal concentrations. As the studies were performed in open systems, the validity of the ecotoxicity tests is questionable. Due to the volatility of the substance the effect values based on measured concentrations may be significantly lower. For that reason a comparison of the effect values found in the above mentioned ecotoxicity studies with effect values predicted by QSAR estimations is performed. According to the ECOSAR calculation for epoxides a 48h-\( LC_{50} \) of 32 mg/l for daphnids and of 20 mg/l for fish can be calculated. These calculated values show that the ecotoxicity tests performed in open systems indeed underestimate the toxicity of 1,2-epoxybutane, however, not by orders of magnitude. Based on the measured and predicted effect data, 1,2-epoxybutane can be classified as moderately toxic.

To consider the lower effect values calculated by QSAR, it is proposed to base the PNECaqua on the lowest predicted effect value (20 mg/l for fish). As only acute tests are available an assessment factor of 1000 is proposed according to the TGD. With this a PNECaqua of 20 \( \mu \)g/l can be derived.

No data are available on terrestrial organisms.
5. CONCLUSIONS AND RECOMMENDATIONS

5.1 Conclusions

In the European Union only one producer of 1,2-epoxybutane is known. The production volume of this chemical in BASF Aktiengesellschaft Ludwigshafen was 5,000-10,000 t in 1999. The total production volume is used at the production site as an intermediate (non-disperse use) for synthesis in closed systems of fuel additives, non-ionic surfactants, defoamers and various other products. Monitoring data showed no emission into the air during production and processing. There is no information on emission of 1,2-epoxybutane into the hydrosphere. The Swedish product register (1999) includes products that contain 1,2-epoxybutane, however, no further information is available. In the USA the substance is used as stabilizer in hydrocarbon solvents. Emissions into the environment during formulation and use of hydrocarbon solvents that contain 1,2-epoxybutane as stabilizer as well as during use of other products that contain the substance cannot be excluded.

The distribution modelling using Mackay, Level I indicates air to be the main target compartment for 1,2-epoxybutane. The substance has no considerable potential for bio- and geoaccumulation (log P_{ow} = 0.68, measured). It is classified as readily biodegradable, failing the 10d-window criterion. In sewage treatment plants the substance will be eliminated by stripping and biodegradation. Hydrolysis and photodegradation are slowly under environmental conditions.

The following aquatic effects concentrations are available:

- *Leuciscus idus*: LC50 (96 h) = 100 – 215 mg/l;
- *Daphnia magna*: EC50 (48 h) = 69.8 mg/l;
- *Scenedesmus subspicatus*: EC50 (72 h) > 500 mg/l;
- *Pseudomonas putida*: EC50 (17 h) = 4,840 mg/l.

All values are related to nominal concentrations. Due to the volatility of the substance the real effect values may be lower. QSAR estimations give effect values of 20 mg/l for fish and 32 mg/l for daphnia and show that the effect values are indeed lower than those found in the tests but not by orders of magnitude. Based on the measured and predicted effect data the substance can be classified as moderately toxic. A PNEC of 20 µg/l can be derived based on the predicted effect value for fish using an assessment factor of 1000.

No data are available on terrestrial organisms.

1,2-Epoxybutane caused acute toxic effects in mammals: LD50 rat (oral) 900 mg/kg body mass, LC50 rat (inhalative, 4 h) > 6,300 ≤ 20,000 mg/m3, LD50 rabbit (dermal) 1,757 (1,255 - 2,546) mg/kg body mass.

It was irritating to the eyes. Irritating effects to the skin were severe (corrosion) if evaporation was minimised due to occlusive application, but there was no effect by semi-occlusive application. 1,2-Epoxybutane was not sensitising in a guinea pig maximisation test. In 90-day inhalation studies with rats and mice 1,2-epoxybutane mainly caused nasal lesions (NOAEC 600 and 150 mg/m3, respectively). Systemic effects occurred at higher concentrations (rat 2400 mg/m3: lower final mean body weight; mice 2400 mg/m3: renal tubular necrosis).

1,2-Epoxybutane was genotoxic in vitro. However, it caused neither chromosomal aberrations in bone marrow nor dominant-lethal mutations in germ cells of rats. This may indicate that the chemical does not reach these organs in sufficient concentrations (spontaneous reactions with cellular nucleophiles and enzymatic detoxification, e.g. by glutathiontransferases have been described).

There is clear evidence for 1,2-epoxybutane being a locally acting carcinogen in male rats (inhalation of 600 mg/m3 caused no tumours and 1,200 mg/m3 caused neoplasms of the nasal cavity and the lung of male rats) and there is equivocal evidence for a carcinogenic activity in female rats. There was no evidence for carcinogenic activity in male or female mice. However, the mortality of
females was increased in this study due to an infection and this raises difficulties in the interpretation of the result. Regarding the overall database on genotoxicity and structural relationship to epoxyethane and -propane, epoxybutane seems to be a genotoxic compound, showing a carcinogenic activity at the site of application only at high concentrations. However, irritating properties of the compound may cause cell proliferation and contribute thereby to tumorinduction.

There are no specific studies on toxicity to reproduction. However, the subchronic and chronic studies with rat and mice did not reveal adverse effects on the reproductive organs. Additionally, the lack of an effect from pre-gestational exposure in the developmental toxicity study and a negative dominant-lethal test may indicate that 1,2-epoxybutane does not reach male and female germ cells in effective concentrations. No developmental toxicity or teratogenicity was detected in rats and rabbits after inhalation of up to 3,000 mg/m³ throughout gestation. (rat: no maternal or foetal toxicity up to 3,000 mg/m³, rabbit: NOAEC maternal = 750 mg/m³, no foetal toxicity up to 3,000 mg/m³).

5.2 Recommendations

If the substance is used in closed systems no further work is recommended. For other uses there is a need for exposure assessment.
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SIDS Dossier
including
Robust Study Summaries

Existing Chemical
ID: 106-88-7
CAS No.: 106-88-7
EINECS Name: 1,2-epoxybutane
EINECS No.: 203-438-2
TSCA Name: Oxirane, ethyl-
Molecular Formula: C4H8O

Producer Related Part
Company: BUA - TU München
Creation date: 07-MAR-2001

Substance Related Part
Company: BUA - TU München
Creation date: 07-MAR-2001

Printing date: 23-MAR-2001
Revision date:
Date of last Update: 23-MAR-2001

Number of Pages: 47

Chapter (profile):
Chapter: 1, 2, 3, 4, 5, 7

Reliability (profile):
Reliability: without reliability, 1, 2, 3, 4

Flags (profile):
1. General Information

1.0.1 OECD and Company Information

**Type:** lead organisation  
**Name:** BASF AG  
**Partner:** Product Safety Regulations, Toxicology, and Ecology  
**Date:** 30-NOV-1999  
**Street:** Carl-Bosch-Str  
**Town:** 67056 Ludwigshafen  
**Country:** Germany  
**Phone:** +49 0621 60 44712  
**Telefax:** +49 0621 60 44711  
**Source:** BASF AG Ludwigshafen  
**Date:** 01-DEC-1999

**Type:** cooperating company  
**Name:** The Dow Chemical Company  
**Partner:** Global Product and Operations Leader Contract Manufacturing Services, Liquid Separations & Polyglycols  
**Date:** 30-NOV-1999  
**Street:** c/o Susan Hearn, MPH  
**Town:** Midland, Michigan 48674  
**Country:** United States  
**Phone:** (517) 636-9192  
**Source:** BASF AG Ludwigshafen  
**Date:** 30-NOV-1999

1.0.2 Location of Production Site

1.0.3 Identity of Recipients

1.1 General Substance Information

**Substance type:** organic  
**Physical status:** liquid  
**Purity:** = 99.9 % w/w  
**Source:** BASF AG Ludwigshafen  
**Date:** 07-DEC-1999

1.1.0 Details on Template

1.1.1 Spectra

1.2 Synonyms

- \(\alpha\)-Butylene oxide  
**Source:** BASF AG Ludwigshafen  
**Date:** 02-DEC-1992

- 1,2-Butene oxide  
**Source:** BASF AG Ludwigshafen  
**Date:** 02-DEC-1992
1. General Information

1,2-Butylene epoxide
Source: BASF AG Ludwigshafen 02-DEC-1992

1,2-Butylene oxide
Source: BASF AG Ludwigshafen 02-DEC-1992

1,2-Epoxybutane
Source: BASF AG Ludwigshafen 02-DEC-1992

1-Butene oxide
Source: BASF AG Ludwigshafen 02-DEC-1992

1-Butylene oxide
Source: BASF AG Ludwigshafen 02-DEC-1992

2-Ethyloxirane
Source: BASF AG Ludwigshafen 02-DEC-1992

Butane, 1,2-epoxy- (8CI)
Source: BASF AG Ludwigshafen 02-DEC-1992

Ethylethylene oxide
Source: BASF AG Ludwigshafen 02-DEC-1992

Ethyloxirane
Source: BASF AG Ludwigshafen 02-DEC-1992

n-Butene 1,2-oxide
Source: BASF AG Ludwigshafen 02-DEC-1992

n-Butylenoxid-1,2
Source: BASF AG Ludwigshafen 02-DEC-1992

Oxirane, ethyl- (9CI)
Source: BASF AG Ludwigshafen 02-DEC-1992

1.3 Impurities

1.4 Additives
1.5 Quantity

**Quantity produced:** 5000 - 10000 tonnes in 1999

**Remark:** not imported in 1999 into European Union by BASF

**Source:** BASF AG Ludwigshafen

07-DEC-1999

1.6.1 Labelling

**Labelling:** provisionally by manufacturer/importer

**Symbols:** F Xn

**R-Phrases:**
- (11) Highly flammable
- (20/21/22) Harmful by inhalation, in contact with skin and if swallowed
- (36/37/38) Irritating to eyes, respiratory system and skin
- (40) Possible risks of irreversible effects

**S-Phrases:**
- (2) Keep out of reach of children
- (3/9) Keep in a cool, well-ventilated place
- (16) Keep away from sources of ignition - No smoking
- (29) Do not empty into drains
- (33) Take precautionary measures against static discharges
- (36/37) Wear suitable protective clothing and gloves

**Source:** BASF AG Ludwigshafen

08-SEP-2000

1.6.2 Classification

**Classification:** provisionally by manufacturer/importer

**Class of danger:**
- carcinogenic, category 3
- harmful
- highly flammable
- irritating

**R-Phrases:**
- (40) Possible risks of irreversible effects
- (20/21/22) Harmful by inhalation, in contact with skin and if swallowed
- (40) Possible risks of irreversible effects
- (11) Highly flammable
- (36/37/38) Irritating to eyes, respiratory system and skin

**Source:** BASF AG Ludwigshafen

08-SEP-2000
1. General Information

1.7 Use Pattern

Type: industrial
Category: Chemical industry: used in synthesis
Source: BASF AG Ludwigshafen
07-SEP-1993

Type: use
Category: Intermediates
Source: BASF AG Ludwigshafen
07-SEP-1993

1.7.1 Technology Production/Use

1.8 Occupational Exposure Limit Values

1.9 Source of Exposure

1.10.1 Recommendations/Precautionary Measures

1.10.2 Emergency Measures

1.11 Packaging

1.12 Possib. of Rendering Subst. Harmless

1.13 Statements Concerning Waste

1.14.1 Water Pollution

Classified by: other
Labelled by: other
Class of danger: 1 (weakly water polluting)
Remark: classified as Appendix 3 in Directive "Allgemeine Verwaltungsvorschrift zum Wasserhaushaltsgesetz über die Einstufung wassergefährdender Stoffe in Wassergefährdungsklassen".
Basis: R-Phrases (R 20/21/22 and R 40)
Source: BASF AG Ludwigshafen
26-SEP-2000 (49)

1.14.2 Major Accident Hazards

1.14.3 Air Pollution

1.15 Additional Remarks
1. General Information

1.16 Last Literature Search

1.17 Reviews

1.18 Listings e.g. Chemical Inventories
2.1 Melting Point

Value: = -129.5 degree C
Method: other: measured
Method: modified ROSSINI-WIECHERS-method, according
ASTM-specification D 1015-55
Source: BASF AG Ludwigshafen
Reliability: (2) valid with restrictions
Discrepancy between documented test parameters and
standard methods, but scientifically acceptable
15-NOV-1999

2.2 Boiling Point

Value: = 63.4 degree C at 1013 hPa
Method: other
Method: static (-10 to 59 °C), dynamic (63.2 to 153.6 °C, under
AR-atmosphere)
Remark: calculated data based on measured data
Source: BASF AG Ludwigshafen
Reliability: (2) valid with restrictions
16-NOV-1999

2.3 Density

Type: density
Value: = .83 g/cm³ at 20 degree C
Method: other: measured
Method: glass- pycnometer
Source: BASF AG Ludwigshafen
Test condition: measured range: -10.0 to 113 °C, average deviation:
0.05 %
Reliability: (2) valid with restrictions
15-NOV-1999

2.3.1 Granulometry

2.4 Vapour Pressure

Value: = 227 hPa at 24 degree C
Method: other (measured)
Method: static (-10 to 59 °C), dynamic (63.2 to 153.6 °C, under
Ar-atmosphere)
2. Physico-chemical Data

Result:

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<th>°C</th>
<th>hPa</th>
</tr>
</thead>
<tbody>
<tr>
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<td>40</td>
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<tr>
<td>0.0</td>
<td>70</td>
</tr>
<tr>
<td>24.0</td>
<td>227</td>
</tr>
<tr>
<td>31.7</td>
<td>315</td>
</tr>
<tr>
<td>40.3</td>
<td>444</td>
</tr>
<tr>
<td>50.6</td>
<td>654</td>
</tr>
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<td>63.2</td>
<td>1003</td>
</tr>
<tr>
<td>74.0</td>
<td>1412</td>
</tr>
<tr>
<td>86.1</td>
<td>2015</td>
</tr>
<tr>
<td>99.7</td>
<td>2949</td>
</tr>
<tr>
<td>121.0</td>
<td>5033</td>
</tr>
<tr>
<td>134.4</td>
<td>6918</td>
</tr>
<tr>
<td>153.6</td>
<td>1003</td>
</tr>
</tbody>
</table>

Source: BASF AG Ludwigshafen
Test condition: measured range: -10.0 to 113 °C, average deviation: 0.05 %
Reliability: (2) valid with restrictions
26-SEP-2000

Value:

Result:

<table>
<thead>
<tr>
<th>°C</th>
<th>hPa</th>
</tr>
</thead>
<tbody>
<tr>
<td>3.3</td>
<td>82.4</td>
</tr>
<tr>
<td>12.8</td>
<td>133.7</td>
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<td>23.2</td>
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<td>34.6</td>
<td>349.6</td>
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<tr>
<td>46.6</td>
<td>562.6</td>
</tr>
<tr>
<td>63.4</td>
<td>1013</td>
</tr>
</tbody>
</table>

Source: BASF AG Ludwigshafen
Reliability: (2) valid with restrictions
26-SEP-2000

2.5 Partition Coefficient

log Pow: = .68 at 25 degree C
Method: other (measured)
Year: 16-NOV-1999

log Pow: = .416
Method: other (calculated)
Year: 16-NOV-1999

Source: BASF AG Ludwigshafen
Reliability: (2) valid with restrictions
2.6.1 Water Solubility

Value: = 6.32 vol% at 60.3 degree C
Method: other: measured
Method: Solubility in boiling condition at 1013 hPa
Source: BASF AG Ludwigshafen
Reliability: (2) valid with restrictions
04-SEP-2000

Value: = 59 g/l at 20 degree C
pH: ca. 7 at 50 g/l and 20 degree C
Source: BASF AG Ludwigshafen
Reliability: (4) not assignable
Manufacturer / producer data without proof
09-AUG-2000

2.6.2 Surface Tension

Test type: Ring method
Value: = 23.5 mN/m at 25 degree C
Method: other: measured
Source: BASF AG Ludwigshafen
Test substance: purity: 99.9%
Reliability: (2) valid with restrictions
16-NOV-1999

2.7 Flash Point

Value: = -25.5 degree C
Type: Method: other: DIN 51755
Year: Source: BASF AG Ludwigshafen
Reliability: (2) valid with restrictions
Manufacturer / producer data without proof
04-SEP-2000

Value: = -15 degree C
Type: Method: Year: Source: BASF AG Ludwigshafen
Reliability: (4) not assignable
09-MAR-2000

2.8 Auto Flammability

Value: = 370 degree C
Method: other: DIN 51794
Remark: Autoignition temperature
Source: BASF AG Ludwigshafen
Reliability: (2) valid with restrictions
Manufacturer / producer data without proof
04-SEP-2000
2.9 Flammability

Result: highly flammable
Source: BASF AG Ludwigshafen
Reliability: (4) not assignable
Manufacturer / producer data without proof
07-DEC-1999

2.10 Explosive Properties

2.11 Oxidizing Properties

2.12 Additional Remarks

Remark: Explosion limits: 3.9 - 20.6 Vol.%
Explosion hazard: Vapours may form explosive mixture with air.
Conditions to avoid:
Protect against moisture
Substances to avoid:
acids, alkalies, organometalsalts, powerful oxidizing agent
Hazardous decomposition products:
None provided product is correctly processed.

Source: BASF AG Ludwigshafen
Reliability: (2) valid with restrictions
Manufacturer / producer data without proof
04-SEP-2000
3.1.1 Photodegradation

Type: air
INDIRECT PHOTOLYSIS
Sensitizer: OH
Conc. of sens.: 500 000 molecule/cm³
Rate constant: = 0.0000000000021 cm³/(molecule * sec)
Degradation: = 50 % after 7.6 day
Method: Year: GLP:
Test substance: Source: BASF AG Ludwigshafen
Test condition: 25 deg C
Reliability: (2) valid with restrictions
11-NOV-1999

Type: air
INDIRECT PHOTOLYSIS
Sensitizer: OH
Conc. of sens.: 500 000 molecule/cm³
Rate constant: = 0.0000000000023988 cm³/(molecule * sec)
Method: Year: GLP:
Test substance: Source: BASF AG Ludwigshafen
Remark: mean tropospheric lifetime of approx. 7 d was calculated based on the equation t1/2 = ln 2/ (KOH*OH)
Reliability: (2) valid with restrictions
17-NOV-1999

3.1.2 Stability in Water

Type: abiotic
t1/2 pH7: = 156 hour(s)
Method: other: hydrolysis
Year: GLP: no data
Test substance: Source: BASF AG Ludwigshafen
Remark: The half-life of 1,2-epoxybutane was determined after incubation at 37°C for various periods of time in 1 mmol/l Tris- HCl buffer (pH 7.4).
Reliability: (2) valid with restrictions
26-SEP-2000

Type: abiotic
t1/2 pH7: = 310 hour(s) at 25 degree C
Method: other: Estimation
Year: GLP:
Test substance: Source: BASF AG Ludwigshafen
Remark: Value based upon measured hydrolysis rates for propylene oxide.
Reliability: (4) not assignable
Handbook
26-SEP-2000
3. Environmental Fate and Pathways

3.1.3 Stability in Soil

Type: Radiolabel:
Concentration: Cation exch.
capac.
Microbial biomass:
Method: other
Year: GLP:
Test substance: Estimation: PCKOCWIN, V 1.63
Method: log Koc = 0.6523, Koc = 4.491
Result: BASF AG Ludwigshafen
Reliability: (1) valid without restriction
17-NOV-1999

Type: Radiolabel:
Concentration: Cation exch.
capac.
Microbial biomass:
Method: other
Year: GLP:
Test substance: based upon estimated aqueous hydrolysis half-lifes
Method: The half-lifes in soil: 168 h - 310 h (7.0 d - 12.0 d).
Result: BASF AG Ludwigshafen
Reliability: (4) not assignable
Handbook
26-SEP-2000

3.2 Monitoring Data (Environment)

3.3.1 Transport between Environmental Compartments

3.3.2 Distribution

Media: air - biota - sediment(s) - soil - water
Method: Calculation according Mackay, Level I
Year: Remark: H = 22.977 Pa m³ mol e⁻¹ (20°C)
Result: air: 88.98 %, water: 11.01 %
Source: BASF AG Ludwigshafen
Reliability: (1) valid without restriction
26-SEP-2000

Media: other (calculation)
Year: Remark: \( \text{H} = 7.6 \times 10^{-4} \) (25 deg C) = 76 Pa m³ mol e⁻¹
Source: BASF AG Ludwigshafen
Reliability: (4) not assignable
04-SEP-2000
3.4 Mode of Degradation in Actual Use

3.5 Biodegradation

Type: aerobic
Inoculum: activated sludge, domestic
Concentration: 28 mg/l related to DOC (Dissolved Organic Carbon)
Degradation: = 90 % after 28 day
Tests substance:
3 day = 0 %
7 day = 17 %
10 day = 20 %
14 day = 34 %
21 day = 86 %
Method: other
Test substance: as prescribed by 1.1 - 1.4
Method: The method is a modification of the DOC-Die Away Test (OECD 301 A). Instead of an open Erlenmeyer flask, the assay was performed in a 1 litre Pyrex bottle locked with a screw cap.
The vessel was equipped with baffles. The bottles contained 500 ml inoculated mineral salt solution to which neat butylene oxide was added directly. The bottles were shaken during the test.
Remark: 1,2-epoxybutane was tested in concentrations well below its water solubility (59 g/l at 20°C). Although the substance is volatile it remained in the water phase under this test conditions (proven by abiotic control).
Result: The test substance reached the pass level (70% DOC-elimination), but failed the 10 day-window. Therefore the test substance is concluded to be biodegradable
Source: BASF AG Ludwigshafen
Reliability: (1) valid without restriction
17-MAR-2000

Type: aerobic
Inoculum: other bacteria
Concentration: 400 mg/l related to DOC (Dissolved Organic Carbon)
Degradation: = 100 % after 6 day
Tests substance: 1 day ca. 90 %
2 day ca. 95 %
3 day ca. 100 %
Method: OECD Guide-line 302 B "Inherent biodegradability: Modified Zahn-Wellens Test"
Year: GLP: yes
Test substance: as prescribed by 1.1 - 1.4
Remark: Elimination by stripping
Result: BOD5 = 5 mg/g
Source: BASF AG Ludwigshafen
Test condition: Inoculum: effluent from laboratory wastewater plants treating municipal sewage
Reliability: (2) valid with restrictions
17-MAR-2000
3. Environmental Fate and Pathways

Type: aerobic
Inoculum: other bacteria
Concentration: 2 mg/l
Degradation: = 17 % after 29 day
Method: OECD Guide-line 301 D "Ready Biodegradability: Closed Bottle Test"

Year: 2000
GLP: no
Test substance: as prescribed by 1.1 - 1.4
Remark: poorly biodegradable
Result: COD 1962 mg/l, BOD5 = 0.1 mg/l
Source: BASF AG Ludwigshafen
Test condition: Inokulum: effluent of domestic waste water from laboratory
plant, test duration 29 days
Reliability: (2) valid with restrictions
17-MAR-2000

Type: aerobic
Inoculum: activated sludge, domestic
Concentration: 4 mg/l related to Test substance
Degradation: 80 - 90 % after 28 day
Result: readily biodegradable
Method: other: CO2-Headspace Test

Year: 2000
GLP: no
Test substance: as prescribed by 1.1 - 1.4
Method: The test is an aquatic batch test method to determine the aerobic biodegradability of a test substance in closed bottles. The biodegradation of a substance is determined by the analysis of the carbon dioxide (CO2) evolution.
Result: Biodegradation: DTIC after 28 days = 80 - 90 %
Elimination: DDOC after 20 days = 90 - 100 %
Source: BASF AG Ludwigshafen
Test condition: test concentration: 34 mg/l
Reliability: (1) valid without restriction
07-SEP-2000

3.6 BOD5, COD or BOD5/COD Ratio

3.7 Bioaccumulation

3.8 Additional Remarks
4.1 Acute/Prolonged Toxicity to Fish

Type: static
Species: Leuciscus idus (Fish, fresh water)
Exposure period: 96 hour(s)
Unit: mg/l
Analytical monitoring: no
NOEC: 46
LC0: 46
LC50: 100 - 215
LC100: 215
Method: other
Year: GLP: no
Test substance: other TS: n-Butylen-1,2-oxid, purity >99%
Method: The method used closely followed the guideline of DIN 38 412 "Testverfahren mit Wasserorganismen (Gruppe L). Allgemeine Hinweise zur Planung, Durchführung und Auswertung Biologischer Testverfahren (L1)" and "Bestimmung der Wirkung von Wasserinhaltsstoffen auf Fische - Fischtest (L15)", June 1982
Remark: nominal concentrations
Source: BASF AG Ludwigshafen
Test condition: dose groups 0, 46, 100, 215, 464, 1000 mg/l, 10 Fishes per group
Reliability: (2) valid with restrictions
19-MAR-2001 (14)

4.2 Acute Toxicity to Aquatic Invertebrates

Type: static
Species: Daphnia magna (Crustacea)
Exposure period: 24 hour(s)
Unit: mg/l
Analytical monitoring:
EC0: 62.5
EC50: 159.7
EC100: 250
Year: GLP: no
Test substance: as prescribed by 1.1 - 1.4
Method: according to OECD 202
Result: EC0, EC50 and EC100 - values are given in nominal concentration, endpoint = swimming ability,
VB 95% (24h) = 142.87 - 178.42
Source: BASF AG Ludwigshafen
Test condition: pH-value: 7.7 - 8.3, water total hardness: 2.80 mmol/l, alkalinility up to pH 4.3: 0.80 ± 0.10 mmol/l, conductivity: 550 - 650 µS/cm, Ca:Mg = 4:1, Na:K = 10:1 illumination: artificial light, type warm white, day:night =16:8 hours, light intensity 5 µE at a wavelength of 400 - 750 nm,
test temperature: 292.0 - 294.9 K,  
test volume: 10 ml, volume/animals: 2 ml, number of  
animals/vessel: 5, total number of  
animals/concentration: 20,  
age of animals: 2-24 hours,  
visually after 0, 3, 6, 24 an 48 h,  
concentration range: 7.81 - 500 mg/l

Reliability:  
19-MAR-2001  
(2) valid with restrictions

Type:  
Species: Daphnia magna (Crustacea)  
Exposure period: 48 hour(s)  
Unit: mg/l  
EC0: = 31.3  
EC50: = 69.8  
EC100: = 125  
Test substance: as prescribed by 1.1 - 1.4  
Method: according to OECD 202  
Result: EC0, EC50 and EC100 - values are given in nominal  
concentration,  
endpoint = swimming ability,  
VB 95% (48h) = 48.95 - 90.67  
Source: BASF AG Ludwigshafen  
Test condition: pH-value: 7.7 - 8.3, water total hardness: 2.80 mmol/l,  
alkanility up to pH 4.3: 0.80 +/- 0.10 mmol/l,  
conductivity: 550 - 650 µS/cm,  
Ca:Mg = 4:1,  
Na:K = 10:1,  
illumination: artificial light, type warm  
white, day:night =16:8 hours, light intensity 5 µE at a  
wave lentgh of 400 - 750 nm,  
test temperature: 292.0 - 294.9 K,  
test volume: 10 ml, volume/animals: 2 ml, number of  
animals/vessel: 5, total number of  
animals/concentration: 20,  
age of animals: 2-24 hours,  
visually after 0, 3, 6, 24 an 48 h,  
concentration range: 7.81 - 500 mg/l

Reliability:  
19-MAR-2001  
(2) valid with restrictions

4.3 Toxicity to Aquatic Plants e.g. Algae

Species: Scenedesmus subspicatus (Algae)  
Endpoint:  
Exposure period: 72 hour(s)  
Unit: mg/l  
EC50: > 500  
EC20 : = 130  
Method: other: DIN 38412, part 9, Determination of inhibitory  
Effect on the cell multiplication  
Test condition: pH-value: 7.7 - 8.3, water total hardness: 2.80 mmol/l,  
alkanility up to pH 4.3: 0.80 +/- 0.10 mmol/l,  
conductivity: 550 - 650 µS/cm,  
Ca:Mg = 4:1,  
Na:K = 10:1,  
illumination: artificial light, type warm  
white, day:night =16:8 hours, light intensity 5 µE at a  
wave lentgh of 400 - 750 nm,  
test temperature: 292.0 - 294.9 K,  
test volume: 10 ml, volume/animals: 2 ml, number of  
animals/vessel: 5, total number of  
animals/concentration: 20,  
age of animals: 2-24 hours,  
visually after 0, 3, 6, 24 an 48 h,  
concentration range: 7.81 - 500 mg/l
4. Ecotoxicity

**Result:**
EC90 (72h) >500 mg/l.
The EC-values are given in nominal concentration.
The EC values are calculated (linear regression analysis) from the concentration-response relationship.

**Source:**
BASF AG Ludwigshafen

**Test condition:**
The test strain of Scenedesmus subspicatus CHODAT SAG 86.81 is obtained of regular intervals from SAG.
Duration of the test: 72 hours,
test temperature: 23 +/− 2°C,
test vessel: reagent tubes, test volume: 100 ml,
Illumination: artificial light - permanent illumination,
light intensity: 50 - 200 µE at a wave length of 400 - 70 nm,
O2-content = 5.0 mg/l, test concentration: 3.91 – 500 mg/l, 8 test concentrations and control, 4 inoculated parallels, 2 uninoculated parallels, pH 8.0 – 9.6,
inoculum density: 10000 cells/ml,
measurements: 0, 24, 48 and 72 h,
parameter: prompt chlorophyll an floorescence at 685 nm as criterion for biomass (excitation with short light impulse at 435 nm)

**Reliability:**
(2) valid with restrictions
16-MAR-2001

**4.4 Toxicity to Microorganisms e.g. Bacteria**

**Type:**
aquatic

**Species:**
Pseudomonas putida  (Bacteria)

**Exposure period:**
17 hour(s)

**Unit:**
mg/l

**EC10:**
= 2920

**EC50:**
= 4840

**EC90 :**
= 7350

**Method:**
other: DIN 38412, part 8, Determination of the inhibitory effect on the cell multiplication

**Year:**
GLP: no

**Test substance:**
as prescribed by 1.1 - 1.4

**Result:**
The test substance was tested in the concentration range between 1250 and 10000 mg/l (nominal).
The results show the nominal concentrations of the test sample that causes after 17 hours an inhibition.

**Source:**
BASF AG Ludwigshafen

**Test condition:**
The test strain of Pseudomonas putida DSM 50026 used is obtained in regular intervals from DSM.
Duration of the test: 17 hours,
temperature during the test: 20 °C,
stem culture: 10 ml, pre cultur: 100 ml, test culture: 10 ml, parameter: optical density 436 nm, 4 inoculated parallels, 1 inoculated parallel, 5 test concentrations and control

**Reliability:**
(2) valid with restrictions
04-SEP-2000

**4.5 Chronic Toxicity to Aquatic Organisms**

**4.5.1 Chronic Toxicity to Fish**

**4.5.2 Chronic Toxicity to Aquatic Invertebrates**
TERRESTRIAL ORGANISMS

4.6.1 Toxicity to Soil Dwelling Organisms
4.6.2 Toxicity to Terrestrial Plants
4.6.3 Toxicity to other Non-Mamm. Terrestrial Species

4.7 Biological Effects Monitoring

4.8 Biotransformation and Kinetics

4.9 Additional Remarks
5. Toxicity

5.1 Acute Toxicity

5.1.1 Acute Oral Toxicity

<table>
<thead>
<tr>
<th>Type</th>
<th>LD50</th>
</tr>
</thead>
<tbody>
<tr>
<td>Species</td>
<td>rat</td>
</tr>
<tr>
<td>Strain</td>
<td></td>
</tr>
<tr>
<td>Sex</td>
<td>male/female</td>
</tr>
<tr>
<td>Number of Animals</td>
<td>5</td>
</tr>
<tr>
<td>Vehicle</td>
<td>CMC</td>
</tr>
<tr>
<td>Value</td>
<td>ca. 900 mg/kg bw</td>
</tr>
<tr>
<td>Method</td>
<td>other: BASF-Test</td>
</tr>
<tr>
<td>GLP</td>
<td>no</td>
</tr>
<tr>
<td>Test substance</td>
<td></td>
</tr>
<tr>
<td>Result</td>
<td>symptoms: dyspnea, apathy, diarrhea</td>
</tr>
<tr>
<td>Source</td>
<td>BASF AG Ludwigshafen</td>
</tr>
<tr>
<td>Test condition</td>
<td>5 animals per dose and gender (values were taken from raw data)</td>
</tr>
<tr>
<td>Reliability</td>
<td>(2) valid with restrictions</td>
</tr>
</tbody>
</table>

05-SEP-2000

Type: LD50
Species: rat
Strain: no data
Sex: no data
Number of Animals: 3
Vehicle: other: corn oil
Value: 500 - 1000 mg/kg bw
Method: other: range finding study
Year: 05-SEP-2000
Test substance: other TS: 1,2-epoxybutane, purity 90-92% and 8-10% cis-2,3-epoxybutane
Result: 500 mg/kg b.m.: slight loss of body mass, 1/3 rats died
1000 mg/kg b.m.: 3/3 animals died within 2 hour
Source: BASF AG Ludwigshafen
Reliability: (2) valid with restrictions
05-SEP-2000

5.1.2 Acute Inhalation Toxicity

<table>
<thead>
<tr>
<th>Type</th>
<th>LC50</th>
</tr>
</thead>
<tbody>
<tr>
<td>Species</td>
<td>rat</td>
</tr>
<tr>
<td>Strain</td>
<td></td>
</tr>
<tr>
<td>Sex</td>
<td>male/female</td>
</tr>
<tr>
<td>Number of Animals</td>
<td>10</td>
</tr>
<tr>
<td>Vehicle</td>
<td></td>
</tr>
<tr>
<td>Exposure time</td>
<td>4 hour(s)</td>
</tr>
<tr>
<td>Value</td>
<td>&gt; 6.3 mg/l</td>
</tr>
<tr>
<td>Method</td>
<td>other: BASF-Test (see Test conditions)</td>
</tr>
<tr>
<td>GLP</td>
<td>no</td>
</tr>
<tr>
<td>Test substance</td>
<td>other TS: 1,2-epoxybutane, purity 99.9%, produced by BASF Aktiengesellschaft</td>
</tr>
<tr>
<td>Result</td>
<td>All animals survived and were killed at the end of the experiment; nothing abnormal was discovered in the postmortem examination.</td>
</tr>
</tbody>
</table>
5. Toxicity

Source: BASF AG Ludwigshafen
Test condition: 10 animals per dose and gender; Sprague-Dawley rats, SPF, 185 ± 15 g bw dynamic inhalation test with analytical monitoring; post exposure observation period: 14 days
Reliability: (2) valid with restrictions
Type: LC50
Species: rat
Strain: male/female
Number of Animals: 10
Vehicle: other: no
Exposure time: 4 hour(s)
Value: 398 - 6550 ppm
Method: other: range finding study of the NTP-Program
Year: GLP: no data
Test substance: other TS: 1,2-epoxybutane, purity > 99%
Result: Mortality: all rats exposed at 6550 ppm died, no other deaths occurred; clinical signs: ocular discharge and dyspnea at 2050 ppm and higher; eye irritations at 1400 ppm and higher
Source: BASF AG Ludwigshafen
Test condition: 5 animals per dose and gender
Doses tested: 398, 721, 1420, 2050, 6550 ppm
Post exposition observation period: 14 days
Reliability: (2) valid with restrictions
Type: other: IRT (inhalation risk test)
Species: rat
Strain: no data
Sex: no data
Number of Animals: other: no
Vehicle: Exposure time:
Value: Method:
Year: GLP: no
Test substance: other TS: n-Butyleneoxide-1,2, obtained from BASF Aktiengesellschaft
Method: IRT: Inhalation Risk Test (results depend on toxicity and volatility of the test substance)
Result: The exposition of 12 rats to an atmosphere saturated with 1,2-epoxybutan at 20 degree C for 3 minutes caused death of 2 animals. 10 minutes exposition of 6 rats caused death of all animals. Irritation of mucosa was observed.
Source: BASF AG Ludwigshafen
Reliability: (2) valid with restrictions
26-SEP-2000
5.1.3 Acute Dermal Toxicity

Type: LD50  
Species: rabbit  
Strain:  
Sex: male  
Number of Animals: 4  
Vehicle:  
Value: 1255 - 2546 mg/kg bw  
Method: other: Smyth et al., 1962, Am Ind Hyg Assoc J, 23, 95)  
Year: 1962  
Test substance: other TS: 1,2-epoxybutane, no further data  
Source: BASF AG Ludwigshafen  
Test condition: contact: 24 hours, occlusive; observation 14 days  
New Zealand rabbits  
Reliability: (2) valid with restrictions  
05-SEP-2000

5.1.4 Acute Toxicity, other Routes

5.2 Corrosiveness and Irritation

5.2.1 Skin Irritation

Species: rabbit  
Concentration: undiluted  
Exposure: Semiocclusive  
Exposure Time: 4 hour(s)  
Number of Animals: 2  
PDII: 0  
Result: not irritating  
EC classification:  
Method: other: BASF-Test  
Year:  
Test substance: other TS: 1,2-epoxybutane, purity 99.9%, produced by BASF Aktiengesellschaft  
Source: BASF AG Ludwigshafen  
Test condition: 0.5 ml were applicated, application area was 2.5 x. 2.5 cm female animals scored 15 minutes, 24, 48 hours and 8 days after removing the tape  
Reliability: (2) valid with restrictions  
19-MAR-2001

Species: rabbit  
Concentration: undiluted  
Exposure: Occlusive  
Exposure Time: 1 hour(s)  
Number of Animals: 4  
PDII:  
Result: corrosive  
EC classification:  
Method: other: BASF-test  
Year:  
Test substance:  
Source:  
Test condition:  
Reliability: (2) valid with restrictions  
19-MAR-2001

Species: rabbit  
Concentration: undiluted  
Exposure: Occlusive  
Exposure Time: 1 hour(s)  
Number of Animals: 4  
PDII:  
Result: corrosive  
EC classification:  
Method: other: BASF-test  
Year:  
Test substance:  
Source:  
Test condition:  
Reliability: (2) valid with restrictions  
19-MAR-2001
5. Toxicity

**Test substance:** other TS: 1,2-epoxybutane, obtained from BASF Aktiengesellschaft

**Method:**
Cotton-tissues (2 x 2 cm) was soaked with the test substance (0.5 ml) and placed on the shaved, intact dorsal skin of four rabbits. The tissues were covered with rubberised patches.

After one hour the the bandages were removed, the skin was rinsed with a mild tenside solution and carefully dried.

Scoring was immediately after the removal of the bandages and 1, 2, 8 days later. At the end of the test, skin effects were checked by section and macroscopic examination.

**Result:**
2/4 animals had full thickness necrosis of the skin, 8 days post application

**Source:** BASF AG Ludwigshafen

**Test condition:** 1 male and 3 females

**Reliability:** (2) valid with restrictions

---

5.2.2 Eye Irritation

**Species:** rabbit

**Concentration:** undiluted

**Dose:** .05 ml

**Exposure Time:**

**Comment:** not rinsed

**Number of Animals:** 2

**Result:** irritating

**EC classificat.:**

**Method:** other: BASF-Test

**Year:** GLP: no

**Test substance:** other TS: 1,2-epoxybutane, purity 99.9%, produced by BASF Aktiengesellschaft

**Result:**
after 1 hour: mild redding and edema; after 24 hours: mild redding, edema and clouding; competely recovered after 8 days

**Source:** BASF AG Ludwigshafen

**Test condition:** one male and one female (values were taken from raw data)

**Reliability:** (2) valid with restrictions

19-MAR-2001

---

5.3 Sensitization

**Type:** Guinea pig maximization test

**Species:** guinea pig

**Concentration:**
Induction undiluted semiocclusive
Challenge undiluted open epicutaneous

**Number of Animals:** 10

**Vehicle:** other: undiluted testsubstance

**Result:** not sensitizing

**Classification:**

**Method:** other: Maguire, 1973, J Soc Cosmet Chem, 24, 151

**Year:** GLP:
Test substance: other TS: 1,2-butylene oxide, obtained from Inorganic
Chemicals Laboratory Midland, Michigan, USA

Result: 9/10 animals responded to the positive control, whereas
0/10 animals treated with the undiluted test material
revealed no signs of sensitisation

Source: BASF AG Ludwigshafen

Test condition:
positive control was an epoxy resin (DER 331)
Two-weeks rest between induction and challenge,
no further details were given in the report

Reliability:
(2) valid with restrictions

5.4 Repeated Dose Toxicity

Species: rat
Sex: male/female
Strain: Fischer 344
Route of admin.: inhalation
Exposure period: 90 days
Frequency of
treatment: 6 hours/day, 5 days/week, 65 exposures in total
Post. obs.
period:
Doses: 0, 50, 100, 200, 400 and 800 ppm (0.15; 0.30; 0.60;
1.18; 2.39 mg/l)
Control Group: yes, concurrent vehicle
NOAEL: 1400 ppm
LOAEL: 1800 ppm
Method: other: NTP Program
Year: GLP:
Test substance: other TS: 1,2-epoxybutane, purity >99% impurity:
1,2-butanediol

Remark: In a preliminary information (OTS 0509932, 1981) the
following was reported:
1 male at 800 ppm and 1 male at 400 ppm had
discoloration of the lungs. 1/10 males and 1/10 females
in controls and sporadically in other exposure groups of
females.
However, thes findings had not been verified in the peer
reviewed final version.

Result: Mortality: 1 female rat in the 100 ppm exposure group
(whatever no substance related deaths);
Body weight: decreased body weight gain at 800 ppm (23%
lower in males and 16% lower in females);
Clinical signs: none;
Histopathology: inflammation of nasal cavity (primarily
the mucosa of the turbinates and the septum including
both areas of olfactory and respiratory epithelium) of
all males and females exposed to 800 ppm but not at
lower concentrations.

Source: BASF AG Ludwigshafen

Test condition:
Necropsy performed on all animals; all controls and the
two highest dose groups examined histologically. Tissue
examined: adrenal glands, brain, esophagus, heart,
kidneys, larynx, liver, lungs and mainstem bronchi,
mandibular and mesenteric lymph nodes, nasal cavity and
nasal turbinates, pancreas, parathyroids, pituitary
gland, prostate or uterus/ovaries, salivary glands, skeletal muscle, skin with mammary gland, spleen, sternebrae or femur or vertebrae including marrow, stomach, thymus, thyroid gland, trachea, and urinary bladder.

Reliability: (2) valid with restrictions

Species: rat
Sex: male/female
Strain: Fischer 344
Route of admin.: inhalation
Exposure period: 14 days
Frequency of treatment: 6 hours/day, 5 days/week
Post. obs. period:
Doses: 0, 400, 800, 1600, 3200 and 6400 ppm (1.20; 2.40; 4.78; 9.57; 19.15 mg/l)
Control Group: yes, concurrent vehicle
NOAEL: = 400 ppm
LOAEL: = 800 ppm
Method: other: NTP-Program

Result:
Mortality: All rats exposed at 3200 or 6400 ppm and 2/5 female rats exposed at 1600 ppm died before the end of the study.
Body weight: Final mean body weight of rats exposed at 800 or 1600 ppm was 12 or 33 % lower than that of the controls for males and 12 or 17 % lower for females.
Clinical signs: Erratic movements and piloerection were substance related effects in rats exposed at 1600 ppm.
Histopathology: Histological examinations were performed on 1 or 2 animals per exposure group. Multifocal pulmonary hemorrhage of moderate severity was observed in 2/2 males and 2/2 females exposed at 1600 ppm. Acute suppurative rhinitis of moderate severity was observed in 2/2 males and 2/2 females exposed at 1600 ppm.

Source: BASF AG Ludwigshafen
Test condition: 5 animals per dose and gender
Reliability: (2) valid with restrictions

Species: rat
Sex: male/female
Strain: Fischer 344
Route of admin.: inhalation
Exposure period: 90 days
Frequency of treatment: 6 hours per day, 5 days per week. There were a total of 66 exposure days.
Post. obs. period:
Doses: 0, 75, 150, 600 ppm (0, 0.23, 0.45, 1.8 mg/l)
Control Group: yes, concurrent vehicle
NOAEL: = 150 ppm
LOAEL: = 600 ppm
Method: other: closely following OECD Guide-line 413
Year: GLP:
Test substance: other TS: 1,2-butylen oxide (single isomer) was
obtained from the production facilities of Dow Chemical USA; purity greater than 99%

Result:

The mean body weight gain for female rats in the 600 ppm group was significantly lower than for controls during the last few weeks of study. In addition, the body weight gains of male rats in the 600 ppm group tended to be lower than for controls, although not statistically significantly so.

Growth of rats in the 75 and 150 ppm groups was not altered by the exposures.

Gross pathologic observations in rats in the 600 ppm group included decreased amounts of abdominal adipose tissue and decreased size of the thymus and mediastinal fat. All other gross pathologic observations in rats were considered spontaneous in nature and unrelated to exposure. There were no treatment-related gross pathologic observations in either rats or mice in the 75 or 150 ppm groups.

Histopathologic examinations of tissues from rats after 13 weeks of exposure to 600 ppm revealed changes in the nasal mucosa which were attributed to primary upper respiratory irritation. The microscopic changes in the nasal turbinates were minimal and were characterized by flattening of the olfactory and respiratory epithelium with some focal thickening of the respiratory epithelium. In addition, increased numbers of inflammatory cells were present in the nasal mucosa and within the lumen of the nasal cavity. Lower portions of the respiratory tract (e.g., trachea and lungs) were apparently unaffected by exposure to butylene oxide vapors, although there were some observations in the lungs and trachea of a few treated female rats which were considered spontaneous in nature and unrelated to exposure.

There were several microscopic changes in rats exposed to 600 ppm which were considered to be indirect effects of exposure to the test material, including decreased hepatocellular size, decreased cell content in the cortex of the thymus gland, and myeloid hyperplasia in vertebral bone marrow (3 of 10 male rats only). All other microscopic observations in rats were considered to be spontaneous in nature and unrelated to exposure. There were no microscopic observations in either male or female rats in the 75 and 150 ppm groups which were considered to be related to exposure to butylene oxide.

Source:

BASF AG Ludwigshafen

Test condition:

All animals were observed daily for signs of toxicity. Body weights were recorded immediately prior to exposure and at selected intervals thereafter. Clinical laboratory studies on each surviving rat and mouse included hematologic analyses [red blood cell counts (RBC), hemoglobin (Hgb), packed cell volume (PCV) and total and differential white blood cell counts (WBC)], and serum clinical chemistry analyses (glucose, urea nitrogen, alkaline phosphatase activity and glutamic pyruvic transaminase activity). Urinalyses (specific gravity, pH, sugar, protein, ketones, blood, bilirubin and urobilinogen) were performed.
Weights of heart, liver, kidneys, brain, thymus and testes (males) were recorded for each animal. Representative sections of adipose tissue, adrenals, aorta, brain, cecum, esophagus, eyes, gonads, gross lesions, heart, small intestine, large intestine, kidneys, lacrimal gland, larynx, liver, lungs, lymph nodes, mammary gland, nasal turbinates, pancreas, peripheral nerve, pituitary, prostate, salivary gland, seminal vesicles, skeletal muscles, skin, spinal cord, spleen, stomach, tongue, trachea, thymus, thyroid, parathyroid, urinary bladder, uterus, vertebrae with bone marrow, in the control and high exposure groups were prepared by conventional histologic techniques. Only selected tissues, based on observations in the high exposure groups, were examined for animals in the lower exposure groups in order to ascertain whether or not there was a dose-response relationship. Each control and exposure group initially consisted of 15 rats per gender; 5 rats from each group were sacrificed after 4 weeks of exposure.

Reliability: (2) valid with restrictions
26-SEP-2000

Species: mouse
Sex: male/female
Strain: B6C3F1
Route of admin.: inhalation
Exposure period: 14 days
Frequency of treatment: 6 hours/day, 5 days/week
Post. obs. period:
Doses: 0, 400, 800, 1600, 3200 and 6400 ppm (1.20; 2.40; 4.78; 9.57; 19.15 mg/l)
Control Group: yes, concurrent vehicle
NOAEL: 400 ppm
LOAEL: 800 ppm
Method: other: NTP-Program
Year: GLP:
Test substance: other TS: 1,2-epoxybutane, purity >99% impurity: 1,2-butanediol
Result: Mortality: all animals died after 1 day in the 1600, 3200 and 6400 ppm groups; one male of the 800 ppm group died on day 3.
Growth: final mean body weights of surviving mice at 800 ppm were 10-12% lower than those of the control;
Hematology: slightly reduced in the 800 ppm groups (both genders);
Clinical signs: dyspnea, listlessness at 800 ppm
Clinical chemistry: no data;
Histopathology: Moderate nephrosis in 2/2 males of the 1600 ppm group, mild to slight nephrosis in 2/2 males and 1/2 females of the 800 ppm group.
Source: BASF AG Ludwigshafen
Test condition: 5 animals per dose and gender
Reliability: (2) valid with restrictions
19-MAR-2001
### Toxicity

<table>
<thead>
<tr>
<th><strong>Species:</strong></th>
<th>mouse</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Strain:</strong></td>
<td>B6C3F1</td>
</tr>
<tr>
<td><strong>Route of admin.:</strong></td>
<td>inhalation</td>
</tr>
<tr>
<td><strong>Exposure period:</strong></td>
<td>90 days</td>
</tr>
<tr>
<td><strong>Frequency of treatment:</strong></td>
<td>6 hours per day, 5 days per week. There were a total of 66 exposure days.</td>
</tr>
<tr>
<td><strong>Post. obs. period:</strong></td>
<td></td>
</tr>
<tr>
<td><strong>Doses:</strong></td>
<td>0, 75, 150, 600 ppm (0, 0.23, 0.45, 1.8 mg/l)</td>
</tr>
<tr>
<td><strong>Control Group:</strong></td>
<td>yes, concurrent vehicle</td>
</tr>
<tr>
<td><strong>NOAEL:</strong></td>
<td>= 150 ppm</td>
</tr>
<tr>
<td><strong>LOAEL:</strong></td>
<td>= 600 ppm</td>
</tr>
<tr>
<td><strong>Method:</strong></td>
<td>other: closely following OECD Guide-line 413</td>
</tr>
<tr>
<td><strong>Test substance:</strong></td>
<td>other TS: 1,2-butylene oxide (single isomer) was obtained from the production facilities of Dow Chemical USA; purity greater than 99%</td>
</tr>
<tr>
<td><strong>Result:</strong></td>
<td>The mean body mass gain for female mice in the 600 ppm group was significantly lower than for controls during the last few weeks of study. In addition, the body weight gains of male mice in the 600 ppm group tended to be lower than for controls, although not statistically significantly so. Growth of mice in the 75 and 150 ppm groups was not altered by the exposures. The mean body weight gain values of male mice in the 75 ppm group were statistically lower than controls on several occasions, but this was not considered to be an adverse treatment-related effect due to the absence of similar changes for male mice in the 150 ppm group. Gross pathologic observations in mice of the 600 ppm group included decreased amounts of abdominal adipose tissue and decreased size of the thymus and mediastinal fat. All other gross pathologic observations in mice were considered spontaneous in nature and unrelated to exposure. There were no treatment-related gross pathologic observations in the 75 or 150 ppm groups. Histopathologic examinations of tissues from mice after 13-weeks of exposure also revealed changes only in the nasal mucosa of animals exposed to 600 ppm which were considered to be direct effects of exposure to the test material. The microscopic changes in the nasal turbinates were characterized by a minimal degree of focal thickening and flattening of the respiratory epithelium. As in rats, there were increased numbers of inflammatory cells present in the nasal mucosa and within the lumen of the nasal cavity; no treatment-related changes were noted in the lungs or trachea of mice. Also, as in rats, there were several other microscopic changes in mice exposed to 600 ppm which were considered to be indirect effects of exposure to the test material including decreased hepatocellular size and decreased cell content in the cortex of the thymus gland.</td>
</tr>
</tbody>
</table>
All other microscopic observations in mice were considered to be spontaneous in nature and unrelated to exposure. There were no microscopic observations in either male or female mice in the 75 and 150 ppm exposure groups which were considered to be related to exposure to the test material.

Source: BASF AG Ludwigshafen

Test condition: All animals were observed daily for signs of toxicity. Body weights were recorded immediately prior to exposure and at selected intervals thereafter. Clinical laboratory studies on each surviving mouse included hematologic analyses (red blood cell counts (RBC), hemoglobin (Hgb), packed cell volume (PCV) and total and differential white blood cell counts (WBC)), and serum clinical chemistry analyses (glucose, urea nitrogen, alkaline phosphatase activity and glutamic pyruvic transaminase activity). Weights of heart, liver, kidneys, brain, thymus and testes (males) were recorded for each animal. Representative sections of adipose tissue, adrenals, aorta, brain, cecum, esophagus, eyes, gallbladder, gonads, gross lesions, heart, small intestine, large intestine, kidneys, lacrimal gland, larynx, liver, lungs, lymph nodes, mammary gland, nasal turbinates, pancreas, peripheral nerve, pituitary, prostate, salivary gland, seminal vesicles, skeletal muscles, skin, spinal cord, spleen, stomach, trachea, thymus, thyroid, parathyroid, urinary bladder, uterus, vertebrae with bone marrow in the control and high exposure groups were prepared by conventional histologic techniques. Only selected tissues, based on observations in the high exposure groups, were examined for animals in the lower exposure groups in order to ascertain whether or not there was a dose-response relationship.

Each control and exposure group initially consisted of 15 rats per gender; 5 rats from each group were sacrificed after 4 weeks of exposure.

Reliability: (2) valid with restrictions

Species: mouse
Sex: male/female
Strain: B6C3F1
Route of admin.: inhalation
Exposure period: 90 days
Frequency of treatment: Post. obs. period:
Doses: 0, 50, 100, 200, 400 and 800 ppm (0.15; 0.30; 0.60; 1.18; 2.39 mg/l)
Control Group: yes, concurrent vehicle
NOAEL: 50 ppm
LOAEL: 100 ppm
Method: other: NTP-Program
Year: GLP:
Test substance: other TS: 1,2-epoxybutane, purity >99% impurity: 1,2-butandiol
Remark:
In a preliminary information (OTS 0509932, 1982) the following was reported:
Gross pathology: red discoloration of the lungs in 4/10 males and all females exposed to 800 ppm and in 1/10 males at 400 ppm; paleness of spleen and distension of the gastrointestinal tract in mice exposed to 800 ppm.
Histological results: thymic necrosis, thymic atrophy, splenic atrophy, splenic necrosis.
Hemorrhage of tracheo-bronchial lymph nodes was observed in 5/8 males and 2/8 females at 800 ppm and 1/10 females of control and sporadically in other exposure groups.
However, these findings had not been verified in the peer reviewed, final report.

Result:
Mortality: all males and females in the 800 ppm exposure group and 2 males in the 50 ppm group died within 10 weeks.
Body mass: no dose-dependent changes;
Clinical signs: listlessness in mice exposed to 800 ppm.
Renal tubular necrosis (6/10 males and 8/10 females) occurred in animals exposed to 800 ppm but not at lower exposure concentrations.
Only inflammation of nasal turbinates occurred at lower levels: all males and females at 400 ppm, all males and females at 200 ppm, 10/10 males and 7/10 females at 100 ppm.

Test condition:
10 animals per dose and gender were used.
Necropsy performed on all animals; all controls and the two highest dose groups examined histologically. Tissue examined: adrenal glands, brain, esophagus, gallbladder, heart, kidneys, larynx, liver, lungs and mainstem bronchi, mandibular and mesenteric lymph nodes, nasal cavity and nasal turbinates, pancreas, parathyroids, pituitary gland, prostate or uterus/ovaries, salivary glands, skeletal muscle, skin with mammary gland, spleen, sternebrae or femur or vertebrae including marrow, stomach, thymus, thyroid gland, trachea, and urinary bladder.

5.5 Genetic Toxicity 'in Vitro'

Type: Ames test
System of testing: Salmonella typhimurium TA 1535, TA 100, TA 1537, TA 98
Concentration: 20 to 7500 µg/plate for TA 100 and 20 to 5000 µg/plate for other strains
Cytotoxic Conc.: with and without
Metabolic activation: positive
Method: OECD Guide-line 471 "Genetic Toxicology: Salmonella typhimurium Reverse Mutation Assay"
Year: no
Test substance: other TS: n-butyleneoxide-1,2, purity: 99.9%, produced by BASF Aktiengesellschaft
**Result:**
weakly positive in TA 1535 and TA 100 with and without S9 mix no signs of bacteriotoxicity

<table>
<thead>
<tr>
<th>STRAIN</th>
<th>S9</th>
<th>CONCENTRATION</th>
<th>REVERTANTS</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>(multiple of control)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>TA1535 with</td>
<td>2500 µg/plate</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td></td>
<td>5000 µg/plate</td>
<td>3</td>
<td></td>
</tr>
<tr>
<td></td>
<td>without 2500 µg/plate</td>
<td>3</td>
<td></td>
</tr>
<tr>
<td></td>
<td>without 5000 µg/plate</td>
<td>3.5</td>
<td></td>
</tr>
<tr>
<td>TA100 with</td>
<td>2500 µg/plate</td>
<td>1.5</td>
<td></td>
</tr>
<tr>
<td></td>
<td>5000 µg/plate</td>
<td>2.5</td>
<td></td>
</tr>
<tr>
<td></td>
<td>without 2500 µg/plate</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td></td>
<td>without 5000 µg/plate</td>
<td>3</td>
<td></td>
</tr>
</tbody>
</table>

**Source:**
BASF AG Ludwigshafen

**Test condition:**
plate incorporation assay

**Reliability:**
(1) valid without restriction

**Type:**
Ames test

**System of testing:**
Salmonella typhimurium TA 1535, TA 100, TA 1537, TA 98 100, 333, 1000, 3333, 10000 µg/plate

**Concentration:**
100, 333, 1000, 3333, 10000 µg/plate

**Cytotoxic Conc.:**
Metabolic activation:
with and without

**Result:**
positive

**Method:**
other: Haworth et al., 1983, Environ Mutagen, 5(Suppl 1), 1

**Year:**
05-SEP-2000  (15)  GLP: no

**Test substance:**
other TS: 1,2-epoxybutane, purity >99% impurity: 1,2-butanediol

**Result:**
positive in TA 100 and TA 1535 with and without S9-Mix at concentrations of 1000 µg/plate and higher

**Source:**
BASF AG Ludwigshafen

**Test condition:**
preincubation assay

**Reliability:**
(2) valid with restrictions

**Type:**
Cytogenetic assay

**System of testing:**
Chinese Hamster Ovary cells

**Concentration:**
16 to 500 µg/ml

**Metabolic activation:**
without

**Result:**
positive

**Method:**
other: Galloway et al., 1985, Environ Mutagen, 7, 1

**Year:**
05-SEP-2000  (40)  GLP: no

**Test substance:**
other TS: 1,2-Epoxybutane, no further data

**Result:**
positive without S9-Mix at highest dose, equivocal with S9-Mix

**Source:**
BASF AG Ludwigshafen

**Reliability:**
(2) valid with restrictions

05-SEP-2000  (1)
### 5. Toxicity

#### 5.6 Genetic Toxicity 'in Vivo'

<table>
<thead>
<tr>
<th>Type:</th>
<th>Cytogenetic assay</th>
</tr>
</thead>
<tbody>
<tr>
<td>Species:</td>
<td>rat</td>
</tr>
<tr>
<td>Sex:</td>
<td>male/female</td>
</tr>
<tr>
<td>Strain:</td>
<td>Sprague-Dawley</td>
</tr>
<tr>
<td>Route of admin.:</td>
<td>inhalation</td>
</tr>
<tr>
<td>Exposure period:</td>
<td>7 hours single exposure or 5 consecutive days</td>
</tr>
<tr>
<td>Doses:</td>
<td>250, 1000 ppm (0.75, 3.0 mg/l)</td>
</tr>
<tr>
<td>Result:</td>
<td>negative</td>
</tr>
<tr>
<td>Method:</td>
<td>other: following OECD Guideline 475 with inhalative exposure</td>
</tr>
<tr>
<td>Year:</td>
<td>GLP: no</td>
</tr>
<tr>
<td>Test substance:</td>
<td>other TS: 1,2-butyleneoxide, purity 99%, obtained from Aldrich Chemical Co. Ltd.</td>
</tr>
<tr>
<td>Remark:</td>
<td>10 animals per dose, gender and time of preparation analytical monitoring of air chamber concentration positive control was EMS, negative control concurrent no test substance</td>
</tr>
<tr>
<td>Result:</td>
<td>No increase of aberrant cells in any group, merely male rats showed an increase of aberrant cells 6 hours after single exposure, if cells only containing gaps were excluded from analysis, this was not statistically significant. No information on general bone marrow toxicity is given in the report.</td>
</tr>
</tbody>
</table>
5. Toxicity

Source: BASF AG Ludwigshafen
Test condition: Sprague-Dawley rats (10 animals per dose, gender and time) were exposed to 1,2-epoxybutane at concentrations of 750 or 3000 mg/m³ (7 hours single exposure or 5 consecutive days). The air chamber concentration was monitored analytically.

Animals were killed and slides of bone marrow cells were prepared 6, 24 and 48 hours after exposure. The exposure groups did not show any increase in the frequency of aberrant cells except in the 6 h sample time males exposed to 3000 mg/m³ butylene oxide (P<0.05). If cells only containing gaps were excluded from the analysis, then the statistical significance of the difference from the air control group was reduced. This result is probably an insufficient evidence on which to base a conclusion for the clastogenic potential of this compound in vivo since the effect was small and was not observed in female rats.

Reliability: (2) valid with restrictions

Type: Dominant lethal assay
Species: rat
Sex: male
Strain: Sprague-Dawley
Route of admin.: inhalation
Exposure period: 7 hours/ day for 5 consecutive days
Doses: 250, 1000 ppm (0.75, 3.0 mg/l)
Result: negative
Method: other: following OECD Guideline 478 with inhalative exposure

Year: 19-MAR-2001
GLP: no
Test substance: other TS: 1,2-butyleneoxide, purity 99%, obtained from Aldrich Chemical Co. Ltd.
Result: under the test conditions no identifiable effect
Source: BASF AG Ludwigshafen
Test condition: 10 male animals per dose mating of 1 treated male on 10 consecutive days following administration, mating with 2 virgin females each day positive control was EMS, negative control concurrent no test substance

Reliability: (2) valid with restrictions

5.7 Carcinogenicity

Species: rat
Sex: male/female
Strain: Fischer 344
Route of admin.: inhalation
Exposure period: 2 years
Frequency of treatment: 6 hours/day, 5 days/week
Post. obs. period: 
Doses: 200, 400 ppm (0.598, 1.197 mg/l)
Result: Control Group: yes, concurrent vehicle
Method: other: NTP-Program

Year: 05-SEP-2000
GLP: no data
Test substance: other TS: 1,2-epoxybutane, purity >99% impurity: 1,2-butanediol

Result:
Survival at termination of the experiment was 30/50, 18/50 and 23/50 for males and 32/50, 21/50 and 22/50 for females in the control, low-dose and high-dose groups, respectively.
Body weights of males were normal until week 86, and body weights of the high dose group decreased by 4-8% afterwards.
Body weights of females were normal until week 22, and body weights of the high dose group decreased by 5-10% afterwards.
Incidence of papillary adenomas of the nasal cavity were 7/50 for high-dose males and 2/50 for high-dose females. No such tumours occurred in controls or in low-dose groups.
Incidence of alveolar/bronchiolar carcinomas were 0/50, 1/50 and 4/49 for males and 1/50, 0/49 and 0/50 for females in the control, low-dose and high-dose groups, respectively.
Incidence of alveolar/bronchiolar adenomas were 0/50, 1/50 and 1/49 for males and 1/50, 0/49 and 1/50 for females. The incidence of alveolar/bronchiolar adenomas and carcinomas in the high-dose group (males) was significantly increased compared to controls.

Treatment-related, non-neoplastic changes in the nose included inflammation, epithelial hyperplasia, squamous metaplasia, hyperostosis of the nasal turbinates bone, and atrophy of the olfactory epithelium at both dose levels.

Conclusion of the authors: Under the conditions of this 2-year inhalation study, there was clear evidence of carcinogenic activity of 1,2-epoxybutane for male F344/N rats and equivocal evidence of carcinogenic activity for female F344/N rats.

Source: BASF AG Ludwigshafen

Test condition: 50 animals per dose and gender
Necropsy and histologic examined performed on all animals; the following tissues examined: adrenal glands, brain, clitoral or preputial gland, colon, esophagus, gross lesions and tissue masses, heart, kidneys, lungs and mainstem bronchi, mammary gland, mandibular lymph nodes, nasal cavity and nasal turbinates, pancreas, parathyroids, pituitary gland, prostate/testes/epididymis or ovaries/uterus, rectum, regional lymph nodes, salivary glands, skin, small intestine, spleen, sternebrae including marrow, stomach, thymus, thyroid gland, trachea, tracheobronchial lymph nodes, and urinary bladder.

Reliability: 26-SEP-2000 (2) valid with restrictions

Species: mouse
Sex: male/female
Strain: B6C3F1
Route of admin.: inhalation
Exposure period: 2 years
Frequency of treatment: 6 hours/day, 5 days/week
Post. obs. period: 

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5. Toxicity

Doses: 50, 100 ppm (0.150, 0.300 mg/l)  
Result: yes, concurrent vehicle  
Control Group: NTP-Program  
Method: other TS: 1,2-epoxybutane, purity >99% impurity: 1,2-butanediol  
Year: GLP: no data  
Test substance: 
Result: Survival at termination of the experiment was 41/50, 45/50 and 33/50 for males and 29/50, 25/50 and 9/50 for females in the control, low-dose and high-dose groups, respectively. The decreased survival was associated with suppurrative inflammation of the ovary and uterus. Klebsiella oxytoca was isolated from the ovarian/uterine lesions. Final body weight of surviving mice was unaffected by exposure. A single squamous-cell papilloma was found in the nasal cavity of a male receiving 100 ppm. This finding was not statistically significant and could not clearly be related to chemical exposure. Treatment-related, non-neoplastic nasal changes included inflammation, emphysema, erosion, regeneration, hyperplasia and squamous metaplasia of the nasal epithelium and atrophy of the olfactory epithelium and inflammation and hyperplasia of the nasolacrimal duct at both dose levels. Conclusion of the authors: Under the conditions of this 2-year inhalation study, there was no evidence of carcinogenic activity of 1,2-epoxybutane for male or female B6C3F1 mice exposed at 50 or 100 ppm.  
Source: BASF AG Ludwigshafen  
Test condition: 50 animals per dose and gender  
Necropsy and histologic examined performed on all animals; the following tissues examined: adrenal glands, brain, clitoral or preputial gland, colon, esophagus, gallbladder, gross lesions and tissue masses, heart, kidneys, lungs and mainstem bronchi, mammary gland, mandibular lymph nodes, nasal cavity and nasal turbinates, pancreas, parathyroids, pituitary gland, prostate/testes/epididymis or ovaries/uterus, rectum, regional lymph nodes, salivary glands, skin, small intestine, spleen, sternebrae including marrow, stomach, thymus, thyroid gland, trachea, tracheobronchial lymph nodes, and urinary bladder.  
Reliability: (2) valid with restrictions

5.8 Toxicity to Reproduction

Type:  
Species:  
Strain:  
Route of admin.:  
Exposure Period:  
Frequency of treatment:  
Duration of test:  
Doses:  
Control Group:
5. Toxicity

Method:
Year: GLP:
Test substance: See repeated-dose toxicity studies (chapter 5.4), dominant-lethal test (chapter 5.6) and developmental toxicity studies (chapter 5.9).
Remark:
Source:
19-MAR-2001

5.9 Developmental Toxicity/Teratogenicity

Species: rat
Sex: female
Strain: Wistar
Route of admin.: inhalation
Exposure period: day 1 to 19 of gestation, additionally groups with pregestational exposure of 21 days
Frequency of treatment: 7 hours/day, 5 days/week
Duration of test: cesarian section on day 21
Doses: 250, 1000 ppm (0.75, 3.0 mg/l)
Control Group:
NOAEL Maternalt.: >= 1000 ppm
NOAEL Teratogen.: >= 1000 ppm
Method:
Year: GLP: no data
Test substance: other TS: butylenoxide, no further data
Method:

On the day prior to initiation of exposure, the animals were placed in the exposure chamber and the food in each housing unit was weighed to allow calculation of the pre-exposure food consumption. The females were weighed prior to placement in the exposure chambers and at least twice weekly during pregestation exposure and on 4 days of gestation. Pregestational exposures were continued for 7 hours per day, 5 days a week, for 3 weeks. The females were transferred to a standard rack unit and caged with males (2:1). Vaginal lavages were performed and examined for the presence of sperm. Sperm positive females were randomly assigned to gestational exposure groups. Gestational exposures were started on the day on which sperm were detected, which was denoted as day 1 of gestation. Mating and initiation of gestational exposures continued for 7-9 days, until about 36 sperm-positive rats were assigned to each experimental group. Gestational exposures were performed 7 hours per day, 7 days per week, through day 19 of gestation. All exposed mated rats were sacrificed at day 21 of exposure. The concentrations to which the rats were exposed were (250 and 1,000 ppm). Based upon the combination of pregestational and gestational exposures, one control and six experimental groups were formed. These groups will be identified by the pregestational and gestational exposure in the presentation of results: Air-Air (Control) - 3 week pregestational exposure to filtered air followed by exposure to filtered air during days 1-19 of gestation.
Air-Low - 3 week pregestational exposure to filtered air followed by low level exposure during days 1-19 of gestation.

Air-High - 3 week pregestational exposure to filtered air followed by high level exposure during days 1-19 of gestation.

Low-Air - 3 week pregestational low level exposure followed by exposure to filtered air during days 1-19 of gestation.

Low-Low - 3 week pregestational low level exposure followed by low level exposure during days 1-19 of gestation.

High-Air - 3 week pregestational high level exposure followed by exposure to filtered air during days 1-19 of gestation.

High-High - 3 week pregestational high level exposure followed by high level exposure during days 1-19 of gestation.

Necropsies were performed on all animals; liver, lung, and kidneys were weighed. Internal abnormalities of the pregnant and nonpregnant animals, e.g., adhesions, tumors, or evidence of infection were also recorded. Samples of the ovaries, uterus, liver, lungs with trachea, and kidneys were taken. Histopathological examination was performed on tissues from 25% (approximately 8 per group) of the pregnant animals, selected at random. The residual tissues and the tissues from the remaining 75% of the animals and from the nonpregnant animals have been preserved for possible future examination.

The uterus, with ovaries attached, was removed from each animal immediately upon sacrifice and the total number of implantation sites was counted. This information and the several other measures to be described were recorded on forms from which computer input was keypunched directly. The ovaries were removed and identified as right or left, the corpora lutea were counted, and the ovaries were subjected to histologic examination. The uterus was opened and counts of living and dead fetuses and of resorptions were made. The resorptions were classified as to the stage of gestation at which death appeared to have occurred. The foetuses were removed from the surrounding membranes in serial order and the amniotic fluid was observed for any abnormalities in color. Concurrently, the placentas were removed, weighed and examined; abnormal placentas were histologically examined.

The each living and recently dead foetuses was weighed, the crown-rump length measured, the sex was determined and examined for gross external abnormalities. Foetuses were randomly (coin-toss) assigned to one of two groups for more detailed teratologic examination. In one group, the heads and internal abnormalities were examined. Slightly more than one-half on the fetuses were examined in this manner(a minimum of 2 fetuses per horn and 4 fetuses per litter). The fetuses of the second group were evaluated for skeletal abnormalities.
Fisher's Exact Probability Test was used on the maternal and fetal data; Bonferroni's method was used to adjust for the problem associated with multiple comparisons against a control group. In all instances, differences from the control group at probability levels of 0.05 or less were accepted as statistically significant.

Maternal toxicity: no mortality without pregestational exposure (0/38) High pregestational exposure caused one death (1/42). However, this death was not regarded as substance-related (the surviving animals showed no signs of severe toxicity; no further details are given in the report) Pregestational exposure to 1,000 ppm of butylene oxide produced a slight, but statistically significant, reduction in the body weight of the rats relative to the controls at most time periods. The differences were transient and were not statistically significant at the end of the pregestation exposure. By 7 days of gestational exposure, the rats exposed at the high levels were significantly lighter than the controls, and remained lighter throughout the study. No remarkable changes in food consumption were produced by pregestational or gestational exposure of rats. The exposure did not affect liver weights. The exposure did not have a major effect on lung weight. No statistically significant differences in placental weight were detected. Apparently normal corpora lutea were noted in the sections of ovary from each rat. The exposure led to a slightly reduced percentage of sperm-positive rats which were pregnant (36/37, 33/37, 28/35, 33/42, 38/44, 33/40, 31/39 for air-air, air-low, air-high, low air, low-low, high-air and high-high respectively) although no clear dose relationship was seen and the decrease was not statistically significant. The exposure had no statistically significant effect on either the weight or length of the fetuses in rats. Statistically significant differences in the sex rations were not observed. Pregestational and/or gestational exposure did not have statistically significant effects on any of the measures of reproductive success. Alterations of the nature or incidence of morphologic changes related to exposure were not noted.

Source:
BASF AG Ludwigshafen

Reliability: (2) valid with restrictions

Species: rabbit  Sex: female
Strain: New Zealand white
Route of admin.: inhalation
Exposure period: day 1 to 24 of gestation
Frequency of treatment: 7 hours/day, 5 days/week
Duration of test: cesarian section on day 30
Doses: 250, 1000 ppm (0.75, 3.0 mg/l)
Control Group: yes, concurrent no treatment
NOAEL Maternatl.: 250 ppm
NOAEL Teratogen.: >= 1000 ppm
Method:
Year: 19-MAR-2001
GLP: no data
Test substance: other TS: butylenoxide, no further data
Method: The females were randomly divided by weight into three
groups of 24 each. They were artificially inseminated in
the afternoon over the course of three successive days,
using pooled semen samples. Ovulation was induced by
nearly simultaneous i.v. injections of 2.5 mg (0.5 ml)
of pituitary luteinizing hormone. The morning following
insemination was defined as day 1 of gestation.
There were three groups of experimental rabbits defined
as follows: LOW level exposure (250 ppm) on days 1-24 of
gestation; HIGH level exposure (1000 ppm) on days 1-24
of gestation; AIR-filtered air exposure on days 1-24 of
gestation.
The rabbits were maintained until day 30 of gestation,
at which time they were sacrificed.
Necropsies were performed on all animals; liver, lung,
and kidneys were weighed. Internal abnormalities of the
pregnant and nonpregnant animals, e.g., adhesions,
tumors, or evidence of infection were also recorded.
Samples of the ovaries, uterus, liver, lungs with
trachea, and kidneys were taken. Histopathological
examination was performed on tissues from 25%
(approximately 8 per group) of the pregnant
animals, selected at random. The residual tissues and
the tissues from the remaining 75% of the animals and
from the nonpregnant animals have been preserved for
possible future examination.
The uterus, with ovaries attached, was removed from each
animal immediately upon sacrifice and the total number
of implantation sites was counted. This information and
the several other measures to be described were recorded
on forms from which computer input was keypunched
directly. The ovaries were removed and identified as
right or left, the corpora lutea were counted, and the
ovaries were subjected to histological examination. The
uterus was opened and counts of living and dead fetuses
and of resorptions were made. The resorptions were
classified as to the stage of gestation at which death
appeared to have occurred. The foetuses were
removed from the surrounding membranes in serial order
and the amniotic fluid was observed for any
abnormalities in color. Concurrently, the placentas were
removed, weighed and examined; abnormal placentas were
histologically examined.
The each living and recently dead foetuses was weighed,
the crown-rump length measured, the sex was determined
and examined for gross external abnormalities. All
fetuses were dissected and examined for visceral
abnormalities.
Fisher's Exact Probability Test was used on the maternal
and fetal data. Bonferronni’s method was used to adjust
for the problem associated with multiple comparisons
against a control group. In all instances, differences
from the control group at probability levels of 0.05 or
less were accepted as statistically significant.
Result: Fourteen of 24 (58%) exposed to 1,000 ppm died during exposure; a significant increase. Suppurative pneumonia was the usual necropsy finding in rabbits which died during exposure.

The exposure did not have a major effect on lung weights; kidney weights were unaffected. No statistically significant differences in placental weight were detected.

The exposure to a reduced percentage of sperm-positive rabbits, based on the results at scheduled sacrifice. Although this might be considered to be influenced by preimplantation mortality of does, nine of 13 does in the high group which died prior to scheduled sacrifice were pregnant. This gives an overall fraction of 11/23 or 48%, as compared to the 42% pregnant in the air group.

The exposure had no statistically significant effect on either the weight or length of the foetuses. The foetuses of the few (2 and 1, respectively) surviving litters of high dose rabbits were markedly smaller than those of the control or low dose groups. Statistically significant differences in the sex rations were not observed.

Gestational exposure did not have statistically significant effects on any of the measures of reproductive success. However, in the two litters exposed to the high level (for which statistical analysis could not be performed) there was a suggestion of a decreased number of live foetuses per litter and an increase in the frequency of resorptions (6.7, 7.0, 4.0 live foetuses per litter in the control, low and high dose group, respectively and 0.85, 0.47, 2.5 resorptions per litter in the control, low and high dose group, respectively).

Alterations of the nature or incidence of morphologic changes related to exposure were not noted.

Source: BASF AG Ludwigshafen

Conclusion: Due to the high maternal toxicity (mortality) a conclusion regarding developmental toxicity can not be drawn!

Reliability: (3) invalid

5.10 Other Relevant Information

Type: Metabolism
Remark: The major sulphur containing metabolite in the urine of rats and rabbits dosed with 1,2-epoxybutane was (2-hydroxybutyl)-mercapturic acid. Rabbits und rats were given 137 mg/kg b.w. and 180.3 mg/kg b.w. respectively by stomach tube. Urine was collected and assayed every 24 h until metabolites were not further detected. The excretion of (2-hydroxybutyl)mercapturic acid in the urine was 4 % (rabbits) and 11 % (rats) of the administered 1,2-epoxybutane, respectively. Butylmercapturic acid could not be detected in the urine of both, rabbits and rats.

Source: BASF AG Ludwigshafen
Reliability: (2) valid with restrictions
Type: Toxicokinetics

Result: Fate of 1,2-epoxybutane (BO) in male rats following inhalative exposure:
BO is extensively metabolised and rapidly eliminated following either inhalation exposure or gavage in F344 male rats. 100, 400, 2000 ppm (300, 1200, 6000 mg/m3) BO caused dose-related depletion of non-protein sulfhydryl groups in liver and kidney tissue. Conjugation of BO with GSH is an important detoxification mechanism in rodents and is less likely overwhelmed by exposure with BO than exposure to EO or PO. The results suggest, that BO would not seriously deplete BO in rats. Steady-state uptake rates of BO were determined to be 0.0433 mg/kg/min at 50 ppm and 0.720 mg/kg/min at 1000 ppm. These rates correspond to an estimated uptake of 15.6 and 252 mg/kg during a six hour exposure. It appears that physical and biological processes involved in absorption, metabolism and elimination of BO are essentially linear throughout the exposure range. In conclusion BO appears to have significantly less biological activity than either EO or PO. This is reflected by the relative toxicities of these substances (EO>PO>BO) as well as their effects in depleting endogenous GSH.

Source: BASF AG Ludwigshafen

Reliability: (2) valid with restrictions

5.11 Experience with Human Exposure

Remark: no data available

Source: BASF AG Ludwigshafen

10-OCT-2000
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