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)

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History: see next page;

Testing: No new SIDS testing (X)
New SIDS testing ( )

Comments:

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)

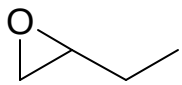
- Review o f validity of structure-activity relationships

- 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)

SIDS INITIAL ASSESSMENT PROFILE

CAS No.	106-88-7
Chemical Name	1,2-epoxybutane
Structural Formula	C_4H_8O 

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.

Environment

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: LC_{50} (96 h) = 100 - 215 mg/l, *Daphnia magna*: EC_{50} (48h) = 69.8 mg/l, *Scenedesmus subspicatus*: ErC_{50} (72 h) > 500 mg/l, *Pseudomonas putida:* EC_{50} (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

FULL SIDS SUMMARY

CAS NO: 106-88-7		SPECIES	PROTOCOL	RESULTS
PHYSICAL-CHEMICAL				
2.1	Melting Point			- 129.5 °C
2.2	Boiling Point			63.4 °C (at 1013 hPa)
2.3	Density			0.83 g/cm^3
2.4	Vapour Pressure			227 hPa (at 24 °C)
2.5	Partition Coefficient (Log P_{ow})		OECD 107	0.68 (at 25 °C)
2.6	Water Solubility			59 g/l at 20 °C
	pH			ca. 7 at 50 g/l 20°C
ENVIRONMENTAL FATE AND PATHWAY				
3.1.1	Photodegradation		Calculated	in air $t_{1/2}$ = 7.6 days
3.1.2	Stability in Water		Measured	$t_{1/2}$ = 156 hours
3.2	Monitoring Data			
3.3	Transport and Distribution		Henry-constant Calculated (Fugacity Level 1 type) acc. to Mackay	22.977 Pa*m^3/mol In Air 88.98 % In Water 11.01 % In Sediment 0 % In Soil 0 % In Biota 0 %
3.5	Biodegradation		ISO 14593	80 - 90 % after 28 days
			OECD 301 D	17 % after 29 days
			OECD 301 A	90 % after 28 days
ECOTOXICOLOGY				
4.1	Acute/Prolonged Toxicity to Fish	*Leuciscus idus*	DIN 38 412	LC_{50} (96 hours) = 100 - 215 mg/l
4.2	Acute Toxicity to Aquatic Invertebrates	*Daphnia magna*	Directive 84/449/EEC, C.2	EC_{50} (24 hours) = 159.7 mg/l
			comparable to OECD 202	EC_{50} (48 hours) = 69.8 mg/l
4.3	Toxicity to Aquatic Plants e.g. Algae	*Scenedesmus subspicatus*	DIN 38412, Part 9 comparable to OECD 201	EC_{50} (72 hours) = > 500 mg/l
4.4	Toxicity to bacteria	*Pseudomonas putida*	DIN 38412, Part 8	EC50 (17 hours) = 4,840 mg/l
(4.6.3)	Toxicity to Other Non-Mammalian Terrestrial Species (Including Birds)			

CAS NO: 106-88-7		SPECIES	PROTOCOL	RESULTS
TOXICOLOGY				
5.1.1	Acute Oral Toxicity	Rat	BASF Test	LD_{50} = 900 mg/kg b.m.
5.1.2	Acute Inhalation Toxicity	Rat	BASF Test	LC_{50} > 6,300 mg/m^3
5.1.3	Acute Dermal Toxicity	Rabbit	According to Smyth 1962	LD_{50} = 1,757 (1,255-2,546) mg/kg bm
5.4	Repeated Dose Toxicity	Rat	90 day inhalation study	NOAEC = 1200 mg/m^3 (nasal lesions)
		Mouse	90 day inhalation study	NOAEC = 150 mg/m^3 (nasal lesions)
5.5	Genetic Toxicity *In Vitro*			
A.	Bacterial Test (Gene mutation)	*Salmonella typhimurium*	OECD 471	+ (With external metabolic activation) + (Without external metabolic activation)
B.	Non-Bacterial *In Vitro* Test (Chromosomal aberrations)	CHO cells	Cytogenetic study	+/- (With metabolic activation) + (Without metabolic activation)
5.6	Genetic Toxicity *In Vivo*	Rat	Cytogenetic study, inhalative exposure	-
		Rat	Dominant lethal-test, inhalative exposure	-
5.8	Toxicity to Reproduction	Rat	(See 5.4, 5.6, 5.9 and *Further Data*	examination of reproductive tissues in subchronic and chronic studies lack of effects in teratogenicity study with pregestational exposure and in dominant-lethal test -
5.9	Developmental Toxicity/ Teratogenicity	Rat	Inhalative exposure pregestational and throughout gestation	NOAEC $\geq$ 3000 mg/m^3 (General toxicity) NOAEC $\geq$ 3000 mg/m^3 (Foetal data)
		Rabbit	Inhalative exposure pregestational and throughout gestation	NOAEC = 600 mg/m^3 (General toxicity) NOAEC > 3000 mg/m^3 (Foetal data)
Further Data	Corrosiveness/Irritation Skin	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	Maximasation Test	Not sensitising
	Carcinogenicity	Rat	2 Years inhalation up to 1,200 mg/m^3	Clear evidence in males (respiratory system) Equivocal evidence in females
		Mouse	2 Years inhalation up to 300 mg/m^3	No evidence in males and females
5.11	Experience with Human Exposure			

SIDS INITIAL ASSESSMENT REPORT

1. IDENTITY

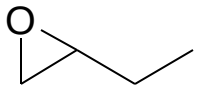
Chemical Name: 1,2-epoxybutane

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: $C_4 H_8 O$

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°C[1] and the vapour pressure is 227 hPa at 24°C [2]. A Henry's law constant of 22.977 $Pa*m^3*mol^{-1}$ 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/cm^3 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-epoxy butane. 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-epoxyutane, 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 intermediat 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 patition coefficient, indicates air to be the main target compartment as 89% partitions to the air and 11% goes into the water [5]. Slow degradation in air is to be expected according to the calculated photodegradation value of $t_{1/2}$ = 7.6 days [6]. Long range distribution via the atmosphere is therefore possible. The substance hydrolyses slowly ($t_{1/2}$ = 156 h) [7].
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 CO_2-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 SIMPLETREAT 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

LD_{50} rat (oral): 900 mg/kg body mass [12]
LC_{50} rat (inhalative): > 6,300 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.
LD_{50} 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 (at-mosphere 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 0.5ml 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 irrita tion. The intensity of the irritating effect depends on the application and the pos sibility 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/m^3, 2 males and 2 females at 4800 mg/m^3, 1 male at 2400 mg/m^3 and for mice: 2 males at 4800 mg/m^3, 2 males and 1 female at 2400 mg/m^3, 1 male at 1200 mg/m^3. Compound-related lesions included pulmonary hemorrhage and rhinitis in rats at 4800 mg/m^3 and nephrosis in mice at 2400 and 4800 mg/m^3

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/m^3) group and 2 male mice in the 150 mg/m^3 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/m^3 to 1200 mg/m^3 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/m^3	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/m^3). No treatment-related mortalities occured. Slight growth retardation was apparent for female rats and female mice in the 1800 mg/m^3 group only. Exposure to 1800 mg/m^3 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 occurence with no toxicologic significance . Hematologic analyses for female mice in the 450 and 1800 mg/m^3 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/m^3

LOAEC (rats and mice) 1800 mg/m^3

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 assay [14, 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 [21]). The use of S9-mix decreased the mutagenic activity.
Several tests with *Drosophila melanogaster* were inconclusive [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-butyleneoxid at doses of 750 or 3000 mg/m3 (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^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 *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^3, five times) [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, *cf*. 3.2.9, Toxicokinetics).

Conclusion
1,2-Epoxybutane is clearly mutagenic *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. [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/m³) no effects on the reproductive organs were observed.
Additionally, the lack of an effect from pre-gestational exposure in the developmental toxicity study (*cf*. 3.2.7) and a negative dominant-lethal test (*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^3 of 1,2-epoxybutane on days 1 through 24 of gestation (7 hours/day, 5 days/week), and foetuses were examined on the 30th 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/4litters 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. [24]

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. [24]

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, tracheabronchial lmyph 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.*" [14]

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 [8]
Daphnia magna:	EC_{50} (48h) = 69.8 mg/l [9]
Scenedesmus subspicatus:	EC_{50} (72 h) > 500 mg/l; EC_{20} (72 h)= 130 mg/l [10]
Pseudomonas putida:	EC_{50} (17 h) = 4,840 mg/l [11].

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 µg/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: LC_{50} (96 h)= 100 – 215 mg/l; *Daphnia magna*: EC_{50} (48 h) = 69.8 mg/l; *Scenedesmus subspicatus*: E_rC_{50} (72 h) > 500 mg/l; *Pseudomonas putida*: EC_{50} (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: LD_{50} rat (oral) 900 mg/kg body mass, 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 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/m^3, respectively). Systemic effects occurred at higher concentrations (rat 2400 mg/m^3: lower final mean body weight; mice 2400 mg/m^3: 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/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 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/m^3 throughout gestation. (rat: no maternal or foetal toxicity up to 3,000 mg/m^3, rabbit: NOAEC maternal = 750 mg/m^3, no foetal toxicity up to 3,000 mg/m^3).

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):	Flags: without flag, confidential, non confidential, WGK (DE), TA-Luft (DE), Material Safety Dataset, Risk Assessment, Directive 67/548/EEC, SIDS

1.0.1 OECD and Company Information

Type: lead organisation
Name: BASF AG
Partner: Product Safety Regulations, Toxicology, and Ecology c/o Dr. Hubert Lendle **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
01-DEC-1999

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

Source: BASF AG Ludwigshafen
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
07-DEC-1999

1.1.0 Details on Template

1.1.1 Spectra

1.2 Synonyms

.alpha.-Butylene oxide
Source: BASF AG Ludwigshafen
02-DEC-1992

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

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
Quantity refers to Germany
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 (29)

1.6.2 Classification

Classification: provisionally by manufacturer/importer
Class of danger: carcinogenic, category 3
R-Phrases: (40) Possible risks of irreversible effects
Source: BASF AG Ludwigshafen
08-SEP-2000 (29)

Classification: provisionally by manufacturer/importer
Class of danger: harmful
R-Phrases: (20/21/22) Harmful by inhalation, in contact with skin and if swallowed
Source: BASF AG Ludwigshafen
08-SEP-2000 (29)

Classification: provisionally by manufacturer/importer
Class of danger: highly flammable
R-Phrases: (11) Highly flammable
Source: BASF AG Ludwigshafen
08-SEP-2000 (29)

Classification: provisionally by manufacturer/importer
Class of danger: irritating
R-Phrases: (36/37/38) Irritating to eyes, respiratory system and skin
Source: BASF AG Ludwigshafen
08-SEP-2000 (29)

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

1.16 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 (26)

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 (23)

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 (24)

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)

Result:

°C	hPa
-10.0	40
0.0	70
24.0	227
31.7	315
40.3	444
50.6	654
63.2	1003
74.0	1412
86.1	2015
99.7	2949
121.0	5033
134.4	6918
153.6	1003

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 (23)

Value:
Method: other (measured)
Result:

°C	hPa
3.3	82.4
12.8	133.7
23.2	215.3
34.6	349.6
46.6	562.6
63.4	1.013

Source: BASF AG Ludwigshafen
Reliability: (2) valid with restrictions
26-SEP-2000 (21)

2.5 Partition Coefficient

log Pow: = .68 at 25 degree C
Method: other (measured)
Year:
Method: according to OECD 107
Source: BASF AG Ludwigshafen
Test substance: purity: 99.9 % (measured with GC)
Reliability: (2) valid with restrictions
16-NOV-1999 (3)

log Pow: = .416
Method: other (calculated)
Year:
Method: Increment method by REKKER with computerprogramm of firm ComuDrug Ltd.
Source: BASF AG Ludwigshafen
Reliability: (2) valid with restrictions
16-NOV-1999 (4)

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 (22)

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 (18)

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 (25)

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 (20)

Value: = -15 degree C
Type:
Method:
Year:
Source: BASF AG Ludwigshafen
Reliability: (4) not assignable
09-MAR-2000 (43)

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 (20)

2.9 Flammability

Result: highly flammable
Source: BASF AG Ludwigshafen
Reliability: (4) not assignable
Manufacturer / producer data without proof
07-DEC-1999 (19)

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 (19)

3.1.1 Photodegradation

Type: air
INDIRECT PHOTOLYSIS
Sensitizer: OH
Conc. of sens.: 500000 molecule/cm3
Rate constant: = .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 (2)

Type: air
INDIRECT PHOTOLYSIS
Sensitizer: OH
Conc. of sens.: 500000 molecule/cm3
Rate constant: = .0000000000023988 cm3/(molecule * sec)
Method:
Year: 1984 **GLP:**
Test substance:
Remark: mean tropospheric lifetime of approx. 7 d was calculated based on the equation t1/2 = ln 2/ (KOH*OH)
Source: BASF AG Ludwigshafen
Reliability: (2) valid with restrictions
17-NOV-1999 (35)

3.1.2 Stability in Water

Type: abiotic
t1/2 pH7: = 156 hour(s)
Method: other: hydrolysis
Year: 1985 **GLP:** no data
Test substance:
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).
Source: BASF AG Ludwigshafen
Reliability: (2) valid with restrictions
26-SEP-2000 (33)

Type: abiotic
t1/2 pH7: = 310 hour(s) at 25 degree C
Method: other: Estimation
Year: **GLP:**
Test substance:
Remark: Value based upon measured hydrolysis rates for propylene oxide.
Source: BASF AG Ludwigshafen
Reliability: (4) not assignable Handbook
26-SEP-2000 (36)

3.1.3 Stability in Soil

Type: **Radiolabel:**
Concentration:
Cation exch. capac.
Microbial biomass:
Method: other
Year: **GLP:**
Test substance:
Method: Estimation: PCKOCWIN, V 1.63
Result: log Koc = 0.6523, Koc = 4.491
Source: BASF AG Ludwigshafen
Reliability: (1) valid without restriction
17-NOV-1999 (5)

Type: **Radiolabel:**
Concentration:
Cation exch. capac.
Microbial biomass:
Method: other
Year: **GLP:**
Test substance:
Method: based upon estimated aqueous hydrolysis half-lifes
Result: The half-lifes in soil: 168 h - 310 h (7.0 d - 12.0 d).
Source: BASF AG Ludwigshafen
Reliability: (4) not assignable
Handbook
26-SEP-2000 (36)

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 (5)

Media:
Method: other (calculation)
Year:
Remark: H= 7.6*10^-4 (25 deg C) = 76 Pa m³ mol e-1
Source: BASF AG Ludwigshafen
Reliability: (4) not assignable
04-SEP-2000 (30)

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
Testsubstance:

3 day	= 0 %
7 day	= 17 %
10 day	= 20 %
14 day	= 34 %
21 day	= 86 %

Method: other
Year: **GLP:** yes
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 with 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 remaind 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 (34)

Type: aerobic
Inoculum: other bacteria
Concentration: 400 mg/l related to DOC (Dissolved Organic Carbon)
Degradation: = 100 % after 6 day
Testsubstance:

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:**
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 trating municipal sewage
Reliability: (2) valid with restrictions
17-MAR-2000 (8)

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: **GLP:** no
Test substance: as prescribed by 1.1 - 1.4
Method: EEC Directive 79-831 Annex V Part C, Closed Bottle Test
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 (11)

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: **GLP:**
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 (6)

3.6 BOD5, COD or BOD5/COD Ratio

3.7 Bioaccumulation

3.8 Additional Remarks

AQUATIC ORGANISMS

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:**
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, Durchfuehrung und Auswertung Biologischer Testverfahren (L1)" und "Bestimmung der Wirkung von Wasserinhaltstoffen aud 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:
Species: Daphnia magna (Crustacea)
Exposure period: 24 hour(s)
Unit: mg/l **Analytical monitoring:**
EC0: = 62.5
EC50: = 159.7
EC100: = 250
Method: Directive 84/449/EEC, C.2 "Acute toxicity for Daphnia"
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, 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 lenght 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: (2) valid with restrictions
19-MAR-2001 (7)

Type:
Species: Daphnia magna (Crustacea)
Exposure period: 48 hour(s)
Unit: mg/l **Analytical monitoring:**
EC0: = 31.3
EC50: = 69.8
EC100: = 125
Method: Directive 84/449/EEC, C.2 "Acute toxicity for Daphnia"
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% (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 lenght 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: (2) valid with restrictions
19-MAR-2001 (7)

4.3 Toxicity to Aquatic Plants e.g. Algae

Species: Scenedesmus subspicatus (Algae)
Endpoint:
Exposure period: 72 hour(s)
Unit: mg/l **Analytical monitoring:**
EC50: > 500
EC20 : = 130
Method: other: DIN 38412, part 9, Determination of inhibitory Effect on the cell multiplication
Year: **GLP:**
Test substance:
Method: according to OECD 201

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 lenght of 400 - 70 nm,
O2-content = 5.0 mg/l, test concentration: 3.91 – 500 mg/l, 8 test concentrations and control, 4 inculated parallels, 2 uninoculated parallels, pH 8.0 - 9.6,
inoculum density: 10000 cells/ml,
mesurements: 0, 24, 48 and 72 h,
parameter: promt chlorophyll an flooresecence at 685 nm as criterion for biomass (excitation with short light impulse at 435 nm
Reliability: (2) valid with restrictions
16-MAR-2001 (10)

4.4 Toxicity to Microorganisms e.g. Bacteria

Type: aquatic
Species: Pseudomonas putida (Bacteria)
Exposure period: 17 hour(s)
Unit: mg/l **Analytical monitoring:**
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 (9)

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

5.1 Acute Toxicity

5.1.1 Acute Oral Toxicity

Type: LD50
Species: rat
Strain:
Sex: male/female
Number of Animals: 5
Vehicle: CMC
Value: ca. 900 mg/kg bw
Method: other: BASF-Test
Year: **GLP:** no
Test substance:
Result: symptoms: dyspnea, apathy, diarrhea
Source: BASF AG Ludwigshafen
Test condition: 5 animals per dose and gender (values were taken from raw data)
Reliability: (2) valid with restrictions
05-SEP-2000 (17)

Type: LD50
Species: rat
Strain:
Sex: no data
Number of Animals: 3
Vehicle: other: corn oil
Value: 500 - 1000 mg/kg bw
Method: other: range finding study
Year: **GLP:** no
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 (46)

5.1.2 Acute Inhalation Toxicity

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

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
14-SEP-2000 (12)

Type: LC50
Species: rat
Strain:
Sex: 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%
Remark: 398 to 6550 ppm = 1,300 to 20,000 mg/m3
Result: Mortality: all rats exposed at 6550 ppm died, no other deaths occured; 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
14-SEP-2000 (40)

Type: other: IRT (inhalation risk test)
Species: rat
Strain:
Sex: no data
Number of Animals:
Vehicle: other: no
Exposure time:
Value:
Method: other: IRT
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 (27)

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 **GLP:**
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 (42)

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 classificat.:
Method: other: BASF-Test
Year: **GLP:** no
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 (13)

Species: rabbit
Concentration: undiluted

Exposure: Occlusive
Exposure Time: 1 hour(s)
Number of Animals: 4
PDII:
Result: corrosive
EC classificat.:
Method: other: BASF-test
Year: **GLP:** no

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
19-MAR-2001 (28)

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 (16)

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 sensitsation
Source: BASF AG Ludwigshafen
Test condition: male Hartley albino guinea pigs
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
19-MAR-2001 (32) (48)

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: = 400 ppm
LOAEL: = 800 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 (however 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: 10 animals per dose and gender
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
19-MAR-2001 (40) (45)

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
Year: **GLP:**
Test substance: other TS: 1,2-epoxybutane, purity >99% impurity: 1,2-butanediol
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 perfomed on 1 or 2 animals per exposure group.Multifocal pulmonary hemorrhage of moderate serverity 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
19-MAR-2001 (40)

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-butylene 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 issue 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 inaffected 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 (39)

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 (40)

Species: mouse **Sex:** male/female
Strain: B6C3F1
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-butylene oxide (single isomer) was obtained from the production facilities of Dow Chemical USA; purity greater than 99%
Result: 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 issue 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.

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

19-MAR-2001 (39)

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-butanediol

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.
Hemmorrhage 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.

19-MAR-2001 (40)

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.:
Metabolic activation: with and without
Result: positive
Method: OECD Guide-line 471 "Genetic Toxicology: Salmonella thyphimurium Reverse Mutation Assay"
Year: **GLP:** 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

STRAIN	S9	CONCENTRATION	REVERTANTS (multiple of control)
TA1535	with	2500 µg/plate	2
	with	5000 µg/plate	3
	without	2500 µg/plate	3
	without	5000 µg/plate	3.5
TA100	with	2500 µg/plate	1.5
	with	5000 µg/plate	2.5
	without	2500 µg/plate	2
	without	5000 µg/plate	3

Source: BASF AG Ludwigshafen
Test condition: plate incorporation assay
Reliability: (1) valid without restriction
05-SEP-2000 (15)

Type: Ames test
System of testing: Salmonella typhimurium TA 1535, TA 100, TA 1537, TA 98
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: **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
05-SEP-2000 (40)

Type: Cytogenetic assay
System of testing: Chinese Hamster Ovary cells
Concentration: 16 to 500 µg/ml
Cytotoxic Conc.:
Metabolic activation: without
Result: positive
Method: other: Galloway et al., 1985, Environ Mutagen, 7, 1
Year: **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)

Type: HGPRT assay
System of testing: human lymphoblastoid cells
Concentration: 8.9 - 33.8 mg/l
Cytotoxic Conc.: 26.6 mg/l
Metabolic activation: without
Result: positive
Method: other
Year: **GLP:** no data
Test substance: other TS: 1,2-Epoxybutane, no further data
Test condition: abstract, no further information was given.
Reliability: (4) not assignable
abstract, no further information was given
23-MAR-2001 (31)

Type: Mouse lymphoma assay
System of testing: L5178Y mouse lymphoma cells
Concentration: 50-800 µg/ml
Cytotoxic Conc.:
Metabolic activation: with and without
Result: positive
Method: other: Clive et al., 1979, Mutat Res, 59, 61
Year: **GLP:** no
Test substance: other TS: 1,2-epoxybutane, purity >99% impurity: 1,2-butanediol
Source: BASF AG Ludwigshafen
Test condition: small and large colonies not distinguished
Reliability: (2) valid with restrictions
05-SEP-2000 (40)

5.6 Genetic Toxicity 'in Vivo'

Type: Cytogenetic assay
Species: rat **Sex:** male/female
Strain: Sprague-Dawley
Route of admin.: inhalation
Exposure period: 7 hours single exposure or 5 consecutive days
Doses: 250, 1000 ppm (0.75, 3.0 mg/l)
Result: negative
Method: other: following OECD Guideline 475 with inhalative exposure
Year: **GLP:** no
Test substance: other TS: 1,2-butyleneoxide, purity 99%, obtained from Aldrich Chemical Co. Ltd.
Remark: 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
Result: 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.

Source: BASF AG Ludwigshafen
Test condition: Sprague-Dawley rats (10 animals per dose, gender and time) were exposed to 1,2-epoxybutane at concentrationss 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
19-MAR-2001 (38) (44)

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: **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 vergin females each day positive control was EMS, negative control concurrent no test substance
Reliability: (2) valid with restrictions
05-SEP-2000 (38) (44)

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: **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.
Incidences 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.
Incidences 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.
Incidences 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 significant increased compared to controls.
Treatment-related, non-neoplastic changes in the nose included inflammation, epithelial hyperplasia, squamous metaplasia, hyperostosis of the nasal turbinate 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, tracheabronchial lmyph nodes, and urinary bladder.

Reliability: (2) valid with restrictions
26-SEP-2000 (40)

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:

Doses: 50, 100 ppm (0.150, 0.300 mg/l)
Result:
Control Group: yes, concurrent vehicle
Method: other: NTP-Program
Year: **GLP:** no data
Test substance: other TS: 1,2-epoxybutane, purity >99% impurity: 1,2-butanediol
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 suppurative 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, tracheabronchial lmyph nodes, and urinary bladder.
Reliability: (2) valid with restrictions
26-SEP-2000 (40)

5.8 Toxicity to Reproduction

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

Method:
Year: **GLP:**
Test substance:
Remark: See repeated-dose toxicity studies (chapter 5.4), dominant-lethal test (chapter 5.6) and developmental toxicity studies (chapter 5.9).
Source: BASF AG Ludwigshafen
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; 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: 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 servere 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
19-MAR-2001 (41)

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 Maternalt.: 250 ppm
NOAEL Teratogen.: >= 1000 ppm
Method:
Year: **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 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. 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. Supperative 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 exposureed 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 were 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 fetuses 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
19-MAR-2001 (41)

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

26-SEP-2000 (37)

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
28-SEP-2000 (47)

5.11 Experience with Human Exposure

Remark: no data available
Source: BASF AG Ludwigshafen
10-OCT-2000

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