
Chemical Name: Chloroprene
CAS No: 126-99-8
Sponsor Country: GERMANY

National SIDS Contact Point in Sponsor Country: Mr. Jan Ahlers

HISTORY:

SIDS Dossier and Testing Plan were reviewed at the SIDS Review Meeting in September 1993 where the following SIDS Testing Plan was agreed:

| no testing | ( X ) |
| testing    | ( )  |

SIAR was already discussed at SIAM 3 (February 1995) where the environmental part of the risk assessment was agreed. It was also decided that the results of NTP studies on carcinogenicity, genotoxicity and reprotoxicity that were conducted at that time should be integrated in the toxicological part of the risk assessment.

COMMENTS:

Deadline for circulation: 31st of July 1998

Date of Circulation: 13th of August 1998
(To all National SIDS Contact Points and the OECD Secretariat)
SIDS INITIAL ASSESSMENT PROFILE

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<td>Chemical Name</td>
<td>Chloroprene</td>
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<tr>
<td>Structural Formula</td>
<td>H₂C=CH-C(Cl)=CH₂</td>
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CONCLUSIONS AND RECOMMENDATIONS

Environment

The chemical is not readily biodegradable and has a low bio- or geoaccumulation potential. PEC/PNEC ratios are calculated as less than one. The chemical is currently considered of low potential risk and low priority for further work.

Human Health

The chemical is considered as a carcinogen. In the Sponsor country, control measures are in place to avoid significant human and environmental impact, including prevention of accidental exposure. In situations where this is not the case, risk assessment and if necessary, risk reduction measures are recommended.

SHORT SUMMARY WHICH SUPPORTS THE REASONS FOR THE CONCLUSIONS AND RECOMMENDATIONS

The production volume of Chloroprene is ca. 52,000 t/a in Germany, 36,000 t/a in France, 35,000 t/a in Northern Ireland, 163,000 t/a in the USA and 87,000 t/a in Japan. It is used as intermediate, for the production of polychloroprene. Chloroprene is "not readily biodegradable" and has a low bio- or geoaccumulation potential. The most sensitive environmental species to chloroprene is *Daphnia magna* (21d-NOEC = 3.2 mg/l). The derived PNEC is 32 µg/l.

In a recent 90-day inhalation study the NOAEL was determined to be 32 ppm for rats and mice. For the hamster the NOAEL for repeated dose (2-year-study) was 10 ppm. For reproductive toxicity no damaging effects were recorded in rats in a study in which two successive generations of rats were exposed up to a concentration of 100 ppm, although other poorly documented tests describe an influence on the male fertility of rats at smaller concentrations. No effect on reproductive parameters was noted for rats and mice in the recent 90-day-study after inhalation up to 80 ppm. No teratogenic effect was observed with rabbits up to 175 ppm. In the recent 2-year inhalation study chloroprene was found to be carcinogenic in rats and mice. The data on short-term mutagenicity are conflicting; however, in the recent micronucleus test with mice of the 90-day inhalation study no induction of micronucleated erythrocytes could be detected.

The aquatic PEC was estimated to be 0.25 µg/l. No data on consumer or workplace exposure is available yet.

NATURE OF FURTHER WORK RECOMMENDED

The chemical is considered as a carcinogen. In the Sponsor country, control measures are in place to avoid significant human and environmental impact, including prevention of accidental exposure. In situations where this is not the case, risk assessment and if necessary, risk reduction measures are recommended.
### Full SIDS Summary

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<td>NA</td>
<td>-130 °C</td>
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<td>2.2 Boiling Point</td>
<td>NA</td>
<td>59.4 °C (at 101.3 kPa)</td>
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<td>NA</td>
<td>959.8 kg/m³</td>
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<td>NA</td>
<td>25 kPa at 20 °C</td>
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<td>2.5 Partition Coefficient (Log Pow)</td>
<td>CLogP</td>
<td>2.2</td>
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<td>2.6 A Water solubility</td>
<td>NA</td>
<td>256-480 mg/l at 20 °C</td>
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<tr>
<td>B pH</td>
<td>/</td>
<td>at °C</td>
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<td>2.12 Oxidation : Reduction potential</td>
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<td>3.1.1 Photodegradation</td>
<td>calc. (Atkinson)</td>
<td>In air $T_{1/2}$ = ca 18 hours</td>
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<td>$T_{1/2}$ = / days</td>
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<td>In air = 0.00036 mg/m³</td>
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<td>calculated (fugacity level 1 type)</td>
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<td>4.2 acute/prolonged toxicity to aquatic invertebrates (daphnia)</td>
<td>OECD GL 202 part 1</td>
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<td>Navicula seminulum</td>
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<td>5.1.1 acute oral toxicity</td>
<td>rat</td>
<td>NA</td>
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<td>mouse</td>
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<td>5.1.2 acute inhalation toxicity</td>
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<td>5.1.3 acute dermal toxicity</td>
<td>rat</td>
<td>NA</td>
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<td>5.4 repeated dose toxicity</td>
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<td>90-day - inhalation</td>
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<td>mouse</td>
<td>90-day - inhalation</td>
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<td>hamster</td>
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<td>5.5 genetic toxicity in vitro</td>
<td>bacterial test (gen mutation) S. Typhimurium</td>
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<td>non-bacterial in vitro test (chromosomal aberrations) Chinese Hamster V79 Human lymphocytes</td>
<td>SCE</td>
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<td>5.6 genetic toxicity in vivo</td>
<td>rat &amp; mouse</td>
<td>dominant lethal as, micronucleus</td>
</tr>
<tr>
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<td>mouse</td>
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<td>rat</td>
<td>2-year - inhalation</td>
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<td>mouse</td>
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<td></td>
<td>hamster</td>
<td>2-year - inhalation</td>
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<td>5.8 toxicity to reproduction</td>
<td>rat (Wistar)</td>
<td>NA (2-generation-study)</td>
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<td>5.9 developmental toxicity / teratogenicity</td>
<td>rat</td>
<td>teratogenicity</td>
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<td></td>
<td>rabbit</td>
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<td>5.11 experience with human exposure</td>
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CAS-NO.: 126-99-8

OECD SIDS CHLOROPRENE

UNEP Publications
SIDS Initial Assessment Report

1. Identity

OECD-name: 2-Chlorbuta-1,3-diene
synonym: Chloroprene
CAS-Nr. 126-99-8
Empirical formula: C₄H₅Cl
Structural formula: H₂C=CH-C(Cl)=CH₂
Purity of industrial product: > 99.7 %
2. Exposure

2.1 General discussion

Production levels (1989):

- Germany 52,000 t (1993)
- France 36,000 t
- Nthrn. Ireland 35,000 t
- USA 163,000 t
- Japan 87,000 t

In Germany all the produced chloroprene is used as an intermediate in chemical industry for the synthesis of polychloroprene. There is no export.

In Sweden as well, chloroprene is used as an intermediate for polymers (no information about volumes). In Denmark, it is found in 35 products with a typical concentration of 10%, and in Finland it is found in two adhesives with a content of 15 - 18 % (no further data available).

According to the producer such high contents of monomers are very unlikely and probably reflect polymeric chloroprene contents. The residual contents of monomeric chloroprene in polymeric products is at maximum 500 ppm (polychloroprene latices).

2.2 Environmental exposure

2.2.1 General

In Germany, the following amounts of chloroprene are released into the environment (one production site):

- air: 268 kg/a from the polymerisation process
- 29.5 t/a from the drying process of polychloroprene
- 22.5 kg/a from the use of polychloroprene endproduct (emission of the monomer)
- 2.25 t/a from the use of Latex (emission of the monomer)
- water 16.5 kg/a waste water treatment effluents (production and processing)

Additionally 1100 t/a of wet waste resulting from polymerisation and further processing are regularly landfilled. It contains up to 500 mg monomere per kg, i.e. a total amount of 550 kg/a of free chloroprene.

According to the producer, the drying process of polychloroprene will be altered in 1994 so as to incinerate all the flue gases. The reduction of the emissions is expected to be ca. 90% i.e. the remaining emissions to the atmosphere will be ca. 3 t/a.

2.2.2 Environmental fate

Chloroprene has a water solubility of 0.256 resp. 0.48 g/l (20°C, two different sources) and a vapour pressure of about 250 hPa at 20°C. The calculated log Pow’s of 1.73, 2.06 and 2.2 (different methods) indicate that there is no relevant potential for bio- or geoaccumulation. With a fragment incrementation method (Meylan et al., 1992), the Koc can be estimated to be 68 l/kg.

Based on the physico-chemical properties, the preferred environmental compartment of chloroprene is the atmosphere (Fugacity model level I: >99.9%).
A closed bottle test according to OECD guideline 301D demonstrated that chloroprene is not readily biodegradable. There are no test data about inherent biodegradability. There are no data about abiotic degradation (photolysis, hydrolysis) in water. Due to the rapid volatilisation from water, those processes are not expected to be of relevance. The calculated half-lives due to photochemical-oxidative degradation in the atmosphere according to the estimation method by Atkinson are 18.3 h (OH-radicals) and 9.9 d (Ozone).

### 2.2.3 Exposure assessment

#### a) Hydrosphere

In Germany 16.5 kg/a are emitted into the river Rhine. For a PEC calculation, a low flow (which is exceeded in 90% of all times) of 690 m$^3$/s is used.

The predicted local environmental concentration is

$$PEC_{\text{local water}} = \frac{16.5 \text{ kg/a}}{690 \text{ m}^3/\text{s}} = 0.76 \text{ ng/l}$$

In the USA a concentration of 2.5 ppb = 2.5 µg/l in waste water effluent was estimated by the US-EPA. A dilution factor of 10 for waste water entering a river should be used. In this case the PEC is:

$$PEC_{\text{local water}} = 2.5 \text{ µg/l} : 10 = 0.25 \text{ µg/l}$$

#### b) Atmosphere

The preferred environmental compartment of chloroprene is the atmosphere, where the compound is rapidly degraded.

As shown above, about 30 t/a resp. 3 t/a are emitted by the producing/processing plant. A gaussian plume model calculation (cf Appendix 1) shows that a maximum downwind concentration of

$$PEC_{\text{local air}} = 23 \text{ µg/m}^3$$

at ground level is predicted. With the planned emission reduction, this concentration should fall to ca. 2.3 µg/m$^3$.

US-EPA estimated a maximum concentration of 5.1 ppb ( = 18.7 µg/m$^3$) for ambient air in the vicinity of a manufacturing plant.

There are no further data available for other countries.

#### c) Soil

Exposure to soil could be expected in the vicinity of production/processing plants due to atmospheric deposition. With the above described emission rates, a deposition rate of $2.85 \times 10^{-13}$ kg.m$^{-2}$.s$^{-1}$ resp. $0.285 \times 10^{-13}$ kg.m$^{-2}$.s$^{-1}$ can be calculated (cf. Appendix 1). Based on a default biodegradation half-live of 500 days and a Koc-value of 68 l/kg, a PEC of 24 µg/kg resp 2.4 µg/kg is calculated. The pore water concentration is

$$PEC_{\text{local soil}} = 20 \text{ µg/l resp. 2 µg/l}$$

if the flue gases are incinerated.

The concentration in groundwater is estimated with the same model at 3.5 µg/l resp. 0.35 µg/l.

#### d) Regional concentrations

Only about 2.25 t/a are released diffusely to the environment through emission of residual monomers from the use of Latex. Compared to the local emission rate at production and processing, the diffuse releases can be neglected.
2.3 Consumer exposure

No data on consumer exposure are available yet.

2.4 Exposure via the Environment

The highest exposure to the general population via the environment would be expected through ambient air in the vicinity of a production/processing plant and through drinking water processed from groundwater.

The local concentration in air was estimated at 2.3 - 23 µg/m³. Based on the physical chemical properties of chloroprene, a significant removal during processing of ca. 50% is to be expected due to its high volatility (EUROPEAN SCIENCE FOUNDATION, 1984). Therefore, the concentration in drinking water is assumed to be 1 - 10 µg/l.

2.5 Workplace exposure

No data on workplace exposure are available yet. Occupational exposure limit values of 10 ppm = 37 mg/m³ have been fixed in several countries.
3. Toxicity

3.1 Human Toxicity

a) Acute Toxicity

**SIDDS data:**

-Animal data:

Independent of the way of application, the acute toxicity of chloroprene is moderate (rat, LD50 oral 251-450 mg/kg bw; rat LC50 inhalation 11800 mg/m³, 4 h; rat, LD50 s.c. 479-1916 mg/kg bw). Acute intoxication is characterized by central nervous system depression. The local irritation after inhalation of lethal concentration caused lesion of the lungs. Single inhalation has a systemic toxic effect on the liver.

-Human experience:

The primary effects of acute exposure to high concentrations (details not available) of chloroprene in air are central nervous system depression, irritation of skin and mucous membranes and respiratory difficulties.

**Conclusion:** moderate acute toxicity

**Recommendation:** no need for follow-up test

**Priority setting:** low priority or concern

b) Repeated Dose Toxicity

**SIDDS data:**

Short term/long term toxicity

-Animal data

Most of the studies deal with the effect of chloroprene after repeated inhalation by rats. Only a small number of studies are adequately conducted and documented.

At concentrations in excess of 144 mg/m³ (four-week study) and ≥ 37 mg/m³ (chronic study) chloroprene causes an increase in liver weight in rats with no histopathological abnormalities. In a subacute study, microscopic liver lesions were visible only after lethal concentrations (≥ 593 mg/m³). 26 weeks’ exposure to 368 mg chloroprene/m³ by inhalation caused no histopathological changes. Slight liver cell lesions are observed more frequently in rats following two years of exposure to 184 mg/m³. The results of clinical biochemistry determinations are normal in all appropriate studies. From the available information it is not possible to derive a NOAEL for the rat. For the hamster the NOAEL was 37 mg/m³ (10 ppm) in a two-year study.

In a recent 90-day inhalation study in rats and mice the NOAEL was determined to be 12 ppm for rats and 32 ppm for mice. In rats and mice exposed to 0, 5, 12, 32 and 80 ppm a generally similar pattern of toxicity was noted. A 200 ppm exposure group was also included for rats only. In mice, no lethality occurred but a slight reduction in body weights was seen at 80 ppm. No effect on
reproductive parameters (sperm count and morphology and female estrous cyclicity or cycle length) was noted. Hematology and clinical parameters were unaffected. Nonprotein sulfhydryl content of lungs and liver were reduced at 80 ppm through wk 12. At necropsy, forestomach epithelial hyperplasia was seen in some 80 ppm mice. In rats, degeneration and metaplasia of olfactory epithelium occurred ≥ 32 ppm. Additionally, anemia, hepatocellular necrosis (reflected in transient increases in serum ALT, GDH, and SDH activities) and reduced sperm mobility was seen at 200 ppm. While renal weights were increased somewhat, no kidney histopathology was noted. Neurobehavioral assessments showed no exposure-related effects on motor activity, forelimb/hindlimb grip strength, or startle response. (Melnick, R.L: et al., Toxicology 108, 79-91 (1996); NTP Technical Report No. 467, 1998).

-Human experience

Many symptoms of chronic chloroprene exposure at the workplace are described. Because the reported data give no information about exposure concentration and the purity of chloroprene, it is not possible to ascribe the findings to chloroprene itself and to interprete them in terms of dose-response relationship.

Carcinogenicity

-Animal data

To investigate the carcinogenic potential of chloroprene, it was tested in rats by oral, subcutaneous and intratracheal administration and in mice by skin application. No carcinogenic effects were found. However these studies are inadequate for drawing reliable conclusions regarding the carcinogenic potential of chloroprene, because they are of bad quality with respect to methodology, information on the purity of chloroprene and the way of reporting.

There was no indications for carcinogenic properties of chloroprene in more recent long term inhalation studies in rats and hamster. However the study with the rats was considered to be also inadequate to allow an evaluation of the carcinogenicity of chloroprene, because the majority of the low dose animals died before the end of the study due to a technical defect in the ventilation system. Three groups of 100 Wistar rats and Syrian golden hamsters of each sex were exposed by inhalation to 0, 10, or 50 ppm (v/v) ß-chloroprene for 6 h/day, 5 days a week for up to 24 and 18 months, respectively. After 72 weeks a technical fault in the chamber operation procedures resulted in the accidental death of 87 male and 73 female rats at 10 ppm unrelated to ß-chloroprene. Otherwise, survival of the remaining 10 ppm rats and the rats exposed at 50 ppm was unaffected by exposure. Survival among both groups of hamsters was higher than the controls. All treated rats exhibited slight restlessness during exposure, but only during the first few weeks of the test. At 50 ppm, rats also showed an increased incidence of alopecia, slight growth retardation, and an increased incidence of foci of altered liver cells, a change frequently seen in aged rats. Hamsters showed only a slight growth retardation and a slight reduction in amyloidosis at 50 ppm. No serious adverse effects were seen in either species at 10 ppm. (Reuzel, P.G.J. & Bosland, M.C., CIVO TNO Report No. R 6328, 1980; Trochimowicz, H.J. et al., 1998)

In another recent study, groups of 50 male and 50 female F344/N rats were exposed to chloroprene at concentrations of 0, 12.8, 32, or 80 ppm by inhalation, 6 hours per day, 5 days per week, for 2 years (NTP Technical Report No. 467, 1998).

Survival of males exposed to 32 or 80 ppm was significantly lower than that of the chamber control group. Mean body weights of males exposed to 80 ppm were lower than those of the chamber controls after week 93. Masses of the torso were observed during the study in exposed female
OECD SIDS CHLOROPRENE

groups, and these clinical findings correlated with mammary gland fibroadenomas observed at necropsy.

The incidences of squamous cell papilloma and squamous cell papilloma or squamous cell carcinoma (combined) of the oral cavity in male rats exposed to 32 ppm and male and female rats exposed to 80 ppm were significantly greater than those in the chamber controls and exceeded the historical control ranges.

The incidences of thyroid gland follicular cell adenoma or carcinoma (combined) in males exposed to 32 or 80 ppm were significantly greater than that in the chamber control group and exceeded the historical control range. Though the incidences of follicular cell adenoma and follicular cell adenoma or carcinoma (combined) in 80 ppm females were not significantly greater than those of the chamber controls, they did exceed the historical control range for these neoplasms.

The incidences of alveolar epithelial hyperplasia of the lung were significantly greater in all exposed groups of males and females compared to those in the control groups. The incidences of alveolar/bronchiolar carcinoma and alveolar/bronchiolar adenoma or carcinoma (combined) in 80 ppm males were slightly greater than those of the chamber control group. Although these incidences were not significant, they exceeded the historical control range for these neoplasms. The incidence of alveolar/bronchiolar adenoma, although not significant, was greater in 80 ppm females than in the control group.

The incidences of multiple fibroadenoma of the mammary gland in all exposed groups of females were greater than that in the chamber control group. The incidences of fibroadenoma (including multiple fibroadenoma) in 32 and 80 ppm females were significantly greater than that in the chamber controls. The incidences of fibroadenoma in the chamber control group and in all exposed groups of females exceeded the historical control range.

The severity of nephropathy in male and female rats was slightly greater than that in the chamber controls. Positive trends in the incidences of renal tubule adenoma and hyperplasia were also observed in males and females. Additional kidney sections from male and female control and exposed rats were examined to provide a clearer indication of the potential effects of chloroprene on the kidney. The combined single- and step-section incidences of renal tubule hyperplasia in 32 and 80 ppm males and 80 ppm females and the incidences of adenoma in all exposed males were significantly greater than those in the controls.

A slight increase in transitional epithelium carcinoma of the urinary bladder was observed in 80 ppm females. In addition, one 32 ppm male had a transitional epithelium carcinoma and one 80 ppm male had a transitional cell papilloma. These findings are noteworthy because no urinary bladder neoplasms have been observed in chamber control male or female 344/N rats.

In the nose, the incidences of atrophy, basal cell hyperplasia, metaplasia, and necrosis of the olfactory epithelium in the nose in 32 and 80 ppm males and females and the incidences of atrophy and necrosis in 12.8 ppm males were significantly greater than those in the chamber control groups. The incidences of chronic inflammation were significantly increased in males exposed to 12.8 or 32 ppm and in males and females exposed to 80 ppm. The incidences of fibrosis and adenomatous hyperplasia in 80 ppm males and females were significantly greater than those in the chamber controls. Generally, lesions in the nasal cavity were minimal to mild in severity.

Groups of 50 male and 50 female B6C3F1 mice were exposed to chloroprene at concentrations of 0, 12.8, 32, or 80 ppm by inhalation, 6 hours per day, 5 days per week, for 2 years (NTP Technical Report No. 467, 1998).
Survival of males exposed to 32 or 80 ppm and of all exposed female groups was significantly lower than that of the chamber controls. The mean body weights of 80 ppm females were significantly less than those of the chamber control group after week 75. Clinical findings included masses of the head, which correlated with harderian gland adenoma and/or carcinoma in 32 ppm males and 80 ppm males and females. Dorsal and lateral torso masses of female mice correlated with mammary gland neoplasms in 32 and 80 ppm females and subcutaneous sarcomas in 12.8, 32, and 80 ppm females.

The incidences of alveolar/bronchiolar neoplasms in the lungs of all groups of exposed males and females were significantly greater than those in the chamber control groups and generally exceeded the historical control ranges. The incidences of multiple alveolar/bronchiolar adenoma and alveolar/bronchiolar carcinoma were increased in all exposed groups of males and females. The incidences of bronchiole hyperplasia in all exposed groups of males and females were significantly greater than those in the chamber control groups.

Male mice had a pattern of nonneoplastic liver lesions along with silver-staining helical organisms within the liver consistent with infection with *Helicobacter hepaticus*. An organism compatible with *H. hepaticus* was confirmed with a polymerase chain reaction restriction fragment length polymorphism (PCR-RFLP)-based assay. In NTP studies with *H. hepaticus*-associated hepatitis, increased incidences of hemangiosarcoma have been seen in the livers of male mice. Therefore, hemangiosarcomas of the liver were excluded from the analyses of circulatory (endothelial) neoplasms in males in this study. Even with this exclusion, the combined occurrence of hemangiona or hemangiosarcoma at other sites was significantly increased at all chloroprene exposure concentrations in males and in 32 ppm females. Incidences of neoplasms at other sites in this study of chloroprene were not considered to have been significantly impacted by the infection with *H. hepaticus* of its associated hepatitis.

The incidences of harderian gland adenoma and harderian gland adenoma or carcinoma (combined) in males exposed to 32 or 80 ppm and females exposed to 80 ppm were significantly greater than those in the chamber controls. The incidences of harderian gland adenoma or carcinoma (combined) in 32 ppm males and 80 ppm males and females exceeded the historical control ranges.

The incidences of mammary gland carcinoma and adenoacanthoma or carcinoma (combined) in 80 ppm females were significantly greater than those in the chamber control group. The incidences of mammary gland carcinoma and of adenoacanthoma in 32 and 80 ppm females exceeded the historical control ranges. Multiple mammary gland carcinomas occurred in exposed females.

The incidences of hepatocellular carcinoma in all exposed female groups and hepatocellular adenoma or carcinoma (combined) in 32 and 80 ppm females were significantly greater than those in the chamber controls; in the 80 ppm group the incidence exceeded the historical control ranges for carcinoma and adenoma or carcinoma (combined). The incidence of eosinophilic foci in 80 ppm females was also significantly greater than that in chamber controls.

The incidences of sarcoma of the skin were significantly greater in all exposed groups of females than in the chamber controls. The incidence of sarcoma of the mesentery were also increased in all exposed groups of females.

The incidences of squamous cell papilloma in 80 ppm females was greater than that in the chamber controls; the difference was not significant, but the incidence exceeded the historical control range. Males also showed a positive trend in the incidence of squamous cell papilloma of the forestomach. In males and females exposed to 80 ppm, the incidences of hyperplasia of the forestomach epithelium were significantly greater than those in the chamber controls.
Carcinomas of the Zymbal's gland were seen in three 80 ppm females; and two carcinomas metastasized to the lung. Zymbal’s gland carcinomas have not been reported in control female mice in the NTP historical database.

The incidence of renal tubule adenoma in 80 ppm males was greater than that in the chamber controls. Though this difference was not significant, the incidence of this rare neoplasm exceeded the historical control range. The incidences of renal tubule hyperplasia in males exposed to 32 or 80 ppm were significantly greater than that in the chamber controls. Additional sections of kidney were examined from control and exposed males to verify these findings. The combined single- and step-section incidence of renal tubule adenomas in 80 ppm males and the combined incidences of renal tubule hyperplasia in all groups of exposed male mice were greater than those in the chamber controls.

The incidences of olfactory epithelial atrophy, adenomatous hyperplasia, and metaplasia in 80 ppm males and females were significantly greater than those in the chamber controls. The incidences of hematopoietic proliferation of the spleen in 32 and 80 ppm males and in all groups of exposed females were significantly greater than those in the chamber controls.1

The results of two short-term carcinogenicity studies are contradictory. Chloroprene did not act as a tumour promoter in a study with dimethylbenzanthracene as initiator.

- Human experience

The results of epidemiologic studies of workers exposed to chloroprene of an unknown concentration and purity are not consistent and cannot be used to substantiate or refute a possible cancer risk in occupationally exposed workers.

Conclusion: Chloroprene is considered as a carcinogen.

Recommendation: In the Sponsor country control measures are in place to avoid significant human and environment impact, including prevention of accidental exposure. In situations where this is not the case, risk assessment and if necessary, risk reduction measures are recommended.

“Specific measures were taken in order to reduce significantly the residual monomer content in polychloroprene latices. By operating a stripping column, chloroprene content could be reduced from 500 ppm to less than 30 ppm.”2

c) Reproductive Toxicity

SID data:

- Animal data

No adverse effects on the male fertility of rats and mice could be determined after repeated exposure to chloroprene in concentrations of up to 368 mg/m³(Appelman, L.M. & Dreef-van der Meulen, H.C., CIVO TNO Report No. R 6634, 1979). Contrary to this, other studies which give no information about the purity of the chloroprene, the generation of the test atmosphere and the analysis of the chloroprene describe an influence on the male fertility of rats even with considerably smaller chloroprene concentrations (e.g. 1.69 mg/m³).

2 refers to correspondence dated October 13, 1999 BAYER AG to BgVV and internal cummunication BAYER AG dated August 16, 2002
The inhalation of chloroprene during gestation is, up to a concentration of 92 mg/m$^3$ (25 ppm), without significant influence on the dams and offspring in rats. Concentrations ≥ 276 mg/m$^3$ (≥ 75 ppm) have little maternal toxic effect. The offspring of these dams show only decreased body weights. A teratogenic effect could not be determined in any concentration (up to 175 ppm) (Koeter, H.B.W.M. & Appelman, L.M., CIVO TNO Report No. 6387, 1980). Contrary to this are the results of some studies that cannot, however, be evaluated due to their inadequate documentation.

Chloroprene was not teratogenic and did not adversely affect female reproductive parameters in the developmental toxicity study in rabbits exposed to 175 ppm or less (Matt, T.J. et al., NTIS/DE94012384, April 1994).

A reproduction study, in which two successive generations of rats (F$_0$ and F$_1$-generation) were exposed to chloroprene (37, 121, 368 mg/m$^3$ i.e. 10, 33, 100 ppm), reveals no adverse effect on the reproductive performance up to a concentration of 368 mg/m$^3$. Growth retardation was observed in the F0-generation at 368 mg/m$^3$ (100 ppm) and in the F1-generation at 121 mg/m$^3$ (33 ppm) and 368 mg/m$^3$ (100 ppm) (Appelman, L.M. & Dreef-van der Meulen, H.C., CIVO TNO Report No. R 6225, 1979).

In the recent 90-day inhalation study in which rats and mice were exposed to 0, 5, 12, 32 and 80 ppm chloroprene no effect on reproductive parameters (sperm count and morphology and female estrous cyclicity or cycle length) was noted for both species. In rats, for which a 200 ppm exposure group was included, reduced sperm mobility was seen at this exposure concentration (Melnick, R.L: et al., Toxicology 108, 79-91 (1996)).

- Human experience

With respect to human reproduction there are weak indications for disturbance of sexual functions in both sexes and for negative influences on pregnancy after exposure of male workers to unknown concentrations of chloroprene (purity not specified). But overall there were not enough reliable data available to draw meaningful conclusions.

Conclusion: The appropriate studies show no adverse effect of chloroprene on reproductive performance and development.

Recommendation: No further studies recommended.

Priority setting: Low priority or concern.

d) Genetic Toxicity

SIDS data:

- Experimental data

The results of genetic toxicity testing are not uniform. The Ames test is positive with and without metabolic activation. Westphal et al. (1994) reported freshly prepared chloroprene was not mutagenic whereas an aged chloroprene preparation was mutagenic, especially in the presence of rat liver S9. No induction of point mutation was observed in Chinese hamster V79 cells. The SCE rate was increased in human lymphocytes (no/no adequate/full information on impurities is given). Repeated inhalation did not cause an increase of SCE in the rat bone marrow. A non-dose dependent increase in recessive lethal mutation was observed in Drosophila melanogaster. Recent sex-linked recessive lethal assays showed no response to chloroprene by either feeding or injection
(Foureman et al., Environ. Mol. Mutagen. 23, 208-227 (1994)). Very low doses of chloroprene (no/no adequate/full information on impurities is given) caused dominant lethal mutation in rats and mice, while corresponding studies involving higher concentrations produced negative results. The results of chromosome aberration studies in vivo are contradictory. The negative result of the recent micronucleus study as part of the 90-d inhalation study with mice (NTP Technical Report No. 467, 1998) supports the assessment that chloroprene does not induce micronucleated erythrocytes in vivo which has been shown in the majority of the data available up to the NTP study.

- Human experience

Because studies which describe an increased frequency of chromosome aberrations in lymphocytes of humans do not specify the concentration and purity of chloroprene to which workers were exposed, it is not possible to draw meaningful conclusions.

**Conclusion:** The conflicting data of the short term mutagenicity tests make a final conclusion with respect to the mutagenic potential of chloroprene difficult. A possible explanation for the positive results, mainly described in the bad reported studies, may be some unknown impurities.

**Recommendation:** Additional investigations would be desirable. In these efforts the purity of chloroprene should taken in account.

**Priority setting:**

e) Other toxicological endpoints

Based on the systemic effect that was described after oral, inhalation and dermal application, it can be assumed that an absorption takes place after these routes of application. There is no knowledge about the distribution of chloroprene in the body. In analogy to structure related substances such as vinyl chloride and isoprene, the formation of a mono- respectively diepoxides appears probable. Also, the further assumption that a conjugation with glutathione follows in the second phase of the biotranformation has been verified.

With rabbits after a contact duration of 24 hours a mild to moderate redness with oedema formation occurred after a dermal application of 200 mg chloroprene/kg bw. The instillation of chloroprene to the conjunctival sac of rabbits led to conjunctivitis lasting 10 days (no further details available).

**Conclusion:** There are no hazards which are still described under the other toxicological endpoints of interest.

**Recommendation:** no need for follow-up test

**Priority setting:** low priority or concern

### 3.2 Ecotoxicity

#### 3.2.1 Aquatic organisms

The following ecotoxic effect concentrations, regarding aquatic organisms, are available:
OECD SIDS

a) fish

*Lepomis macrochirus*  
96h-LC_{50} 245 mg/l  
(flow through system; nominal concentration)

*Leuciscus idus*  
96h-LC_{0} 200 mg/l  
4.5h-LC_{100} 500 mg/l  
(static, open system; nominal conc.; range finding test)

*goldfish*  
24h-LC_{50} 10 mg/l  
(original literature not available, test result could not be validated; data not included in the SIDS)

b) invertebrates

*Daphnia magna*  
24h-EC_{50} 348 mg/l  
21d-NOEC 3.2 mg/l  
(effect: reproduction; semi-static; nominal conc.)

c) algae

*Navicula seminulum*  
7d-EC_{50} 380 mg/l  
7d-EC_{11} 87 mg/l  
(effect: growth inhibition; static; nominal conc.)

d) microorganisms

*Escherichia coli*  
24h-NOEC 1000 mg/l  
(nominal conc., effect: growth inhibition)

*Pseudomonas fluorescens*  
24h-NOEC 1000 mg/l  
(nominal conc., effect: growth inhibition)

3.2.2 Terrestrial organisms

There are no data available.
4. Initial Assessment

4.1 Human toxicity

On the basis of the recent NTP 2-year inhalation study with rats and mice a carcinogenic potential of chloroprene is assumed. However the recent data on genotoxicity, \textit{in vivo}, are negative.

4.2 Assessment of environmental hazards

a) Hydrosphere

According to the EU-Technical Guidance Document for the risk assessment of existing substances, the value of the safety factor is $F = 100$, as no long-term test has been performed with the acutely most sensitive species (fish), although long-term NOECs are available for daphnids and algae. The low acute effect concentration with goldfish is discarded, as its validity could not be evaluated. With the lowest long-term NOEC of 3.2 mg/l and the highest PEC of 0.25 µg/l:

\[
PNEC = \frac{3200}{100} = 32 \mu g/l
\]

\[
PEC/PNEC = \frac{0.25}{32} = 0.008
\]

As PEC/PNEC < 1, chloroprene represents presently no risk for the aquatic compartment.

b) Soil compartment

As no effect data with terrestrial organisms are available, the aquatic PNEC is used on a first approach to indicate if these tests are necessary or not. With a PEC of 20 µg/l resp. 2 µg/l in pore water:

\[
(PEC/PNEC)_{indic} = \frac{20}{32} = 0.62
\]

As PEC/PNEC < 1, no tests with terrestrial organisms are currently necessary.
5. Conclusions and Recommendations

Toxicity

Due to the carcinogenic potential of chloroprene, there is need for limiting the risk. Risk reduction measures have to be considered.

Ecotoxicity

A comparison of estimated environmental concentrations and the predicted no-effect concentration for aquatic ecosystems, based on long-term tests, indicates that no risk of damage to aquatic ecosystems is to be expected. For the terrestrial compartment, there are presently no indications for the need of testing.
6. References


Internal communication BAYER AG dated August 16, 2002


Matt, T.J. et al., NTIS/DE94012384, April 1994

Melnick, R.L: et al., Toxicology 108, 79-91 (1996)


Trochimowicz, H.J. et al., Inhalation Toxicology 10, 443-472 (1998)

Westphal, G. et al., Arch. Toxicol. 68, 79-84 (1994)
Appendix 1: Calculations

ad 2.2.3 Exposure assessment

Local concentration in air and atmospheric deposition:

The atmospheric concentration and the deposition fluxes are proportional to the emission rate:

\[ C_{\text{air}} = \text{Emission} \cdot C_{\text{stdair}} \]

with:
- \( C_{\text{air}} \): concentration in air at 100 m from a point source \([\text{kg.m}^{-3}]\)
- \( \text{Emission} \): emission rate to air \([\text{kg.s}^{-1}]\)
- \( C_{\text{stdair}} \): standard concentration in air at source strength of 1 kg/s = \(24 \cdot 10^{-6} \text{ kg m}^{-3}\)

\[ C_{\text{air}} = 23 \mu\text{g/m}^3 \text{ resp. 2.3 } \mu\text{g/m}^3 \]

Furthermore the deposition flux is dependent on the fraction of the chemical that is associated with the aerosols:

\[ \text{DEP}_{\text{total}} = \text{Emission} \cdot \left[ \text{FR}_{\text{aerosol}} \cdot D_{\text{stdaer}} + (1 - \text{FR}_{\text{aerosol}}) \cdot D_{\text{stdgas}} \right] \]

with:
- \( \text{DEP}_{\text{total}} \): total deposition flux \([\text{kg.m}^{-2}.\text{s}^{-1}]\)
- \( \text{FR}_{\text{aerosol}} \): fraction of the chemical bound to aerosol [-]
- \( D_{\text{stdaer}} \): standard deposition flux of aerosol bound compounds at source strength of 1 kg/s (= \(1 \cdot 10^{-8} \text{ kg.m}^{-2}.\text{s}^{-1}\))
- \( D_{\text{stdgas}} \): standard deposition flux of gaseous compounds as a function of the Henry's law constant:

\[ 10\log H < -2 \quad 5 \cdot 10^{-10} \]
\[ -2 < 10\log H < 2 \quad 4 \cdot 10^{-10} \]
\[ 10\log H > 2 \quad 3 \cdot 10^{-10} \]

The fraction of the chemical associated with aerosol particles can be estimated on the basis of the chemical's vapour pressure, according to Junge (described in TGD):

\[ \text{CON}_{\text{junge}} \cdot \text{SURF}_{\text{aer}} \]
\[ \text{FR}_{\text{aerosol}} = \frac{\\text{CON}_{\text{junge}} \cdot \text{SURF}_{\text{aer}}}{\text{VP} + \text{CON}_{\text{junge}} \cdot \text{SURF}_{\text{aer}}} \]

with:
- \( \text{CON}_{\text{junge}} \): constant of Junge-equation \([\text{Pa.m}]\)
- \( \text{SURF}_{\text{aer}} \): surface area of aerosol particles \([\text{m}^2.\text{m}^{-3}]\)
- \( \text{VP} \): vapour pressure \([\text{Pa}]\) (here 25000 Pa)
As a default, the product of $\text{CON}_{\text{junge}}$ and $\text{SURF}_{\text{aer}}$ is set to $10^{-4}$ Pa (TGD).

$$=> \text{DEP}_{\text{total}} = 2.85 \cdot 10^{-13} \text{ kg.m}^{-2}.\text{s}^{-1} \text{ resp. } 0.285 \cdot 10^{-13} \text{ kg.m}^{-2}.\text{s}^{-1}$$

Calculation of the soil concentration due to atmospheric deposition

With the PESTLA-computer-model (described in TGD), the equilibrium concentration in the top soil layer can be determined. With a default biodegradation half-life of 500 days and a $K_{oc}$-value of 68 l/kg, a concentration of 24 µg/kg resp. 2.4 µg/kg is calculated.

The pore water concentration can be estimated with

$$\text{PEC}_{\text{soil}} \cdot \text{RHO}_{\text{soil}}$$

$$\text{PEC}_{\text{soil pore water}} = \frac{\Theta_{w} + \Theta_{s} \cdot \text{RHO}_{\text{solid}}}{\Theta_{w} + \Theta_{s} \cdot \text{RHO}_{\text{solid}}} \text{ [kg/l]}$$

with:

- $K_{p}$ = soil-water partition coefficient (here 1.34 kg/l)
- $\Theta_{w}$ = volume fraction of pore water in soil (0.4)
- $\Theta_{s}$ = volume fraction of solids in soil (0.4)
- $\text{RHO}_{\text{soil}}$ = density of bulk soil (1.5 kg/l)
- $\text{RHO}_{\text{solid}}$ = density of solid phase (2.5 kg/l)

$$=> \text{PEC}_{\text{soil pore water}} = 20 \mu g/l \text{ resp. } 2 \mu g/l$$

The concentration in groundwater is estimated with the same model at 3.5 µg/l resp. 0.35 µg/l.
**IUCLID Data Set**

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<th>Existing Chemical</th>
<th>Substance ID: 126-99-8</th>
</tr>
</thead>
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<td>CAS No.</td>
<td>126-99-8</td>
</tr>
<tr>
<td>EINECS Name</td>
<td>2-chlorobuta-1,3-diene</td>
</tr>
<tr>
<td>EINECS No.</td>
<td>204-818-0</td>
</tr>
<tr>
<td>Molecular Weight</td>
<td>88.54</td>
</tr>
<tr>
<td>Molecular Formula</td>
<td>C4H5Cl</td>
</tr>
</tbody>
</table>

**Producer Related Part**
- Company: Bayer AG
- Creation date: 06-MAY-94

**Substance Related Part**
- Company: Bayer AG
- Creation date: 06-MAY-94

**Memo:** AKTUELL EEC

**Printing date:** 03-SEP-98
**Revision date:** 02-JUN-94
**Date of last Update:** 06-AUG-98

**Number of Pages:** 98

**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
1.0.1 OECD and Company Information

Type: cooperating company
Name: Du Pont UK Ltd.
Town: SG1 4QN Stevenage
Country: United Kingdom

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: > 99.7 % w/w
Remark: Cooperationing company: DuPont UK Ltd., United Kingdom

1.1.1 Spectra

1.2 Synonyms

2-chloro-1,3-butadiene
2-chloroprene
beta-chloroprene

1.3 Impurities

CAS-No:
EINECS-No:
EINECS-Name: 1-chlorobuta-1,3-diene
Contents: <= .3 % w/w

1.4 Additives

CAS-No:
EINECS-No:
EINECS-Name:
Remark: 92-84-2 10-phenothiazine < 0.2 or
98-29-3 1,2-benzenediol,4-(1,1-dimethylethyl)- < 0.2

1.5 Quantity

Production during the last 12 months: yes
Quantity produced: 10 000 - 50 000 tonnes in 1993

Remark: no change of production volume 1996
19-JUN-97
1.6.1 Labelling

Labelling: as in Directive 67/548/EEC
Symbols: F
          Xn
Nota: D
Specific limits: no
R-Phrases: (11) Highly flammable
          (20/22) Harmful by inhalation and if swallowed
          (36) Irritating to eyes
S-Phrases: (2) Keep out of reach of children
          (16) Keep away from sources of ignition - No smoking

1.6.2 Classification

Classification: as in Directive 67/548/EEC
Class of danger: harmful
R-Phrases: (20/22) Harmful by inhalation and if swallowed

Classification: as in Directive 67/548/EEC
Class of danger: highly flammable
R-Phrases: (11) Highly flammable

Classification: as in Directive 67/548/EEC
Class of danger: irritating
R-Phrases: (36) Irritating to eyes

1.7 Use Pattern

Type: type
Category: Use in closed system

Type: industrial
Category: Chemical industry: used in synthesis

Type: use
Category: Intermediates
Remark: Chloroprene is only used as monomer in the production of polychloroprene rubber

1.7.1 Technology Production/Use

1.8 Occupational Exposure Limit Values

Type of limit: MAK (DE)
Limit value: 36 mg/m³
Short term expos.
Limit value: 72 mg/m³
Schedule: 30 minute(s)
Frequency: 4 times

1.9 Source of Exposure

1.10.1 Recommendations/Precautionary Measures
OECD SIDS CHLOROPRENE

1. GENERAL INFORMATION

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

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. PHYSICO-CHEMICAL DATA

2.1 Melting Point

Value: -130 degree C
GLP: no

2.2 Boiling Point

Value: 59.4 degree C at 1013 hPa
GLP: no

2.3 Density

Type: 
Value: .9598 at 20 degree C

2.3.1 Granulometry

2.4 Vapour Pressure

Value: 230.04 hPa at 20 degree C
Method: other (calculated)
GLP: no

Value: 239 hPa at 20 degree C

Value: 250 hPa at 20 degree C

Value: 267 hPa at 20 degree C

2.5 Partition Coefficient

log Pow: 1.73
Method: other (calculated): according to Hansch and Leo
Year: 
GLP: no

log Pow: 2.06
Method: other (calculated): according to Leo
Year: 
GLP: no

log Pow: 2.2
Method: other (calculated): Leo, A., CLOGP-3.6 (1991) Daylight, Chemical Information Systems Inc. Irvine, CA, USA
Year: 
2.6.1 Water Solubility

Value: 0.256 g/l at 20 degree C
GLP: no

Value: 0.48 g/l at 20 degree C

Value: 0.25 g/l at 25 degree C

2.6.2 Surface Tension

2.7 Flash Point

Value: -20 degree C
Type: Method: other: DIN 51758
Year: GLP: no

2.8 Auto Flammability

2.9 Flammability

Result: GLP: no
Remark: 320 degree C

2.10 Explosive Properties

2.11 Oxidizing Properties

2.12 Additional Remarks

Remark: Henry-constant
7.97 x 1000 Pa m3/mol at 20 degree C
3.1.1 Photodegradation

Type: air
INDIRECT PHOTOLYSIS
Sensitizer: OH
Method: other (calculated): estimation method by Atkinson
Year: GLP:
Test substance: t1/2 18.3 h
Remark:

Type: air
Method: other (calculated): estimation according to Hendry and Kenley (EPA-560/12-79-001)
Year: GLP:
Test substance: as prescribed by 1.1 - 1.4
Remark: photolysis-air: t1/2 4.2 h (OH-Radicals)
         t1/2 3.56 h (OH-Radicals + Ozone) (29)

Type: air
Method: 
Year: GLP:
Test substance: as prescribed by 1.1 - 1.4
Remark: photolysis-air: t1/2 1.5 h (EPA) (42)

3.1.2 Stability in Water

3.1.3 Stability in Soil

3.2 Monitoring Data (Environment)

Type of measurement:
Medium:
Remark: air: US: 0.36 ug/m3 (mean value) (1981) *
         waste disposal sites: 0.31 ug/m3 (1 sample),
         n.d. (94 samples) (1985) *
         * detection limit: 0.04 ug/m3
         water: Germany: no information

3.3.1 Transport between Environmental Compartments

3.3.2 Distribution

Media:
Method: Calculation according Mackay, Level I
Year: 
Remark: Chloroprene is to be expected to about 100 % in the atmosphere.
Air          : 99.96    %
Water        : 0.036   %
Soil/Sediment: 0.00054 %
Partition between water and soil/sediment is not to
be expected. The half-life for partitioning from water
to air is about 4.9 h up to 1-4 days.

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3.4 Mode of Degradation in Actual Use

Remark: Photolytical degradation in air

3.5 Biodegradation

Type: aerobic
Inoculum: domestic sewage
Degradation: 10 % after 28 day
Method: OECD Guide-line 301 D "Ready Biodegradability: Closed Bottle
Test"
Year: 1988 GLP: no
Test substance: as prescribed by 1.1 - 1.4

(139)

3.6 BOD5, COD or BOD5/COD Ratio

3.7 Bioaccumulation

Species:
Exposure period:
Concentration:
BCF:
Elimination:
Method:
Year:
GLP:
Test substance:
Remark: Bioaccumulation and geoaccumulation are only to be expected
to a small extent (no measured values).

3.8 Additional Remarks
AQUATIC ORGANISMS

4.1 Acute/Prolonged Toxicity to Fish

Type: flow through
Species: Lepomis macrochirus (Fish, fresh water)
Exposure period: 96 hour(s)
Unit: mg/l
LC50: 245
Method: 
Year: 
Test substance: other TS: chloroprene, no indic. about purity
Remark: Nominal concentration, high volatility
Test condition: 18 degree C; DO = 5-9 ppm

Type: other: static, open system
Species: Leuciscus idus (Fish, fresh water)
Exposure period: 96 hour(s)
Unit: mg/l
LC0: 200
Method: other: Bestimmung der akuten Wirkung von Stoffen auf Fische.
Arbeitskreis "Fischtest" im Hauptausschuss "Detergentien" (15.10.73)
Year: 1974
GLP: no
Test substance: as prescribed by 1.1 - 1.4
Remark: Nominal concentration, high volatility, range finding test open system

Type: other: static, open system
Species: Leuciscus idus (Fish, fresh water)
Exposure period: 
Unit: mg/l
LC100: 500
Method: other: Bestimmung der akuten Wirkung von Stoffen auf Fische.
Arbeitskreis "Fischtest" im Hauptausschuss "Detergentien" (15.10.73)
Year: 1974
GLP: no
Test substance: as prescribed by 1.1 - 1.4
Remark: Exposure period: 4.5 h
Nominal concentration, exceeding water solubility, high volatility; range finding test

4.2 Acute Toxicity to Aquatic Invertebrates

Species: Daphnia magna (Crustacea)
Exposure period: 24 hour(s)
Unit: mg/l
EC0: 100
EC50: 348
EC100: 800
Method: OECD Guide-line 202, part 1 "Daphnia sp., Acute Immobilisation Test"
Year: 1988
GLP: no
Test substance: as prescribed by 1.1 - 1.4
4. ECOTOXICITY

Remark: Nominal concentration;
Type: open system;
EC50/EC100 exceeding water solubility

4.3 Toxicity to Aquatic Plants e.g. Algae

Species: Navicula seminulum (Algae)
Endpoint: other: growth reduction
Exposure period: 7 day
Unit: mg/l Analytical monitoring: no
EC50: 380
Method:
Year: GLP: no
Test substance: other TS: chloroprene, no indic. about purity
Remark: Type: static, batch growth rate test
Nominal concentration, EC50 exceeding water solubility, high volatility
EC11 87 mg/l, nominal concentration
Test condition: 18 +/- 1 degree C

4.4 Toxicity to Microorganisms e.g. Bacteria

Type: other: static
Species: Escherichia coli (Bacteria)
Exposure period: 24 hour(s)
Unit: mg/l Analytical monitoring: no
EC0: 1000
Method:
Year: 1974 GLP: no
Test substance: as prescribed by 1.1 - 1.4
Remark: Nominal concentration, exceeding water solubility
Endpoint: growth inhibition

Type: other: static
Species: Pseudomonas fluorescens (Bacteria)
Exposure period: 24 hour(s)
Unit: mg/l Analytical monitoring: no
EC0: 1000
Method:
Year: 1974 GLP: no
Test substance: as prescribed by 1.1 - 1.4
Remark: Nominal concentration, exceeding water solubility
Endpoint: growth inhibition

4.5 Chronic Toxicity to Aquatic Organisms

4.5.1 Chronic Toxicity to Fish

Species:
Endpoint:
Exposure period:
4. ECOTOXICITY

4.5.2 Chronic Toxicity to Aquatic Invertebrates

| Species:    | Daphnia magna (Crustacea) |
| Endpoint:   | reproduction rate          |
| Exposure period: | 21 day                     |
| Unit:       | mg/l                       |
| Analytical monitoring: | no                     |
| Method:     | OECD Guide-line 202, part 2 "Daphnia sp., Reproduction Test" |
| Year:       | 1988                       |
| GLP:        | no                         |
| Test substance: | as prescribed by 1.1 - 1.4 |

<table>
<thead>
<tr>
<th>Concentration (mg/l)</th>
<th>Reproduction rate (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.0</td>
<td>74.1</td>
</tr>
<tr>
<td>3.2</td>
<td>97.5</td>
</tr>
<tr>
<td>10.0</td>
<td>87.2</td>
</tr>
<tr>
<td>31.6</td>
<td>67.0</td>
</tr>
<tr>
<td>100.0</td>
<td>54.7</td>
</tr>
</tbody>
</table>

Type: semi-static; nominal concentration. Based on the concentration-response relationship and considering the biological variability, the NOEC for the reproduction rate is 3.2 mg/l.

(139)
TERRESTRIAL ORGANISMS

4.6.1 Toxicity to Soil Dwelling Organisms

Type:
Species:
Endpoint:
Exposure period:
Unit:
Method:
   Year: GLP:
Test substance: no information
Remark: no information

4.6.2 Toxicity to Terrestrial Plants

Species:
Endpoint:
Expos. period:
Unit:
Method:
   Year: GLP:
Test substance: no information
Remark: no information

4.6.3 Toxicity to other Non-Mamm. Terrestrial Species

Species:
Endpoint:
Expos. period:
Unit:
Method:
   Year: GLP:
Test substance: no information
Remark: no information

4.7 Biological Effects Monitoring

Remark: no information

4.8 Biotransformation and Kinetics

Type:
Remark: no information

4.9 Additional Remarks

Remark: Terrestrial Organisms:
   It will be assumed that under normal conditions of production and processing chloroprene does not contaminate the terrestrial environment.
5.1 Acute Toxicity

5.1.1 Acute Oral Toxicity

<table>
<thead>
<tr>
<th>Type</th>
<th>LD50</th>
</tr>
</thead>
<tbody>
<tr>
<td>Species</td>
<td>rat</td>
</tr>
<tr>
<td>Sex:</td>
<td></td>
</tr>
<tr>
<td>Number of</td>
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</tr>
<tr>
<td>Animals:</td>
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<td>Vehicle:</td>
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</tr>
<tr>
<td>Value:</td>
<td>251 mg/kg bw</td>
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<td>Year:</td>
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<td>GLP:</td>
<td>(11)</td>
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<tr>
<td>Test substance:</td>
<td>freshly destilled chloroprene</td>
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<table>
<thead>
<tr>
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<tbody>
<tr>
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<td>Sex:</td>
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<td>Value:</td>
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<td></td>
</tr>
<tr>
<td>Animals:</td>
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<td>Vehicle:</td>
<td></td>
</tr>
<tr>
<td>Value:</td>
<td>50 mg/kg bw</td>
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<td>Method:</td>
<td>other: Class B poison test</td>
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<td>GLP:</td>
<td></td>
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<td>Test substance:</td>
<td>no deaths were observed</td>
</tr>
<tr>
<td>Remark:</td>
<td></td>
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<tr>
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<tr>
<td>Species:</td>
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<td>Sex:</td>
<td></td>
</tr>
<tr>
<td>Number of</td>
<td></td>
</tr>
<tr>
<td>Animals:</td>
<td></td>
</tr>
<tr>
<td>Vehicle:</td>
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<tr>
<td>Value:</td>
<td>384 mg/kg bw</td>
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<td>Method:</td>
<td></td>
</tr>
<tr>
<td>Year:</td>
<td></td>
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<tr>
<td>GLP:</td>
<td></td>
</tr>
<tr>
<td>Test substance:</td>
<td></td>
</tr>
<tr>
<td>Remark:</td>
<td>The minimal fatal dose (MFD); MFD is taken as the amount necessary to cause between 70 and 100 % of the animals to die acute death</td>
</tr>
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</table>

<table>
<thead>
<tr>
<th>Type:</th>
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<tbody>
<tr>
<td>Species:</td>
<td>mouse</td>
</tr>
<tr>
<td>Sex:</td>
<td></td>
</tr>
<tr>
<td>Number of</td>
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</tr>
<tr>
<td>Animals:</td>
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<td>Vehicle:</td>
<td></td>
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<tr>
<td>Value:</td>
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<tr>
<td>Method:</td>
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<tr>
<td>Year:</td>
<td></td>
</tr>
<tr>
<td>GLP:</td>
<td></td>
</tr>
<tr>
<td>Test substance:</td>
<td></td>
</tr>
</tbody>
</table>

Remarks:
Sex: 
Number of Animals: 
Vehicle: 
Value: = 260 mg/kg bw 
Method: 
Year: GLP: 
Test substance: 

5.1.2 Acute Inhalation Toxicity

Type: LD50 
Species: mouse 
Sex: 
Number of Animals: 
Vehicle: 
Value: = 146 mg/kg bw 
Method: 
Year: GLP: 
Test substance: 

Type: other: (see method) 
Species: rat 
Sex: 
Number of Animals: 
Vehicle: 
Exposure time: 4 hour(s) 
Value: = 11.8 mg/l 
Method: 
Year: GLP: 
Test substance: 
Remark: no deaths were observed; nominal concentration 
Test substance: freshly distilled chloroprene 

Type: other: (see method) 
Species: rat 
Sex: 
Number of Animals: 
Vehicle: 
Exposure time: 1 hour(s)
Value: = 72.4 mg/l
Method: other: Class B poison test
Year: GLP:
Test substance: no deaths were observed; analytical concentration
Remark: (37)

Type: other: (see remarks)
Species: rat
Sex: Number of Animals:
Vehicle: Exposure time: 1 hour(s)
Value: = 57.5 mg/l
Method: Year: GLP:
Test substance: no deaths were observed; nominal concentration
Remark: (36)

Type: other: (see remarks)
Species: rat
Sex: Number of Animals:
Vehicle: Exposure time: 4 hour(s)
Value: = 8.42 mg/l
Method: Year: GLP:
Test substance: The Approximate Lethal Concentration (ALC)
Remark: chloroprene freshly distilled
Test substance: (27)

Type: other: (see remarks)
Species: rat
Sex: Number of Animals:
Vehicle: Exposure time: 8 hour(s)
Value: 15 - 21 mg/l
Method: Year: GLP:
Test substance: The minimal fatal dose (MFD); MFD is taken as the amount necessary to cause between 70 and 100 % of the animals to die acute death
Remark: (145)

Type: LC100
Species: mouse
Sex: Number of Animals:
Vehicle: Exposure time: 1 hour(s)
Value: 3 mg/l
Method: GLP:
Test substance:

Type: LC50
Species: mouse
Sex:
Number of Animals:
Vehicle:
Exposure time: 2 hour(s)
Value: 3.48 mg/l
Method: GLP:
Test substance:

Type: LC50
Species: mouse
Sex:
Number of Animals:
Vehicle:
Exposure time: 2 hour(s)
Value: 1.3 mg/l
Method: GLP:
Test substance:

Type: LC50
Species: mouse
Sex:
Number of Animals:
Vehicle:
Exposure time:
Value: 2.3 mg/l
Method: GLP:
Test substance:

Type: other (see remarks)
Species: mouse
Sex:
Number of Animals:
Vehicle:
Exposure time: 8 hour(s)
Value: .6 mg/l
Method: GLP:
Test substance:
Remark: The minimal fatal dose (MFD); MFD is taken as the amount necessary to cause between 70 and 100% of the animals to die acute death
<table>
<thead>
<tr>
<th>Type</th>
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<tbody>
<tr>
<td>Species</td>
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<td>Vehicle</td>
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<tr>
<td>Exposure time</td>
<td>1 hour(s)</td>
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<tr>
<td>Value</td>
<td>= 1 mg/l</td>
</tr>
<tr>
<td>Method</td>
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</tr>
<tr>
<td>Year</td>
<td>GLP:</td>
</tr>
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<td>Test substance</td>
<td></td>
</tr>
<tr>
<td>Remark</td>
<td>no deaths were observed</td>
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<tr>
<td>Vehicle</td>
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</tr>
<tr>
<td>Exposure time</td>
<td>2 hour(s)</td>
</tr>
<tr>
<td>Value</td>
<td>= 2.3 mg/l</td>
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<td>Method</td>
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<td>Test substance</td>
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<tr>
<td>Remark</td>
<td>mortality &gt; 50 %</td>
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<tr>
<td>Sex</td>
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<td>Number of Animals</td>
<td></td>
</tr>
<tr>
<td>Vehicle</td>
<td></td>
</tr>
<tr>
<td>Exposure time</td>
<td>2 hour(s)</td>
</tr>
<tr>
<td>Value</td>
<td>= 1.91 mg/l</td>
</tr>
<tr>
<td>Method</td>
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</tr>
<tr>
<td>Year</td>
<td>GLP:</td>
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<tr>
<td>Test substance</td>
<td></td>
</tr>
<tr>
<td>Remark</td>
<td>mortality &gt; 50 %</td>
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<tr>
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<td>(94)</td>
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<table>
<thead>
<tr>
<th>Type</th>
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<tbody>
<tr>
<td>Species</td>
<td>rabbit</td>
</tr>
<tr>
<td>Sex</td>
<td></td>
</tr>
<tr>
<td>Number of Animals</td>
<td></td>
</tr>
<tr>
<td>Vehicle</td>
<td></td>
</tr>
<tr>
<td>Exposure time</td>
<td>8 hour(s)</td>
</tr>
<tr>
<td>Value</td>
<td>ca. 7.5 mg/l</td>
</tr>
<tr>
<td>Method</td>
<td></td>
</tr>
<tr>
<td>Year</td>
<td>GLP:</td>
</tr>
<tr>
<td>Test substance</td>
<td></td>
</tr>
<tr>
<td>Remark</td>
<td>The minimal fatal dose (MFD); MFD is taken as the amount necessary to cause between 70 and 100 % of the animals to die acute death</td>
</tr>
<tr>
<td></td>
<td>(145)</td>
</tr>
</tbody>
</table>
5. TOXICITY

5.1 Acute Toxicity

5.1.1 Oral Toxicity

Type: other (see remarks)
Species: rabbit
Sex: 
Number of Animals:
Vehicle: 
Exposure time: 2 hour(s)
Value: 6.8 - 8 mg/l
Method: 
Year: GLP:
Test substance: 
Remark: mortality > 50 %

Type: other (see remarks)
Species: cat
Sex: 
Number of Animals:
Vehicle: 
Exposure time: 8 hour(s)
Value: = 2.5 mg/l
Method: 
Year: GLP:
Test substance: 
Remark: The minimal fatal dose (MFD); MFD is taken as the amount necessary to cause between 70 and 100 % of the animals to die acute death

Type: other (see remarks)
Species: cat
Sex: 
Number of Animals:
Vehicle: 
Exposure time: 2 hour(s)
Value: = 11 mg/l
Method: 
Year: GLP:
Test substance: 
Remark: mortality > 50 %

5.1.2 Skin Toxicity

5.1.3 Acute Dermal Toxicity

Type: other (see method)
Species: rat
Sex: 
Number of Animals:
Vehicle: 
Value: = 200 mg/kg bw
Method: other: Class B poison test
Year: GLP:
Test substance: 
Remark: no deaths were observed
Test substance: freshly distilled chloroprene
### 5.1.4 Acute Toxicity, other Routes

**Type:** LD50  
**Species:** rat  
**Sex:**  
**Number of Animals:**  
**Vehicle:**  
**Route of admin.:** s.c.  
**Value:**  
- **Value:** 1916 mg/kg bw  
**Method:**  
- **Year:**  
**Test substance:** chloroprene freshly distilled stored under nitrogen  
**Remark:** with an observation period of 2 days  
**Test substance:** chloroprene freshly distilled stored under nitrogen  

(121)

**Type:** LD50  
**Species:** rat  
**Sex:**  
**Number of Animals:**  
**Vehicle:**  
**Route of admin.:** s.c.  
**Value:**  
- **Value:** 958 mg/kg bw  
**Method:**  
- **Year:**  
**Test substance:** chloroprene freshly distilled stored under nitrogen  
**Remark:** with an observation period of 7 days  
**Test substance:** chloroprene freshly distilled stored under nitrogen  

(121)

**Type:** LD50  
**Species:** rat  
**Sex:**  
**Number of Animals:**  
**Vehicle:**  
**Route of admin.:** s.c.  
**Value:**  
- **Value:** 479 mg/kg bw  
**Method:**  
- **Year:**  
**Test substance:** chloroprene freshly distilled, stabilized and stored for several days under air  
**Remark:** with an observation period of 2 days  
**Test substance:** chloroprene freshly distilled, stabilized and stored for several days under air  

(121)
Remark: with an observation period of 7 days
Test substance: chloroprene freshly distilled, stabilized and stored for several days under air

Type: LD100
Species: mouse
Sex: 
Number of Animals: 
Vehicle: 
Route of admin.: s.c.
Value: = 958 mg/kg bw
Method: Year: GLP:
Test substance: 

Type: other: (see remarks)
Species: rat
Sex: 
Number of Animals: 
Vehicle: 
Route of admin.: s.c.
Value: = 19166 mg/kg bw
Method: Year: GLP:
Test substance: 
Remark: The minimal fatal dose (MFD); MFD is taken as the amount necessary to cause between 70 and 100 % of the animals to die acute death

Type: other: (see remarks)
Species: mouse
Sex: 
Number of Animals: 
Vehicle: 
Route of admin.: s.c.
Value: = 1000 mg/kg bw
Method: Year: GLP:
Test substance: 
Remark: mortality > 50 %

Type: other: (see remarks)
Species: rabbit
Sex: 
Number of Animals: 
Vehicle: 
Route of admin.: s.c.
Value: = 958 other: mg/animal
Method: Year: GLP:
Test substance:
Remark: lethal dose

Type: other: (see remarks)
Species: cat
Sex: 
Number of Animals: 
Vehicle: 
Route of admin.: s.c.
Value: = 287 mg/kg bw
Method: 
Year: GLP:
Test substance: 
Remark: The minimal fatal dose (MFD); MFD is taken as the amount necessary to cause between 70 and 100 % of the animals to die acute death

Type: other: (see remarks)
Species: cat
Sex: 
Number of Animals: 
Vehicle: 
Route of admin.: s.c.
Value: = 4792 other: mg/animal
Method: 
Year: GLP:
Test substance: lethal dose
Remark: lethal dose

Type: other: (see remarks)
Species: rabbit
Sex: 
Number of Animals: 
Vehicle: 
Route of admin.: i.v.
Value: = 383 other: mg/animal
Method: 
Year: GLP:
Test substance: lethal dose
Remark: lethal dose

Type: LD50
Species: rat
Sex: 
Number of Animals: 
Vehicle: 
Route of admin.: other
Value: ca. 520 mg/kg bw
Method: 
Year: GLP:
Test substance: the route of application is not clear, s.c. or i.p.
5.2 Corrosiveness and Irritation

5.2.1 Skin Irritation

Species: rabbit
Concentration:

Exposure:
Exposure Time:
Number of Animals:
PDII:
Result:
EC classificat.:
Method: other: a single dose of 200 mg/kg bw was applied to the clipped trunk (occlusive) for 24 h, the wrapping was removed and the skin washed with water; the animals were observed for 48h

Year: GLP:
Test substance:
Remark: effects: 1 day - mild to moderate erythema with edema
2 day - generally mild to moderate erythema

Species: mouse
Concentration:

Exposure:
Exposure Time:
Number of Animals:
PDII:
Result:
EC classificat.:
Method: other: undiluted chloroprene was applied onto the interscapular region of the skin on backs in the quiescent phase of the hair cycle (no further information)

Year: GLP:
Test substance:
Remark: effects: after repeated application, thickening and scab-forming were observed on the 5th day

Species: rat
Concentration:

Exposure:
Exposure Time:
Number of Animals:
PDII:
Result:
EC classificat.:
Method: other: 480 mg/animal was rubbed into the skin of the back, daily for one week

Year: GLP:
5.2.2 Eye Irritation

Species: rabbit
Concentration: 
Dose: 
Exposure Time: 
Comment: 
Number of Animals: 
Result: 
EC classificat.: 
Method: other: no further information
Year: GLP:
Test substance: 
Remark: effects: conjunctivitis which lasted for 10 days (49)

5.3 Sensitization

5.4 Repeated Dose Toxicity

Species: rat Sex: male
Strain: Wistar
Route of admin.: inhalation
Exposure period: 5d,
Frequency of treatment: 6h/d, daily
Post. obs. period: 56d
Doses: 0.184, 0.368 mg/l (50, 100 ppm)
Control Group: yes, concurrent no treatment
Method: 
Year: GLP:
Test substance: 
Remark: During the exposure: reduced food consumption and bw loss in both dose groups; afterwards the bw gain was comparable with the controls.
Test substance: chloroprene freshly distilled under nitrogene (58)

Species: rat Sex: male/female
Strain: Wistar
Route of admin.: inhalation
Exposure period: 5d
Frequency of treatment: 6h/d, daily
Post. obs. period: no
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Doses: 0.368 mg/l, (100 ppm)
Control Group: yes, concurrent no treatment
Method: 
  Year: GLP:
  Test substance: 
  Remark: 
  Result: body weight gain was decreased
  Test substance: 

Species: rat
Strain: Wistar
Route of admin.: inhalation
Exposure period: 14d
Frequency of treatment: 5d/w, 6h/d
Post. obs. period: 
Doses: 0.0883, 0.1693 mg/l (24, 46 ppm)
Control Group: yes, concurrent no treatment
Method: 
  Year: GLP:
  Test substance: 
  Remark: 
  Result: Slight behavioural disturbance and very slight growth retardation at both exposure levels.
  Test substance: 

Species: rat
Strain: other: ChR-CD
Route of admin.: inhalation
Exposure period: 22d
Frequency of treatment: 4h/d, daily
Post. obs. period: 
Doses: 0.085 mg/l (23 ppm)
Control Group: yes, concurrent no treatment
Method: 
  Year: GLP:
  Test substance: 
  Remark: 
  Result: No clinical signs; weight gain pattern similar to controls; gross and histopathologic examination revealed no changes
  Test substance: 

Species: rat
Strain: Wistar
Route of admin.: inhalation
Exposure period: 28d
Frequency of treatment: 5d/w, 6h/d
Post. obs. period: 
Doses: 0.144, 0.593, 2.3 mg/l (39, 161, 625 ppm)
Control Group: yes, concurrent no treatment
Method: 
  Year: GLP:
  Test substance: 
  Remark: 
  Result: 
  Test substance: 

(148) (131) (53)

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5. TOXICITY

Date: 03-09-98
Id: 126-99-8

Test substance: analytical concentration
Result: deaths (161, 625 ppm); decreased food consumption and body weight gain at all concentration levels; increased relative organ weights of kidneys, liver and lung (all concentrations); slight to severe degree of centrilobular liver degeneration and necrosis (625 ppm and 161 ppm, only the animals which died during the experiment); slightly enlarged tubular epithelial cells in the kidneys (625 ppm); hemorrhages, perivascular edema of the lungs (all animals which died during the experiment); blood and urine examinations: normal.

Test substance: chloroprene freshly distilled under nitrogen

Species: rat
Sex: male/female
Strain: Wistar
Route of admin.: inhalation
Exposure period: 91d
Frequency of treatment: 5d/w, 6h/d
Post. obs. period: 20d (males), until litters had been weaned (females)
Doses: 0.037, 0.121, 0.368 mg/l (10, 33, 100 ppm)
Control Group: yes, concurrent no treatment
Method: Year: GLP:
Test substance: nominale concentration
Result: No deaths; decreased bw gain (females of the highest dose level); gross and microscopic pathological examinations did not reveal any treatment-related abnormalities.

Test substance: chloroprene freshly purified

Species: rat
Sex: female
Strain: Wistar
Route of admin.: inhalation
Exposure period: 24d
Frequency of treatment: 5d/w, 6h/d
Post. obs. period: no
Doses: 0.736 mg/l (200 ppm)
Control Group: yes, concurrent no treatment
Method: Year: GLP:
Test substance: nominale concentration
Result: No deaths; growth retardation; alopecia (the occurrence of alopecia may depend on the typ of diet used).

Test substance: chloroprene freshly purified

Species: rat
Sex: male/female
Strain: Wistar
Route of admin.: inhalation
Exposure period: 26w
Frequency of treatment: 5d/w, 6h/d
Post. obs. period: no
Doses: 0.037, 0.121, 0.368 mg/l (10, 33, 100 ppm)
Control Group: yes, concurrent no treatment
Method: Year: GLP:
Test substance: nominale concentration
Remark: No deaths; clinical symptoms during the first weeks (100 ppm); slight growth retardation (100 ppm, males); slight increase in the percentage of neutrophils and a decrease in the percentage of lymphocytes (100 ppm, males); more urine with a lower creatinine content (100 ppm, females); increase of the relative liver weights (all females in a dose-related manner, 100 ppm, males); increase of the relative kidney weights (100 ppm, both sex, 30 ppm, females); the microscopic pathological examination revealed no treatment-related abnormalities.

Test substance: chloroprene freshly purified

Species: rat Sex: male/female
Strain: Wistar
Route of admin.: inhalation
Exposure period: 2a
Frequency of treatment: 5d/w, 6h/d
Post. obs. period: no
Doses: 0.0368, 0.184 mg/l (10, 50 ppm)
Control Group: yes, concurrent no treatment
Method: Year: GLP:
Test substance: analytical concentrations; in week 72 an interruption of the ventilation in one of the inhalation chambers caused death by suffocation of 87 males and 73 females from 100 animals each sex.
Result: Mortality was not influenced by exposure to chloroprene; slight restlessness (10, 50 ppm) during the first few weeks; growth retardation (50 ppm) diminished in the course of the second year; relative lung weights were decreased (10, 50 ppm); increased number of animals with small foci of cellular alterations in the liver (50 ppm); animals of the high dose group were less severely affected by chronic respiratory disease.

Test substance: chloroprene freshly purified

Species: rat Sex: no data
Strain: no data
Route of admin.: inhalation
Exposure period: max. 100d
Frequency of treatment: 2h/d
Post. obs. period:
5. TOXICITY

Doses: 6 mg/l
Control Group: yes
Method: 
Year: GLP:
Test substance: 
Remark: increased adrenal weight and cholesterol content in the adrenals; decreased spleen weight
Result: 
Species: rat
Sex: no data
Strain: no data
Route of admin.: inhalation
Exposure period: max. 90d
Frequency of treatment: 2h/d
Post. obs. period:

Doses: 4 mg/l
Control Group: yes
Method: 
Year: GLP:
Test substance: 
Remark: glutaminase activity (brain): unchanged (30d), decreased (60d), unchanged (90d)
Result: glutamine synthetase (brain): decreased (30d, 60d), increased (90d)
Species: rat
Sex: no data
Strain: no data
Route of admin.: inhalation
Exposure period: max. 60d
Frequency of treatment: 2h/d
Post. obs. period:

Doses: 6 - 30 mg/l
Control Group: no data specified
Method: 
Year: GLP:
Test substance: 
Remark: Reserves of endogenous thiosulfate in the tissue increased.
Result: 
Species: rat
Sex: no data
Strain: no data
Route of admin.: inhalation
Exposure period: 2- 3 months
Frequency of treatment: 2h/d
Post. obs. period:

Doses: 8 mg/l
Control Group: yes
Method: 
Year: GLP:
Test substance: no detailed information, evaluation impossible
Result: aminotransferase activity decreased (blood, liver, kidney, spleen)

Species: rat  Sex: male/female
Strain: no data
Route of admin.: inhalation
Exposure period: 75d
Frequency of treatment: 2h/d
Post. obs. period:
Doses: 6 mg/l
Control Group: yes
Method: GLP:
Test substance: no detailed information, evaluation impossible
Result: The amount of glycogen in the liver and muscles decreased; the pyruvic acid content in the blood increased.

Species: rat  Sex: male/female
Strain: no data
Route of admin.: inhalation
Exposure period: 90d
Frequency of treatment: 2h/d
Post. obs. period:
Doses: 4 mg/l
Control Group: yes
Method: GLP:
Test substance: no detailed information, evaluation impossible
Result: The amount of glycogen in the liver and muscles decreased; the pyruvic acid content in the blood increased.

Species: rat  Sex: male/female
Strain: no data
Route of admin.: inhalation
Exposure period: max. 3 months
Frequency of treatment: 2h/d
Post. obs. period:
Doses: 2 mg/l
Control Group: yes
Method: GLP:
Test substance: no detailed information, evaluation impossible
Result: Time dependent increase of the glycogen content in the brain.
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<tr>
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<tr>
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<td>GLP:</td>
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<td>Remark:</td>
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<tr>
<td>Result:</td>
<td>The content of free ammonia in the brain increased; the content of glutamine in the brain decreased. (92) (102)</td>
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<td>Post. obs. period:</td>
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<tr>
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<td>Year:</td>
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<td>Remark:</td>
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<tr>
<td>Result:</td>
<td>The respiration rate of brain mitochondria was temporary decreased. (1)</td>
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<td>Method:</td>
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<td>Year:</td>
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<td>Remark:</td>
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<tr>
<td>Result:</td>
<td>tissue respiration in liver and brain was reduced; altered enzyme activities in liver and brain (111)</td>
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### 5. TOXICITY

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<td>2h/d</td>
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<td>brain tissue: the level of glutamate temporary decreased, the level of aspartate and alanine increased (91) (93)</td>
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<td>Result: activity of the carbonic anhydrase decreased in blood, brain and gastric mucosa. (108)</td>
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<td>Result: bones: changes in the collagen fibers and in the bone tissue (128)</td>
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<td>Regeneration of bone fractures was prolonged.</td>
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<tr>
<td>cathepsin activity decreased in brain, liver and kidney (brain &gt; liver &gt; kidney)</td>
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<tr>
<td>13/25 rats died; decreased activity of alkaline and acid phosphatase in liver, kidney and brain</td>
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<th>Year:</th>
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<tbody>
<tr>
<td>histochemical changes in the liver; a protective effect was observed with an protein rich diet</td>
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<td>(12)</td>
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Species: rat  Sex: no data
Strain: no data
Route of admin.: inhalation
Exposure period: max. 180d
Frequency of treatment: 2h/d
Post. obs. period:
Doses: 8 mg/l
Control Group: yes
Method:
Year: GLP:
Test substance:
Remark: no detailed information, evaluation impossible
Result: the cholinesterase activity in the brain decreased

(103)

Species: rat  Sex: no data
Strain: no data
Route of admin.: inhalation
Exposure period: 24w
Frequency of treatment: 5h/d
Post. obs. period:
Doses: 0.000088, 0.00022, 0.00048 mg/l
Control Group: no data specified
Method:
Year: GLP:
Test substance:
Remark: no detailed information, evaluation impossible
Result: 0.00022 mg/l: cholinesterase activity in the brain increased, sulphydryl groups in the brain tissue decreased, ATP activity increased, adrenal weight increased
0.00048 mg/l: cholinesterase activity in the brain decreased, elevated adrenal weight

(113)

Species: rat  Sex: no data
Strain: no data
Route of admin.: inhalation
Exposure period: 24w
Frequency of treatment: 5h/d
Post. obs. period:
Doses: 0.00056, 0.00306 mg/l
Control Group: yes
Method:
Year: GLP:
Test substance:
Remark: no detailed information, evaluation impossible
Result: dystrophy (brain) at both concentrations

(112) (117)

Species: rat  Sex: no data
Strain: no data
Route of admin.: inhalation
Exposure period: 28w
Frequency of
treatment: 2h/d  
Post. obs. period: 
Doses: 2 mg/l  
Control Group: no data specified  
Method: 
Year: GLP:  
Test substance: no detailed information, evaluation impossible  
Remark: some animals were exposed during 2 weeks with a recovery period of 4 months  
Result: increased adrenal weights; macroscopically and microscopically visible alterations in the adrenal glands (irreversible?)

Species: rat  
Sex: no data  
Strain: no data  
Route of admin.: inhalation  
Exposure period: max. 9 months  
Frequency of treatment: 2h/d  
Post. obs. period: 
Doses: 8 mg/l  
Control Group: yes  
Method: 
Year: GLP:  
Test substance: no detailed information, evaluation impossible  
Remark: After 3 and 6 months ammonia level in liver and kidneys has increased, in the liver after 9 months reached the control level again.

Species: rat  
Sex: male/female  
Strain: no data  
Route of admin.: inhalation  
Exposure period: 150 - 160d  
Frequency of treatment: 2h/d  
Post. obs. period: 
Doses: 8 mg/l  
Control Group: yes  
Method: 
Year: GLP:  
Test substance: no detailed information, evaluation impossible  
Remark: hexokinase activity was depressed (skin > kidneys > brain > heart muscles)

Species: rat  
Sex: male/female  
Strain: no data  
Route of admin.: inhalation  
Exposure period: max. 180d  
Frequency of treatment:  
Post. obs.
5. TOXICITY

Test substance: freshly distilled chloroprene

Remark: no detailed information, evaluation impossible

Result: the amount of free gangliosides in the brain was reduced

Species: rat
Sex: male/female
Strain: no data
Route of admin.: inhalation
Exposure period: max. 120d
Frequency of treatment: 2h/d
Post. obs. period:
Doses: 8 mg/l
Control Group: yes
Method:
Year: GLP:

Test substance:
Remark: no detailed information, evaluation impossible
Result: brain content of free cerebrosides increased, content of bonded cerebrosides remained unchanged.

Species: rat
Sex: male/female
Strain: no data
Route of admin.: inhalation
Exposure period: 30d
Frequency of treatment: 2h/d
Post. obs. period:
Doses: 8 mg/l
Control Group: yes
Method:
Year: GLP:

Test substance:
Remark: no detailed information, evaluation impossible
Result: The content of SH groups decreased in the brain, spleen, liver, blood serum and kidneys.

Species: rat
Sex: male/female
Strain: Fischer 344
Route of admin.: inhalation
Exposure period: 16 days
Frequency of treatment: 6h/day; 5 days/week
Post. obs. period: no
Doses: 0, 32, 80, 200 or 500 ppm
Control Group: yes, concurrent no treatment
Method: other
Year: GLP: no data
<table>
<thead>
<tr>
<th>Test substance</th>
<th>other TS: purity: approx. 96 %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Result</td>
<td>increased mortality (200 ppm/500 ppm) but the mortality pattern did not reflect the effect of chloroprene exposure; reduced body weight gain (200 ppm/500 ppm (f)); anemia and thrombocytopenia (200 ppm (f)/500 ppm); increased liver enzyme activities (200 ppm (f)/500 ppm), increased liver weights (200 ppm (f)/500 ppm); liver necrosis (200 ppm/500 ppm); epithelial degeneration in all exposed animals</td>
</tr>
</tbody>
</table>

28-OCT-97

Species: rat
Sex: male/female
Strain: Fischer 344
Route of admin.: inhalation
Exposure period: 13 weeks
Frequency of treatment: 6h/day; 5 days/week
Post. obs. period: no
Doses: 0, 5, 12, 32, 80 or 200 ppm
Control Group: other
Method: GLP: no data
Year: no data

<table>
<thead>
<tr>
<th>Test substance</th>
<th>other TS: purity &gt; 97.9 %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Result</td>
<td>no effects on survival and body weight gain; anemia (200 ppm); thrombocytopenia (200 ppm/80 ppm (f)); transient increase of liver enzyme activities; liver nonprotein sulfhydryl concentrations decreased (200 ppm); increase of horizontal activity in neurobehavioral assessment (&gt;= 32 ppm); increased kidney weights (200 and 80 ppm (f)); increased incidence of olfactory epithelial degeneration (&gt;= 32 ppm); liver necrosis (200 ppm)</td>
</tr>
</tbody>
</table>

28-OCT-97

Species: rat
Sex: male/female
Strain: Fischer 344
Route of admin.: inhalation
Exposure period: 2 years
Frequency of treatment: 6h/day; 5 days/week
Post. obs. period: no
Doses: 0, 12.8, 32, 80 ppm
Control Group: yes, concurrent no treatment
Method: GLP: no data
Year: no data

<table>
<thead>
<tr>
<th>Test substance</th>
<th>other TS: purity: approx. 96 %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Result</td>
<td>reduced survival (32 and 80 ppm (m)); decreased mean body weights (80 ppm (m)); for pathology findings s. chapter 5.7</td>
</tr>
</tbody>
</table>

28-OCT-97

Species: rat
Sex: male
Strain: no data
Route of admin.: gavage
Exposure period: 20d
Frequency of treatment: Post. obs. period: no
Doses: 0.5 mg/kg bw
<table>
<thead>
<tr>
<th>Control Group:</th>
<th>yes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Method:</td>
<td>GLP:</td>
</tr>
<tr>
<td>Year:</td>
<td></td>
</tr>
<tr>
<td>Test substance:</td>
<td>purified chloroprene in water</td>
</tr>
<tr>
<td>Remark:</td>
<td>no detailed information, evaluation impossible</td>
</tr>
<tr>
<td>Result:</td>
<td>relative organ weights of liver, spleen and gonads were unchanged; activity of beta-galactosidase in the blood serum increased and decreased in the seminal fluid; isoenzyme spectrum of LDH in the seminal fluid has changed.</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Species:</th>
<th>rat</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex:</td>
<td>male</td>
</tr>
<tr>
<td>Strain:</td>
<td>no data</td>
</tr>
<tr>
<td>Route of admin.:</td>
<td>gavage</td>
</tr>
<tr>
<td>Exposure period:</td>
<td>28d</td>
</tr>
<tr>
<td>Frequency of treatment:</td>
<td></td>
</tr>
<tr>
<td>Post. obs. period:</td>
<td></td>
</tr>
<tr>
<td>Doses:</td>
<td>0.0005, 0.005, 0.05 mg/kg bw</td>
</tr>
<tr>
<td>Control Group:</td>
<td></td>
</tr>
<tr>
<td>Method:</td>
<td></td>
</tr>
<tr>
<td>Year:</td>
<td></td>
</tr>
<tr>
<td>Test substance:</td>
<td></td>
</tr>
<tr>
<td>Remark:</td>
<td>no detailed information, evaluation impossible</td>
</tr>
<tr>
<td>Result:</td>
<td>0.0005 mg/kg bw: relative organ weights unchanged; activity of beta-galactosidase in blood serum increased 0.005 mg/kg bw: activity of beta-galactosidase in seminal fluid increased 0.05 mg/kg bw: relative organ weights unchanged; activity of beta-galactosidase in blood serum increased</td>
</tr>
<tr>
<td>Test substance:</td>
<td>purified chloroprene in water</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Species:</th>
<th>rat</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex:</td>
<td>male</td>
</tr>
<tr>
<td>Strain:</td>
<td>no data</td>
</tr>
<tr>
<td>Route of admin.:</td>
<td>gavage</td>
</tr>
<tr>
<td>Exposure period:</td>
<td>24w</td>
</tr>
<tr>
<td>Frequency of treatment:</td>
<td></td>
</tr>
<tr>
<td>Post. obs. period:</td>
<td></td>
</tr>
<tr>
<td>Doses:</td>
<td>0.0005, 0.005, 0.05 mg/kg bw</td>
</tr>
<tr>
<td>Control Group:</td>
<td></td>
</tr>
<tr>
<td>Method:</td>
<td></td>
</tr>
<tr>
<td>Year:</td>
<td></td>
</tr>
<tr>
<td>Test substance:</td>
<td></td>
</tr>
<tr>
<td>Remark:</td>
<td>0.005 and 0.05 mg/kg bw: lethargy, body weight declined, relative organ weights increased (liver, spleen, gonads), activity of beta-galactosidase increased (liver)</td>
</tr>
<tr>
<td>Test substance:</td>
<td>purified chloroprene in water</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Species:</th>
<th>rat</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex:</td>
<td>no data</td>
</tr>
<tr>
<td>Strain:</td>
<td>no data</td>
</tr>
<tr>
<td>Route of admin.:</td>
<td>gavage</td>
</tr>
<tr>
<td>Exposure period:</td>
<td>9 months</td>
</tr>
</tbody>
</table>
### Frequency of treatment
- **Post. obs. period:** daily

### Doses:
- 0.15, 0.8, 1.5 mg/kg bw

### Control Group:
- yes

### Test substance:
- chloroprene with 0.5-0.8 % dimers and polymers in water

### Remark:
- no detailed information, evaluation impossible

### Result:
- death, loss of body weight, lowered blood pressure (0.8 and 1.5 mg/kg bw); alterations in the heart, liver and spleen (gross necropsy) in the 1.5 mg/kg bw dose group.

### Test substance:
- chloroprene with 0.5-0.8 % dimers and polymers in water

### Species:
- rat

### Sex:
- male/female

### Strain:
- other: BDIV

### Route of admin.:
- gavage

### Exposure period:
- 114 weeks

### Frequency of treatment:
- once per week

### Post. obs. period:
- until 120 weeks

### Doses:
- 50 mg/kg bw

### Control Group:
- yes, concurrent vehicle

### Test substance:
- chloroprene, purity 99 %, containing 0.8 % 1-chlorobutadiene

### Species:
- rat

### Sex:
- no data

### Route of admin.:
- dermal

### Exposure period:
- 41d

### Frequency of treatment:
- 1 week once a day, followed by an interruption of 14d, then again 34d daily

### Post. obs. period:
- at the end of 71 days

### Doses:
- 1. phase 480 mg/rat; 2. phase 1440 mg/rat

### Control Group:
- yes

### Test substance:
- only one control animal

### Remark:
- Some signs of local irritation; mild nephrosis, the spleen was hyperemic, testicles were more or less degenerated and calcified in certain areas, the liver of 2 animals showed signs of degeneration.
5. TOXICITY

Species: rat  
Sex: no data

Strain: no data

Route of admin.: s.c.

Exposure period: 30d

Frequency of treatment: daily

Post. obs. period:

Doses: 0.5 mg/kg bw

Control Group: yes

Method:

Year: GLP:

Test substance: 

Remark: no detailed information, evaluation impossible

Result: increased adrenal weight and cholesterol content in the adrenals; decreased spleen weight

Species: rat  
Sex: no data

Strain: no data

Route of admin.: i.p.

Exposure period: max. 60d

Frequency of treatment: daily

Post. obs. period:

Doses: 51.1 mg/kg bw

Control Group: no data specified

Method:

Year: GLP:

Test substance: 

Remark: no detailed information, evaluation impossible

Result: time dependent damage of the liver (elevated activity of uro-cinase and histidase in the blood, decreased enzyme activity in the liver)

Species: mouse  
Sex: male

Strain: Swiss

Route of admin.: inhalation

Exposure period: 14d

Frequency of treatment: 5d/w, 6h/d

Post. obs. period: 56d

Doses: 0.0368, 0.368 mg/l (10, 100 ppp)

Control Group: yes, concurrent no treatment

Method:

Year: GLP:

Test substance: 

Remark: 

Result: No deaths in the 10 ppm group, 8/11 died during the first week of treatment (100 ppm); food intake and bw gain were comparable with the controls.

Test substance: chloroprene freshly distilled under nitrogen

Species: mouse  
Sex: no data

Strain: other: C57BL/6

Route of admin.: inhalation
OECD SIDS

CHLOROPRENE

5. TOXICITY

Date: 03-09-98
Id: 126-99-8

Exposure period: no data
Frequency of treatment: no data
Post. obs. period:

Doses: 0.000054, 0.000064, 0.00013, 0.00032, 0.00185, 0.035 mg/l
Control Group: no data specified
Method:
Year: GLP:
Test substance: no detailed information, evaluation impossible
Remark: no systemic effects
Result: (136)

Species: mouse
Strain: B6C3F1
Route of admin.: inhalation
Exposure period: 16 days
Frequency of treatment: 6h/day; 5 days/week
Post. obs. period:

Doses: 0, 12, 32, 80 or 200 ppm
Control Group:
Method:
Year: GLP: no data
Test substance: other TS: purity: approx. 96 %
Result: all animals exposed to 200 ppm died; reduced body weight gain (32 ppm and 80 ppm (m)); no deviations in hematology and clinical chemistry parameters; reduced thymus weights (80 ppm); increased relative liver weights (80 ppm); liver and thymic necrosis (200 ppm); squamous epithelial hyperplasia of the forestomach (80 ppm)

28-OCT-97

Species: mouse
Strain: B6C3F1
Route of admin.: inhalation
Exposure period: 13 weeks
Frequency of treatment: 6h/day; 5 days/week
Post. obs. period:

Doses: 0, 5, 12, 32 or 80 ppm
Control Group: yes, concurrent no treatment
Method:
Year: GLP: no data
Test substance: other TS: purity > 97.9 %
Result: no effect on survival; reduced final body weights (80 ppm (m)); changes of hematology parameters (32 and 80 ppm (f)); no biologically significant organ weight effects; an increased incidence of squamous epithelial hyperplasia of the forestomach

28-OCT-97

Species: mouse
Strain: B6C3F1
Route of admin.: inhalation
Exposure period: 2 years
OECD SIDS CHLOROPRENE

5. TOXICITY

Date: 03-09-98
Id: 126-99-8

Frequency of treatment: 6h/day; 5 days/week
Post. obs. period: no
Doses: 0, 12.8, 32 or 80 ppm
Control Group: other

Method: Year: GLP: no data
Test substance: other TS: purity: approx. 96 %
Result: reduced survival in all females and 32 and 80 ppm males;
decreased mean body weights (80 ppm(f)); for pathology
findings s. chapter 5.7

Species: mouse Sex: no data
Strain: no data
Route of admin.: dermal
Exposure period: 14d
Frequency of treatment: daily
Post. obs. period:
Doses: 5 drops
Control Group: no

Method: Year: GLP:
Test substance: purified chloroprene
Result: At the end of 2 weeks half of the animals were dead and the
rest were stuporous, no change in the hair.

Species: rabbit Sex: no data
Strain: no data
Route of admin.: inhalation
Exposure period: 24w
Frequency of treatment: 4h/d
Post. obs. period:
Doses: 0.1 - 0.5 mg/l
Control Group: yes

Method: Year: GLP:
Test substance: no detailed information, evaluation impossible
Result: reduced liver glycogen content; increased blood pyruvic acid content

Species: rabbit Sex: no data
Strain: no data
Route of admin.: inhalation
Exposure period: 180d
Frequency of treatment: 4h/d
Post. obs. period:
Doses: 0.8 - 1 mg/l
Control Group: yes
Method: GLP:
Test substance: no detailed information, evaluation impossible
Remark: decreased activity of the carbonic anhydrase in the brain:
cerebral cortex > cerebellum > medulla oblongata
Result: decreased activity of the carbonic anhydrase in the brain:
cerebral cortex > cerebellum > medulla oblongata

Species: dog
Sex: no data
Strain: no data
Route of admin.: inhalation
Exposure period: 20d
Frequency of treatment: 
Post. obs. period:
Doses: 8 - 20 mg/l
Control Group: no data specified
Method: GLP:
Test substance: no detailed information, evaluation impossible
Remark: jaundice; the filtering and reabsorption actions of the kidneys were changed.
Result: jaundice; the filtering and reabsorption actions of the kidneys were changed.

Species: dog
Sex: no data
Strain: no data
Route of admin.: inhalation
Exposure period: 21d
Frequency of treatment: 4h/d
Post. obs. period:
Doses: 0.1 - 0.5 mg/l
Control Group: no
Method: GLP:
Test substance: no detailed information, evaluation impossible
Remark: reversible hypoglycaemia
Result: reversible hypoglycaemia

Species: dog
Sex: no data
Strain: no data
Route of admin.: inhalation
Exposure period: 3.5 - 4 months
Frequency of treatment: 4h/d
Post. obs. period:
Doses: 0.1 - 0.5 mg/l
Control Group: no
Method: GLP:
Test substance: no detailed information, evaluation impossible
Remark: no detailed information, evaluation impossible
Result: reversible hypoglycaemia

Species: dog  Sex: male
Strain: no data
Route of admin.: inhalation
Exposure period: 24w
Frequency of treatment: 2h/d
Post. obs. period:
Doses: 6 - 20 mg/l
Control Group: yes
Method: GLP:
Test substance: no detailed information, evaluation impossible
Remark:
Result: suppression in the absorption of glucose and pyruvic acid by the brain, amount of pyruvic acid in the blood increased and the amount of glucose decreased.

Species: dog  Sex: male
Strain: no data
Route of admin.: i.v.
Exposure period: repeated
Frequency of treatment:
Post. obs. period:
Doses: 10, 20, 40, 80, 160, 320, 640, 1000 mg
Control Group: yes
Method: GLP:
Test substance: no detailed information, evaluation impossible
Remark:
Result: 60-100 mg: hyperactivity, salivation, mydriasis
1000 mg: death
repeated chloroprene administration caused a decrease in blood coagulation time

Species: guinea pig  Sex: no data
Strain: no data
Route of admin.: inhalation
Exposure period: max. 6 weeks
Frequency of treatment: 2h/d
Post. obs. period:
Doses: up to 0.34 mg/l
Control Group: no data specified
Method: GLP:
Test substance: no detailed information, evaluation impossible
Remark:
Result: liver damage, altered lipid and carbohydrate metabolism
Species: guinea pig  
Sex: no data  
Strain: no data  
Route of admin.: dermal  
Exposure period: 14d  
Frequency of treatment:  
Post. obs. period:  
Doses: 1 ml  
Control Group: no  
Method:  
Year:  
Test substance:  
Remark: no detailed information, evaluation impossible  
Result: At the end of 2 weeks half of the animals were dead and the rest were stuporous, no change in the hair.  
Test substance: pure chloroprene  
(132)

Species: other: Syrian Golden hamster  
Sex: male/female  
Strain:  
Route of admin.: inhalation  
Exposure period: 28d  
Frequency of treatment: 5d/w, 6h/d  
Post. obs. period: no  
Doses: 0.144, 0.596, 2.391 mg/l (39, 162, 630 ppm)  
Control Group: yes, concurrent no treatment  
Method:  
Year:  
Test substance:  
Remark: analytical concentration  
Result: 100 % mortality at the highest concentration within 24 hr after the first exposure, some deaths at 162 ppm, no deaths at 39 ppm; body weight gain: normal (39, 162 ppm); irritation of the mucous membrane of the nasal cavity (all concentrations); alveolar and perivascular edema of the lungs (animals which died); necrosis and degeneration of hepatocytes (most of the survivors of the 162 ppm-group).  
Test substance: chloroprene freshly distilled under nitrogen  
(27)

Species: other: Syrian Golden hamster  
Sex: male/female  
Strain:  
Route of admin.: inhalation  
Exposure period: 18 months  
Frequency of treatment: 5d/w, 6h/d  
Post. obs. period: no  
Doses: 0.0368, 0.184 mg/l (10, 50 ppm)  
Control Group: yes, concurrent no treatment  
Method:  
Year:  
Test substance:  
Remark: analytical concentrations  
Result: Mortality in both test groups was lower than in the
controls; no abnormalities in behavior; growth retardation (50 ppm); a slight reduction in amyloidosis (50 ppm)
Test substance: chloroprene freshly purified

5.5 Genetic Toxicity 'in Vitro'

<table>
<thead>
<tr>
<th>Type</th>
<th>Ames test</th>
</tr>
</thead>
<tbody>
<tr>
<td>System of testing:</td>
<td>Salmonella typhimurium TA 100</td>
</tr>
<tr>
<td>Concentration:</td>
<td>up to 5 µmol/plate</td>
</tr>
<tr>
<td>Metabolic activation:</td>
<td>with and without</td>
</tr>
<tr>
<td>Result:</td>
<td></td>
</tr>
<tr>
<td>Year:</td>
<td>GLP: no data</td>
</tr>
<tr>
<td>Test substance:</td>
<td>other TS: freshly prepared (distillation from a commercial solution in xylene) and aged chloroprene</td>
</tr>
<tr>
<td>Remark:</td>
<td>result: negative (freshly distilled chloroprene); weak positive (aged chloroprene without S9 mix); positive (aged chloroprene with S9 mix)</td>
</tr>
<tr>
<td>28-OCT-97</td>
<td></td>
</tr>
</tbody>
</table>

Type: Ames test
System of testing: Salmonella typhimurium TA 1535, TA 1537, TA 1538
Concentration: with and without
Result: negative
Method: 
Year: GLP: 
Test substance: 
Remark: result: negative, positive (TA 1535 with activation)
OECD SIDS

5. TOXICITY

CHLOROPRENE

Date: 03-09-98
Id: 126-99-8

Method: Ames test
Test substance: chloroprene purity 99%
Result: positive

Type: Ames test
System of testing: Salmonella typhimurium TA 1530, TA 100
Concentration: with and without metabolic activation
Result: positive
<table>
<thead>
<tr>
<th>Test substance:</th>
<th>(18) (21)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Type:</strong></td>
<td>Ames test</td>
</tr>
<tr>
<td><strong>System of testing:</strong></td>
<td>Salmonella typhimurium TA 100, Ta 98, TA 1535</td>
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<tr>
<td><strong>Concentration:</strong></td>
<td></td>
</tr>
<tr>
<td><strong>Metabolic activation:</strong></td>
<td>with and without</td>
</tr>
<tr>
<td><strong>Result:</strong></td>
<td></td>
</tr>
<tr>
<td><strong>Method:</strong></td>
<td></td>
</tr>
<tr>
<td><strong>Year:</strong></td>
<td></td>
</tr>
<tr>
<td><strong>Remark:</strong></td>
<td>result: positive (TA 100, TA 1535)</td>
</tr>
<tr>
<td><strong>GLP:</strong></td>
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</table>

<table>
<thead>
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<tr>
<td><strong>System of testing:</strong></td>
<td>Salmonella typhimurium TA 1535, TA 1537, TA 1538, TA 100, TA 98</td>
</tr>
<tr>
<td><strong>Concentration:</strong></td>
<td></td>
</tr>
<tr>
<td><strong>Metabolic activation:</strong></td>
<td>with and without</td>
</tr>
<tr>
<td><strong>Result:</strong></td>
<td></td>
</tr>
<tr>
<td><strong>Method:</strong></td>
<td></td>
</tr>
<tr>
<td><strong>Year:</strong></td>
<td></td>
</tr>
<tr>
<td><strong>Remark:</strong></td>
<td>result: positive (TA 100, TA 1535)</td>
</tr>
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<td><strong>GLP:</strong></td>
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<tbody>
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<td><strong>Type:</strong></td>
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<tr>
<td><strong>System of testing:</strong></td>
<td>Salmonella typhimurium TA 1537, TA 1535, TA 100, TA 98</td>
</tr>
<tr>
<td><strong>Concentration:</strong></td>
<td></td>
</tr>
<tr>
<td><strong>Metabolic activation:</strong></td>
<td>with and without</td>
</tr>
<tr>
<td><strong>Result:</strong></td>
<td>negative</td>
</tr>
<tr>
<td><strong>Method:</strong></td>
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<td><strong>Year:</strong></td>
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<td><strong>Remark:</strong></td>
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<tr>
<td><strong>GLP:</strong></td>
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</table>

<table>
<thead>
<tr>
<th>Test substance:</th>
<th>chloroprene purity 50 %</th>
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</thead>
<tbody>
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<td>Ames test</td>
</tr>
<tr>
<td><strong>System of testing:</strong></td>
<td>Salmonella typhimurium TA 1535</td>
</tr>
<tr>
<td><strong>Concentration:</strong></td>
<td></td>
</tr>
<tr>
<td><strong>Metabolic activation:</strong></td>
<td>with</td>
</tr>
<tr>
<td><strong>Result:</strong></td>
<td>positive</td>
</tr>
<tr>
<td><strong>Method:</strong></td>
<td></td>
</tr>
<tr>
<td><strong>Year:</strong></td>
<td></td>
</tr>
<tr>
<td><strong>Remark:</strong></td>
<td></td>
</tr>
<tr>
<td><strong>GLP:</strong></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Test substance:</th>
<th>(43)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Type:</strong></td>
<td>Ames test</td>
</tr>
<tr>
<td><strong>System of testing:</strong></td>
<td>Salmonella typhimurium TA 100</td>
</tr>
<tr>
<td><strong>Concentration:</strong></td>
<td></td>
</tr>
<tr>
<td><strong>Method:</strong></td>
<td></td>
</tr>
<tr>
<td><strong>Year:</strong></td>
<td></td>
</tr>
<tr>
<td><strong>Remark:</strong></td>
<td></td>
</tr>
<tr>
<td><strong>GLP:</strong></td>
<td></td>
</tr>
</tbody>
</table>
5. TOXICITY

Metabolic activation: with and without
Result: positive
Method: GLP:
Test substance:

Type: Mammalian cell gene mutation assay
System of testing: Chinese Hamster V 79
Concentration: Metabolic activation: with
Result: negative
Method: GLP:
Test substance: chloroprene purity 99 %

Type: Sister chromatid exchange assay
System of testing: human lymphocytes
Concentration: Metabolic activation: no data
Result: positive
Method: GLP:
Test substance: chloroprene purity 99 %

Type: Yeast gene mutation assay
System of testing: Saccharomyces cerevisiae D4
Concentration: Metabolic activation: with and without
Result: negative
Method: GLP:
Test substance: chloroprene purity 99 %

5.6 Genetic Toxicity 'in Vivo'

Type: Dominant lethal assay
Species: mouse Sex: male
Strain: Swiss
Route of admin.: inhalation
Exposure period: 14d, 5d/w, 6h/d
Doses: 0.0368, 0.368 mg/l
Result: No dominant lethal mutations were induced.
Method: GLP:
Test substance: chloroprene purity 99 %
5. TOXICITY

<table>
<thead>
<tr>
<th>Type:</th>
<th>Dominant lethal assay</th>
</tr>
</thead>
<tbody>
<tr>
<td>Species:</td>
<td>mouse</td>
</tr>
<tr>
<td>Sex:</td>
<td>male</td>
</tr>
<tr>
<td>Strain:</td>
<td>other: C57BL/6</td>
</tr>
<tr>
<td>Route of admin.:</td>
<td>inhalation</td>
</tr>
<tr>
<td>Exposure period:</td>
<td>no data</td>
</tr>
<tr>
<td>Doses:</td>
<td>0.000064, 0.00032, 0.0035 mg/l</td>
</tr>
<tr>
<td>Result:</td>
<td></td>
</tr>
<tr>
<td>Method:</td>
<td></td>
</tr>
<tr>
<td>Test substance:</td>
<td>no detailed information, evaluation difficult</td>
</tr>
<tr>
<td>Remark:</td>
<td>The frequency of dominant lethal mutations was significantly increased at the highest concentration.</td>
</tr>
<tr>
<td>Result:</td>
<td></td>
</tr>
</tbody>
</table>

Type:         Dominant lethal assay
Species:      mouse
Sex:          male
Strain:       other: C57BL/6
Route of admin.: inhalation
Exposure period: no data
Doses:        0.000054, 0.00013, 0.00185 mg/l
Result:       No dominant lethal mutations were induced.

Type:         Dominant lethal assay
Species:      rat
Sex:          male
Strain:       Wistar
Route of admin.: inhalation
Exposure period: 5d, 6h/d
Doses:        0.184, 0.368 mg/l
Result:       No dominant lethal mutations were induced.

Type:         Dominant lethal assay
Species:      rat
Sex:          male
Strain:       other: white rat
Route of admin.: inhalation
Exposure period: 10w
Doses:        0.000057, 0.00014 mg/l
Result:       No dominant lethal mutations were induced.
<table>
<thead>
<tr>
<th>Type</th>
<th>Dominant lethal assay</th>
<th>Sex: male</th>
</tr>
</thead>
<tbody>
<tr>
<td>Species:</td>
<td>rat</td>
<td></td>
</tr>
<tr>
<td>Strain:</td>
<td>other: white rat</td>
<td></td>
</tr>
<tr>
<td>Route of admin.:</td>
<td>inhalation</td>
<td></td>
</tr>
<tr>
<td>Exposure period:</td>
<td>22w, 4h/d</td>
<td></td>
</tr>
<tr>
<td>Doses:</td>
<td>0.000051, 0.00015, 0.00169 mg/l</td>
<td></td>
</tr>
<tr>
<td>Result:</td>
<td>no detailed information, evaluation impossible</td>
<td></td>
</tr>
<tr>
<td>Result:</td>
<td>An increase of overall embryonic mortality (accounted for by pre-implantation losses) was observed at the highest concentration.</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Type</th>
<th>Dominant lethal assay</th>
<th>Sex: male</th>
</tr>
</thead>
<tbody>
<tr>
<td>Species:</td>
<td>rat</td>
<td></td>
</tr>
<tr>
<td>Strain:</td>
<td>other: white rat</td>
<td></td>
</tr>
<tr>
<td>Route of admin.:</td>
<td>inhalation</td>
<td></td>
</tr>
<tr>
<td>Exposure period:</td>
<td>10w</td>
<td></td>
</tr>
<tr>
<td>Doses:</td>
<td>0.000051, 0.00015 mg/l</td>
<td></td>
</tr>
<tr>
<td>Result:</td>
<td>no detailed information, evaluation impossible</td>
<td></td>
</tr>
<tr>
<td>Result:</td>
<td>No influence on the overall embryonic mortality was observed at both concentrations.</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Type</th>
<th>Dominant lethal assay</th>
<th>Sex: male</th>
</tr>
</thead>
<tbody>
<tr>
<td>Species:</td>
<td>rat</td>
<td></td>
</tr>
<tr>
<td>Strain:</td>
<td>other: white rat</td>
<td></td>
</tr>
<tr>
<td>Route of admin.:</td>
<td>inhalation</td>
<td></td>
</tr>
<tr>
<td>Exposure period:</td>
<td>48d, 4h/d</td>
<td></td>
</tr>
<tr>
<td>Doses:</td>
<td>0.0000038, 0.000039 mg/l</td>
<td></td>
</tr>
<tr>
<td>Result:</td>
<td>no detailed information, evaluation impossible</td>
<td></td>
</tr>
<tr>
<td>Result:</td>
<td>An increase of the overall embryonic mortality (accounted for by pre-implantation losses) was observed at both concentrations.</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Type</th>
<th>Drosophila SLRL test</th>
<th>Sex: male</th>
</tr>
</thead>
<tbody>
<tr>
<td>Species:</td>
<td>other: Drosophila melanogaster</td>
<td></td>
</tr>
<tr>
<td>Strain:</td>
<td>other: feeding and injection</td>
<td></td>
</tr>
<tr>
<td>Route of admin.:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Exposure period:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Doses:</td>
<td>0, 1800 ppm</td>
<td></td>
</tr>
<tr>
<td>Result:</td>
<td>negative</td>
<td></td>
</tr>
<tr>
<td>Method:</td>
<td>GLP: no data</td>
<td></td>
</tr>
<tr>
<td>Test substance:</td>
<td>other TS: purity approx. 99.9 %</td>
<td></td>
</tr>
<tr>
<td>Date:</td>
<td>06-AUG-98</td>
<td></td>
</tr>
</tbody>
</table>

---
5. TOXICITY

Type: Drosophila SLRL test
Species: other: Drosophila melanogaster  Sex: male
Strain: other: wild-type strain Berlin K
Route of admin.: other: feeding
Exposure period: up to 72 hours
Doses: up to 34.3 mM
Result:
Method: GLP: no data
Year: 06-AUG-98
Test substance: other TS: purity 99 %
Result: no indication of a concentration-effect relationship; when all the data were pooled and compared with the pooled material from 7 control experiments, the difference was significant at the 1 % confidence level

Type: Micronucleus assay
Species: mouse  Sex: male/female
Strain: B6C3F1
Route of admin.: inhalation
Exposure period: 13 weeks
Doses: 0, 5, 12, 32 and 80 ppm
Result:
Method: other: as presented in Mac Gregor et al. (1990)
Year: 06-AUG-98
Test substance: other TS: purity approx. 96 %
Result: no induction of micronucleated erythrocytes in peripheral blood

Type: Micronucleus assay
Species: mouse  Sex: male
Strain: B6C3F1
Route of admin.: inhalation
Exposure period: 12d, 6h/d
Doses: 0.044, 0.118, 0.294, 0.736 mg/l
Result:
Method: GLP:
Year: 06-AUG-98
Test substance: 100 % mortality in the highest dose group
Result: No significant alterations in the frequency of micronucleated normochromatic and polychromatic erythrocytes in the peripheral blood
Test substance: chloroprene purity 98 %

Type: Micronucleus assay
Species: rat  Sex: male/female
Strain: Wistar
Route of admin.: inhalation
Exposure period: 5d, 6h/d
Doses: 0, 0.368 mg/l
Result:
Method: GLP:
Year: 06-AUG-98
Test substance: body weight gain was decreased compared with controls

Remark: No significant alterations in the frequency of micronucleated normochromatic and polychromatic erythrocytes in the peripheral blood

Test substance: chloroprene purity 98 %

Remark: body weight gain was decreased compared with controls
### OECD SIDS

**CHLOROPRENE**

**5. TOXICITY**

<table>
<thead>
<tr>
<th>Result:</th>
<th>The incidence of micronucleated erythrocytes and the ratio of poly- and normochromatic erythrocytes in the bone marrow was not affected by treatment.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Type:</td>
<td>Micronucleus assay</td>
</tr>
<tr>
<td>Species:</td>
<td>mouse</td>
</tr>
<tr>
<td>Strain:</td>
<td>no data</td>
</tr>
<tr>
<td>Route of admin.:</td>
<td>inhalation</td>
</tr>
<tr>
<td>Exposure period:</td>
<td>2d, 2h/d</td>
</tr>
<tr>
<td>Doses:</td>
<td>0.0015, 0.0666, 0.4643, 0.763 mg/l</td>
</tr>
<tr>
<td>Result:</td>
<td></td>
</tr>
<tr>
<td>Method:</td>
<td>GLP:</td>
</tr>
<tr>
<td>Test substance:</td>
<td></td>
</tr>
<tr>
<td>Sex:</td>
<td>no data</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Result:</th>
<th>The micronucleated polychromatic erythrocytes were elevated in a dose dependent manner (no information about the number of normochromatic erythrocytes).</th>
</tr>
</thead>
<tbody>
<tr>
<td>Type:</td>
<td>Sister chromatid exchange assay</td>
</tr>
<tr>
<td>Species:</td>
<td>mouse</td>
</tr>
<tr>
<td>Strain:</td>
<td>B6C3F1</td>
</tr>
<tr>
<td>Route of admin.:</td>
<td>inhalation</td>
</tr>
<tr>
<td>Exposure period:</td>
<td>12d, 6h/d</td>
</tr>
<tr>
<td>Doses:</td>
<td>0.044, 0.118, 0.294, 0.736 mg/l</td>
</tr>
<tr>
<td>Result:</td>
<td></td>
</tr>
<tr>
<td>Method:</td>
<td>GLP:</td>
</tr>
<tr>
<td>Test substance:</td>
<td></td>
</tr>
<tr>
<td>Sex:</td>
<td>male</td>
</tr>
</tbody>
</table>

| Remark: | 100 % mortality in the highest dose group                                                                                               |
| Result: | No significant increase in sister chromatid exchange                                                                                     |
| Test substance: | chloroprene purity 98 %                                                                                                                  |

| Type:   | other: (see remarks)                                                                                                                    |
| Species:| mouse                                                                                                                                  |
| Strain: | B6C3F1                                                                                                                                  |
| Route of admin.: | inhalation                                                                                                         |
| Exposure period: | 12d, 6h/d                                                                                                      |
| Doses: | 0.044, 0.118, 0.294, 0.736 mg/l                                                                                                    |
| Result: |                                                                                                                                         |
| Method: | GLP:                                                                                                                                   |
| Test substance: |                                                                                                                                        |
| Sex: | male                                                                                                                                   |

| Remark: | 100 % mortality in the highest dose group test type: bone marrow average generation was examined |
| Result: | No significant alteration in the bone marrow average generation time                                                                 |
| Test substance: | chloroprene purity 98 %                                                                                                                  |

| Type:   | other: (see remarks)                                                                                                                    |
| Species:| mouse                                                                                                                                  |
| Strain: | B6C3F1                                                                                                                                  |
| Route of admin.: | inhalation                                                                                                         |
| Exposure period: | 12d, 6h/d                                                                                                      |
| Doses: | 0.044, 0.118, 0.294, 0.736 mg/l                                                                                                    |
OECD SIDS
CHLOROPRENE

5. TOXICITY

Date: 03-09-98
Id: 126-99-8

<table>
<thead>
<tr>
<th>Year:</th>
<th>GLP:</th>
</tr>
</thead>
<tbody>
<tr>
<td>Test substance:</td>
<td>chloroprene purity 98 %</td>
</tr>
<tr>
<td>Remark:</td>
<td>100 % mortality in the highest dose group</td>
</tr>
<tr>
<td>Result:</td>
<td>The mitotic index was elevated, with the increase being significant only at the highest dose evaluated.</td>
</tr>
</tbody>
</table>

| Type: | other: Cytogenetic assay bone marrow |
| Species: | rat |
| Sex: | male |
| Strain: | no data |
| Route of admin.: | inhalation |
| Exposure period: | 16 w, 5d/w, 4h/d |
| Doses: | see remarks |
| Result: | |
| Method: | |

| Test substance: | no details reported, evaluation impossible |
| Result: | increased chromosomenaberrations |
| Test substance: | mixtures of chloroprene (0.00196 mg/l)/dodecylmercaptan (0.00502 mg/l)/ammonia (0.0198 mg/l) and chloroprene (0.0028 mg/l)/methylacrylate (0.004 mg/l) |

| Type: | other: Cytogenetic assay bone marrow |
| Species: | rat |
| Sex: | female |
| Strain: | no data |
| Route of admin.: | inhalation |
| Exposure period: | 48 d, 4h/d |
| Doses: | 0.00000038, 0.000039 mg/l |
| Result: | |
| Method: | |

| Year: | GLP: |
| Test substance: | no data |
| Remark: | no details reported, evaluation impossible |
| Result: | increased chromosomenaberrations |

| Type: | other: Cytogenetic assay bone marrow |
| Species: | mouse |
| Sex: | no data |
| Strain: | other: C57BL/6 |
| Route of admin.: | inhalation |
| Exposure period: | 8 w |
| Doses: | 0.000064, 0.00032, 0.035 mg/l |
| Result: | |
| Method: | |

| Year: | GLP: |
| Test substance: | no data |
| Remark: | no details reported, evaluation impossible |
| Result: | increased chromosomenaberrations |

| Type: | other: Cytogenetic assay bone marrow |
| Species: | mouse |
| Sex: | no data |
| Strain: | other: C57BL/6 |
| Route of admin.: | inhalation |
| Exposure period: | 8 w |
5. TOXICITY

Doses: 0.000054, 0.00013, 0.00185 mg/l
Result: 
Method: 
Year: GLP:
Test substance: 
Remark: no details reported, evaluation impossible
Result: increased chromosomenaberrations

Type: other: Cytogenetic assay bone marrow
Species: mouse
Strain: B6C3F1
Route of admin.: inhalation
Exposure period: 12 d, 6h/d
Doses: 0.044, 0.118, 0.297, 0.736 mg/l
Result: 100 % mortality in the highest dose group
Method: 
Year: GLP:
Test substance: 
Remark: No significant increase in chromosomal aberrations
Test substance: chloroprene purity 98 %

5.7 Carcinogenicity

Species: mouse
Strain: other: Mongrel albino mice
Route of admin.: dermal
Exposure period: no data
Frequency of treatment: once
Post. obs. period: 30d
Doses: 
Result: Control Group: no data specified
Method: other: Sebaceous gland test
Year: GLP:
Test substance: 
Remark: no detailed information, evaluation impossible
Result: The sebaceous glands showed no particular changes.

Species: rat
Strain: Wistar
Route of admin.: inhalation
Exposure period: 2a
Frequency of treatment: 5d/w, 6h/d
Post. obs. period: no
Doses: 0.0368, 0.184 mg/l (10, 50 ppm)
Result: Control Group: yes, concurrent no treatment
Method: 
Year: GLP:
Test substance: 
Remark: analytical concentrations; most of the animals of
the low-level group died in week 72 by suffocation because the ventilation was interrupted. 
see also chapter 4.4

**Result:** No evidence of carcinogenic activity in rats at the 50 ppm level

**Test substance:** freshly purified chloroprene

06-AUG-98

<table>
<thead>
<tr>
<th>Species:</th>
<th>rat</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Sex:</strong></td>
<td>male/female</td>
</tr>
<tr>
<td><strong>Strain:</strong></td>
<td>Fischer 344</td>
</tr>
<tr>
<td><strong>Route of admin.:</strong></td>
<td>inhalation</td>
</tr>
<tr>
<td><strong>Exposure period:</strong></td>
<td>2 years</td>
</tr>
<tr>
<td><strong>Frequency of treatment:</strong></td>
<td>6h/day; 5 days/week</td>
</tr>
<tr>
<td><strong>Post. obs. period:</strong></td>
<td>no</td>
</tr>
<tr>
<td><strong>Doses:</strong></td>
<td>0, 12.8, 32, 80 or 200 ppm</td>
</tr>
<tr>
<td><strong>Result:</strong></td>
<td>Control Group: yes, concurrent no treatment</td>
</tr>
<tr>
<td><strong>Method:</strong></td>
<td>other</td>
</tr>
<tr>
<td><strong>Year:</strong></td>
<td>(130) (141)</td>
</tr>
<tr>
<td><strong>Test substance:</strong></td>
<td>other TS: purity: approx. 96 %</td>
</tr>
<tr>
<td><strong>Result:</strong></td>
<td>concentration dependent increase of incidences of nonneoplastic effects in the nose; increased incidences of neoplasms of oral cavity, thyroid gland and kidney in males and females; increased incidences of neoplasms of lung (m) and mammary gland (f)</td>
</tr>
</tbody>
</table>

28-OCT-97

<table>
<thead>
<tr>
<th>Species:</th>
<th>mouse</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Sex:</strong></td>
<td>no data</td>
</tr>
<tr>
<td><strong>Strain:</strong></td>
<td>other: Kunming albino mice</td>
</tr>
<tr>
<td><strong>Route of admin.:</strong></td>
<td>inhalation</td>
</tr>
<tr>
<td><strong>Exposure period:</strong></td>
<td>28 w</td>
</tr>
<tr>
<td><strong>Frequency of treatment:</strong></td>
<td>6d/w, 4h/d</td>
</tr>
<tr>
<td><strong>Post. obs. period:</strong></td>
<td>4 w</td>
</tr>
<tr>
<td><strong>Doses:</strong></td>
<td>0.0029, 0.01918, 0.189 mg/l</td>
</tr>
<tr>
<td><strong>Result:</strong></td>
<td>Control Group: other: yes</td>
</tr>
<tr>
<td><strong>Method:</strong></td>
<td>other: short term test for the induction of lung tumor</td>
</tr>
<tr>
<td><strong>Year:</strong></td>
<td>GLP:</td>
</tr>
<tr>
<td><strong>Test substance:</strong></td>
<td>No lung tumors were found before the 6th month. The tumor incidence in the 0.0029 mg/l group increased significantly; the higher the concentration, the higher the incidence (no information about mortality).</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Species:</th>
<th>mouse</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Sex:</strong></td>
<td>male/female</td>
</tr>
<tr>
<td><strong>Strain:</strong></td>
<td>B6C3F1</td>
</tr>
<tr>
<td><strong>Route of admin.:</strong></td>
<td>inhalation</td>
</tr>
<tr>
<td><strong>Exposure period:</strong></td>
<td>2 years</td>
</tr>
<tr>
<td><strong>Frequency of treatment:</strong></td>
<td>6h/day; 5 days/week</td>
</tr>
<tr>
<td><strong>Post. obs. period:</strong></td>
<td>no</td>
</tr>
<tr>
<td><strong>Doses:</strong></td>
<td>0, 12.8, 32 or 80 ppm</td>
</tr>
<tr>
<td><strong>Result:</strong></td>
<td></td>
</tr>
</tbody>
</table>
Control Group: yes, concurrent no treatment
Method: other

Year: GLP: no data
Test substance: other TS: purity: approx. 96 %
Result: concentration dependent increase of incidences of nonneoplastic effects in the nose and spleen of both sexes; increased incidences of neoplasms of the lung, circulatory system and harderian gland in males and females; increased incidences of the forestomach and kidney (m) and mammary gland, liver, skin and mesentery (f)

28-OCT-97                                                                 (120)

Species: hamster                                          Sex: male/female
Strain: other: Syrian golden
Route of admin.: inhalation
Exposure period: 18 months
Frequency of treatment: 5d/w, 6h/d
Post. obs. period: no
Doses: 0.0368, 0.184 mg/l (10, 50 ppm)
Result: Control Group: yes, concurrent no treatment
Method: GLP:

Test substance: analytical concentrations; see also chapter 4.4
Result: No evidence of carcinogenic activity in hamster up to an exposure level of 50 ppm.

Test substance: freshly purified chloroprene
06-AUG-98                                                                 (129) (141)

Species: rat                                              Sex: female
Strain: other: BDIV
Route of admin.: oral unspecified
Exposure period: once
Frequency of treatment: 
Post. obs. period: 120w
Doses: 100 mg/kg bw
Result: Control Group: other: yes, vehicle
Method: GLP:

Test substance: on the 17th day of pregnancy the animals got the single dose, see also chapter 4.8
Result: No evidence of carcinogenicity of chloroprene.

Test substance: chloroprene purity 99 %

Species: rat                                              Sex: male/female
Strain: other: BDIV
Route of admin.: oral unspecified
Exposure period: 117w
Frequency of treatment: twice a week
Post. obs. period: no
### 5. TOXICITY

**Doses:** 50 mg/kg bw  
**Result:**  
**Control Group:** yes, concurrent vehicle  
**Method:**  
**Year:** GLP:  
**Test substance:** see also chapter 4.4 and 4.8  
**Result:** No evidence of carcinogenicity of chloroprene.  
**Test substance:** chloroprene purity 99 %  

**Species:** other: (see remarks)  
**Sex:**  
**Strain:**  
**Route of admin.:**  
**Exposure period:**  
**Frequency of treatment:**  
**Post. obs. period:**  
**Doses:**  
**Result:**  
**Control Group:** yes, concurrent no treatment  
**Method:**  
**Year:** GLP:  
**Test substance:** Chloroprene does not cause neoplasms in mice and rats when applied by gavage, intratracheally, s.c. and dermally. In combination with dimethylbenzanthracene chloroprene showed no promoting activity (incomplete reporting of the studies, insufficient duration of the experiments).  

**5.8 Toxicity to Reproduction**

**Type:** Fertility  
**Species:** rat  
**Sex:** male  
**Strain:** Wistar  
**Route of admin.:** inhalation  
**Exposure Period:** 5d  
**Frequency of treatment:** 6h/d, daily  
**Duration of test:**  
**Doses:** 0.184, 0.368 mg/l (50, 100 ppm)  
**Control Group:** yes, concurrent no treatment  
**Method:**  
**Year:** GLP:  
**Test substance:** nominale concentration; see also chapter 5.4 and 5.6  
**Result:** No adverse effects on fertility.  
**Test substance:** chloroprene freshly distilled under nitrogen  

**Type:** Fertility  
**Species:** rat  
**Sex:** male  
**Strain:** other: Charles River  
**Route of admin.:** inhalation
Exposure Period: 22d
Frequency of treatment: 4h/d, daily
Duration of test: 
Doses: 0.092 mg/l (25 ppm)
Control Group: yes, concurrent no treatment
Method:
Year: GLP:
Test substance: 
Remark: The reproductive capability of the males was not impaired.
Test substance: chloroprene 99.9+% pure and contained fewer than 50 ppm dimers

Type: Fertility
Species: rat Sex: male
Strain: 
Route of admin.: inhalation
Exposure Period: 48d
Frequency of treatment: 4h/d
Duration of test: 
Doses: 0.0000038, 0.000039 mg/l
Control Group: yes
Method:
Year: GLP:
Test substance: no detailed information, evaluation impossible
Remark: see also chapter 5.6
Result: The fertilizing ability of the males did not suffer; the motility of the spermazooa was unchanged.

Type: Fertility
Species: rat Sex: male
Strain: Wistar
Route of admin.: inhalation
Exposure Period: 91d
Frequency of treatment: 5d/w, 6h/d
Duration of test: 
Doses: 0.037, 0.121, 0.368 mg/l (10, 33, 100 ppm)
Control Group: yes, concurrent no treatment
Method:
Year: GLP:
Test substance: nominal concentration, see also chapter 5.4
Remark: Fertility was not adversely affected; microscopic examination of the testicles did not show any abnormality.
Result: freshly purified chloroprene

Type: Fertility
Species: rat Sex: female
Strain: no data
Route of admin.: inhalation
Exposure Period: 24w
Frequency of
Treatment: 6d/w, 5h/d
Duration of test: 13 weeks
Doses: 0.030 mg/l
Control Group: yes
Method: Year: GLP:
Test substance: no detailed information, evaluation impossible
Remark: No adverse effects on the female fertility.
Result: (86)

Type: Fertility
Species: rat Sex: male/female
Strain: Fischer 344
Route of admin.: inhalation
Exposure Period: 13 weeks
Frequency of treatment: 6h/day; 5 days/week
Doses: 0, 5, 32 or 200 ppm
Control Group: yes, concurrent no treatment
Method: other: sperm morphology and vaginal cytology evaluations on subchronic study rats
Year: GLP:
Test substance: other TS: purity: approx. 96 %
Result: a decrease of sperm motility (200 ppm)
28-OCT-97 (88) (120)

Type: Fertility
Species: mouse Sex: male
Strain: no data
Route of admin.: inhalation
Exposure Period:
Frequency of treatment: 8h
Duration of test: Doses: 0.548 mg/l
Control Group: yes
Method: Year: GLP:
Test substance: no detailed information, evaluation impossible;
Remark: The number of pregnant mice decreased; the litter size was unchanged.
Result: (145)

Type: Fertility
Species: mouse Sex: female
Strain: no data
Route of admin.: inhalation
Exposure Period:
Frequency of treatment: 8h
Duration of test: Doses: 0.544 mg/l
Control Group: yes
Method: Year: GLP:
Test substance: no detailed information, evaluation impossible; 
Remark: The number of pregnant rats was unchanged; normal litter size. 

Type: Fertility 
Species: mouse 
Strain: Swiss 
Route of admin.: inhalation 
Exposure Period: 14d 
Frequency of treatment: 5d/w, 6h/d 
Duration of test: 
Doses: 0.0368, 0.368 mg/l 
Control Group: yes, concurrent no treatment 
Method: 
Year: GLP: 
Test substance: 
Remark: nominale concentration; see also chapter 5.4 and 5.6 
Result: There was no indication of antifertility effects. 

Test substance: chloroprene freshly distilled under nitrogen 

Type: Fertility 
Species: mouse 
Strain: B6C3F1 
Route of admin.: inhalation 
Exposure Period: 13 weeks 
Frequency of treatment: 6h/day; 5 days/week 
Duration of test: 13 weeks 
Doses: 0, 12, 32 or 80 ppm 
Control Group: yes, concurrent no treatment 
Method: other: sperm morphology and vaginal cytology evaluations on subchronic study rats 
Year: GLP: no 
Test substance: other TS: purity: approx. 96 % 
Result: no effects in comparison to the chamber controls 

Type: 
Species: rat 
Strain: Wistar 
Route of admin.: inhalation 
Exposure Period: 13 or 26 weeks 
Frequency of treatment: 5d/w, 6h/d 
Duration of test: 
Doses: 0.037, 0.121, 0.368 mg/l (10, 33, 100 ppm) 
Control Group: yes, concurrent no treatment 
Method: 
Year: GLP: 
Test substance: nominal concentration, sperm cell abnormalities 
Remark: 
Result: No induction of sperm cell abnormalities or changes in the sperm concentration 

(145) 

(55) 

(88) (120) 

(56)
5. TOXICITY

**Type:** other: (see remarks)

**Species:** rat  
**Sex:** male

**Strain:** no data

**Route of admin.:** inhalation

**Exposure Period:** 22w

**Frequency of treatment:** 4h/d

**Duration of test:**

**Doses:** 0.000051, 0.00015, 0.00169 mg/l

**Control Group:** yes

**Method:**

**Year:** GLP:

**Test substance:**

**Remark:** no detailed information, evaluation impossible, see also chapter 5.6

**Result:**

- 0.000051 mg/l: no effects
- 0.00015 and 0.00169 mg/l: an increase in the over-all embryonic mortality; cases of atrophy of the testicles; spermatozoa with reduced resistance to an acid medium and reduced mobility

---

**Type:** other: (see remarks)

**Species:** rat  
**Sex:** male

**Strain:** no data

**Route of admin.:** inhalation

**Exposure Period:** 10w

**Frequency of treatment:**

**Duration of test:**

**Doses:** 0.000051, 0.00015 mg/l

**Control Group:** yes

**Method:**

**Year:** GLP:

**Test substance:**

**Remark:** no detailed information, evaluation impossible, see also chapter 5.6

**Result:**

- 0.000051 mg/l: no effects
- 0.00015 mg/l: spermatozoa with reduced resistance to an acid medium and reduced mobility

---

**Type:** other: (see remarks)

**Species:** rat  
**Sex:** female

**Strain:** no data

**Route of admin.:** inhalation

**Exposure Period:** 16w

**Frequency of treatment:** 5h/d

**Duration of test:**

**Doses:** 0.5 mg/l

**Control Group:** yes, concurrent no treatment

**Method:**

**Year:** GLP:

**Test substance:**

**Remark:** no detailed information, evaluation impossible

**Result:** The esteral period was prolonged; changed vaginal smears

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(87)
5. TOXICITY

Type: other: (see remarks)
Species: rat
Sex: female
Strain: no data
Route of admin.: inhalation
Exposure Period: 28w
Frequency of treatment: 5h/d
Duration of test:
Doses: 0.5 mg/l
Control Group: yes, concurrent no treatment
Method:
Year: GLP:
Test substance: no detailed information, evaluation impossible
Remark: The estral period was prolonged; changed vaginal smears; during the estral period the number of primordial follicles decreased; the number of atretic follicles increased; the weight of ovaries increased.

Type: other: (see remarks)
Species: rat
Sex: male
Strain: no data
Route of admin.: gavage
Exposure Period: 20d
Frequency of treatment:
Duration of test:
Doses: 0.5 mg/kg bw
Control Group: yes
Method:
Year: GLP:
Test substance: no detailed information, evaluation impossible; see also chapter 5.4
Remark: relative weight of gonads unchanged
Test substance: purified chloroprene in water

Type: other: (see remarks)
Species: rat
Sex: male
Strain: no data
Route of admin.: gavage
Exposure Period: 28d
Frequency of treatment:
Duration of test:
Doses: 0.0005, 0.005, 0.05 mg/kg bw
Control Group:
Method:
Year: GLP:
Test substance: no detailed information, evaluation impossible; see also chapter 5.4
Remark: weight of gonads and the semen were unchanged
Test substance: purified chloroprene in water
5. TOXICITY

Type: other: (see remarks)  
Species: rat  
Sex: male  
Strain: no data  
Route of admin.: gavage  
Exposure Period: 24w  
Frequency of treatment:  
Duration of test:  
Doses: 0.0005, 0.005, 0.05 mg/kg bw  
Control Group:  
Method:  
Year: GLP:  
Test substance:  
Remark: no detailed information, evaluation impossible; see also chapter 5.4  
Result: 0.005 and 0.05 mg/kg bw: relative weight of gonads increased; the motility time of the spermatozoids decreased 0.05 mg/kg bw: reduction in the osmotic resistance of the spermatozoids

Test substance: purified chloroprene in water

(73)

Type: other: (see remarks)  
Species: mouse  
Sex: no data  
Strain: other: C57BL/6  
Route of admin.: inhalation  
Exposure Period: 8w  
Frequency of treatment:  
Duration of test:  
Doses: 0.00006, 0.00032, 0.0035 mg/l  
Control Group: yes  
Method:  
Year: GLP:  
Test substance:  
Remark: no detailed information, evaluation impossible; see also chapter 5.6  
Result: 0.00032 and 0.0035 mg/l: adverse changes in spermatogenesis 0.00006 mg/l: no adverse effect

(136)

5.9 Developmental Toxicity/Teratogenicity

Species: rat  
Sex: female  
Strain: Wistar  
Route of admin.: inhalation  
Exposure period: 11d  
Frequency of treatment: 6.-16. gestation day  
Duration of test:  
Doses: 0.037, 0.092, 0.276, 0.644 mg/l (10, 25, 75, 175 ppm)  
Control Group: yes, concurrent no treatment  
Method:  
Year: GLP:  
Test substance: NOEL Maternal Toxicity: 10 ppm  
Remark: analytical concentration
<table>
<thead>
<tr>
<th>Test substance:</th>
<th>chloroprene freshly purified</th>
</tr>
</thead>
<tbody>
<tr>
<td>Species:</td>
<td>rat</td>
</tr>
<tr>
<td>Sex:</td>
<td>female</td>
</tr>
<tr>
<td>Strain:</td>
<td>Wistar</td>
</tr>
<tr>
<td>Route of admin.:</td>
<td>inhalation</td>
</tr>
<tr>
<td>Exposure period:</td>
<td>13d</td>
</tr>
<tr>
<td>Frequency of treatment:</td>
<td>4.-16. gestation day</td>
</tr>
<tr>
<td>Duration of test:</td>
<td></td>
</tr>
<tr>
<td>Doses:</td>
<td>0.037, 0.092, 0.276, 0.644 mg/l (10, 25, 75, 175 ppm)</td>
</tr>
<tr>
<td>Control Group:</td>
<td>yes, concurrent no treatment</td>
</tr>
<tr>
<td>Method:</td>
<td>GLP:</td>
</tr>
<tr>
<td>Year:</td>
<td></td>
</tr>
<tr>
<td>Test substance:</td>
<td>NOEL Maternal Tox.: 10 ppm</td>
</tr>
<tr>
<td>Remark:</td>
<td>analytical concentration</td>
</tr>
<tr>
<td>Result:</td>
<td>0.276 anf 0.644 mg/l: some foetal growth depression At concentrations up to 0.644 mg/l chloroprene did not exert any teratogenic effect.</td>
</tr>
<tr>
<td>Test substance:</td>
<td>freshly purified chloroprene</td>
</tr>
<tr>
<td>Species:</td>
<td>rat</td>
</tr>
<tr>
<td>Sex:</td>
<td>female</td>
</tr>
<tr>
<td>Strain:</td>
<td>other: Charles River</td>
</tr>
<tr>
<td>Route of admin.:</td>
<td>inhalation</td>
</tr>
<tr>
<td>Exposure period:</td>
<td>18d</td>
</tr>
<tr>
<td>Frequency of treatment:</td>
<td>3.-20. gestation day</td>
</tr>
<tr>
<td>Duration of test:</td>
<td></td>
</tr>
<tr>
<td>Doses:</td>
<td>0.0037, 0.037, 0.092 mg/l (1, 10, 25 ppm)</td>
</tr>
<tr>
<td>Control Group:</td>
<td>yes, concurrent no treatment</td>
</tr>
<tr>
<td>Method:</td>
<td>GLP:</td>
</tr>
<tr>
<td>Year:</td>
<td></td>
</tr>
<tr>
<td>Test substance:</td>
<td>NOEL Maternal Tox.: 25 ppm</td>
</tr>
<tr>
<td>Remark:</td>
<td>analytical concentration</td>
</tr>
<tr>
<td>Result:</td>
<td>A significant increase was found in the number of dams that had resorptions following exposure to 10 ppm. An increase in the average body weight of fetuses from dams exposed to chloroprene. Fetuses from dams exposed to 10 and 25 ppm were significantly longer. No skeletal or soft tissue malformations were observed</td>
</tr>
<tr>
<td>Test substance:</td>
<td>chloroprene 99.9+% pure and contained fewer than 50 ppm dimers</td>
</tr>
<tr>
<td>Species:</td>
<td>rat</td>
</tr>
<tr>
<td>Sex:</td>
<td>female</td>
</tr>
<tr>
<td>Strain:</td>
<td>other: Charles River</td>
</tr>
<tr>
<td>Route of admin.:</td>
<td>inhalation</td>
</tr>
<tr>
<td>Exposure period:</td>
<td>12d</td>
</tr>
<tr>
<td>Frequency of treatment:</td>
<td>1.-12. gestation day</td>
</tr>
<tr>
<td>Duration of test:</td>
<td></td>
</tr>
<tr>
<td>Doses:</td>
<td>0.0037, 0.037, 0.092 mg/l (1, 10, 25 ppm)</td>
</tr>
<tr>
<td>Control Group:</td>
<td>yes, concurrent no treatment</td>
</tr>
</tbody>
</table>
### Method:
**Year:** 03-09-98

**Test substance:**
NOEL Maternal Tox: 25 ppm

**Remark:**
remark: analytical concentration, embryotoxicity study

**Result:**
No embryonal toxicity at chloroprene levels up to 25 ppm was observed.

**Test substance:**
chloroprene 99.9+% pure and contained fewer than 50 ppm dimers

### Species:
rat

### Sex:
female

### Strain:
no data

### Route of admin.:
inhalement

### Exposure period:
22d

### Frequency of treatment:
1.-22. gestation day

### Duration of test:
0.0000156, 0.000013, 0.0006, 0.003, 0.004 mg/l

### Control Group:
yes

### Result: Exposure to concentrations of 0.003 and 0.004 mg/l led to reduced fetal weight, an increase in the overall embryonal mortality and to teratogenic effects (reduced length of the diaphase (?) of the femur and fibula, disturbances in the vascular permeability). No such changes were demonstrated in the other dose groups.

### Species:
rat

### Sex:
male/female

### Strain:
Wistar

### Route of admin.:
inhalement

### Exposure period:
13w (Fo), 10w (F1)

### Frequency of treatment:
5d/w, 6h/d

### Duration of test:
0.037, 0.121, 0.368 mg/l (10, 33, 100 ppm)

### Control Group:
yes, concurrent no treatment

### Method:

**Year:**

**Test substance:**
NOEL Parental: 33 ppm
NOEL F1 Offspring: 10 ppm
NOEL F2 Offspring: remark: nominal concentration

**Result:**
Fertility of males and females, number of young born per litter, general condition, appearance, male/female ratio, and mortality of the young were not adversely affected. There was no indication of increased intra-uterine mortality. Growth retardation was observed in the Fo-generation at the high dose level and in the F1-generation at the mid- and high-dose levels. The relative weights of the liver and the ovaries of the high-level female rats (descendants from untreated females and treated males) were elevated.

**Test substance:**
chloroprene freshly purified
Species: rabbit  Sex: female
Strain: New Zealand white
Route of admin.: inhalation
Exposure period: 6 through 28 days of gestation
Frequency of treatment: 6 h/day, 7 days/week
Duration of test: day 29 of gestation
Doses: 0, 10, 40, 175 ppm
Control Group: yes
Method: other: no data
Year: GLP: no data
Test substance: no data
Result: chloroprene did not result in observable toxicity to either the dam or the offspring at any concentration tested; no increased of fetal malformations (no further information available from the abstract)

06-AUG-98
Species: rat  Sex: female
Strain: other: BDIV
Route of admin.: gavage
Exposure period: 1d
Frequency of treatment: 17. gestation day
Duration of test: 
Doses: 100 mg/kg bw
Control Group: yes, concurrent vehicle
Method: GLP: 
Year: 
Test substance: see also chapter 4.4 and 4.7
Result: Litter sizes and pre-weaning mortality were not different in chloroprene treated animals from those in controls.
Test substance: chloroprene, purity 99 %, containing 0.8 % 1-chlorobutadiene

5.10 Other Relevant Information

Type: Immunotoxicity
Remark: Chlorobutadiene can exert inhibitory effects on cellular and primary humoral immune function, toxic effects on thymus and bone marrow when inhaled for 2-3 weeks at concentrations up to 0.4 mg/l in mice (no detailed information, evaluation impossible)
Test substance: chlorobutadiene

Type: Metabolism
Remark: After incubation with mouse-liver microsomes volatile alkylating metabolites could be trapped by reaction with an excess of 4-(4-nitrobenzyl)pyridine.
Test substance: chloroprene, purity 99%

Type: Metabolism
In homogenates of liver, kidney, spleen and brain of rats the content of SH groups decreased after incubation with chloroprene (no further information).

Test material: (109)

A review of the data on health effects in man is given by IARC. (54)

A decrease in the immunity to transplantation was observed in rats when administered 1-5 s.c. injections at 0.5 ul/kg (no detailed information, evaluation possible)

Test substance: (4)

The antibody forming cells in the spleen decreased when injected s.c. at 0.5 ul/g into rats before, during or after they were immunized with sheep erythrocytes (no detailed information, evaluation impossible)

Test substance: (3)

Inhalation of 0.001 mg/l for 5h/d for 7 months delayed the reversal of primary or secondary motor-defense conditioned reflexes. However chronic inhalation of 0.03 and 1.4 mg/l accelerated the reversal of conditioned reflexes.

Test substance: (5)

rat (male, wistar), 0, 50, 100 mg/kg bw, single dose by stomach tube: rapid decrease of hepatic GSH, dose dependent increase in the excretion of urinary thioethers. (138)

Normal hamster lung cells treated with chloroprene showed malignant transformations 14 weeks after treatment. (81) (89)

In primary cell cultures of Syrian hamster embryo cells treated prior to virus inoculation with chloroprene no increased frequency of adenovirus transformation was seen. But chloroprene will enhance the transformation when added after virus adsorption and cell transfer. (25)

The TC50 for primary rat hepatocytes is reported to be 0.78 mg/ml. After incubation with chloroprene >= 0.96 mg/ml the activities of GOT and LDH decreased. (81) (89)
5. TOXICITY

Type: other: Hepatoxicity in vitro
Remark: LDH release of primary rat hepatocytes did not rise significantly above control until addition of 885 μg chloroprene/ml. Within 15 and 30 min 46 and 55 % of the total LDH activity was found in the cell medium.
Test Substance: unstablized chloroprene, purity > 99.7%

Type: other: acute inhalation toxicity
Remark: Fed and fasted rats (Sprague Dawley, male) were exposed to concentrations of 500, 1000, 2000, 4600, 10000 ppm (1.84, 3.68, 7.36, 16.928, 36.8 mg/l) for 4h. Fed rats: one death in the 10000 ppm group, elevated serum alanine-alpha-ketoglutarate transaminase AKT activity (4600 and 10000 ppm). Fasted rats: deaths in all dose groups, dose dependent increase of the serum AKT activity.

5.11 Experience with Human Exposure

Remark: Exposure of man to high concentrations of chloroprene vapour produces similar effects to those seen in animals.

Remark: A wide range of adverse effects are described in chloroprene exposed workers. Among these are effects on the central, peripheral and autonomic nervous system, the respiratory system, the liver, the kidneys, adrenal glands, blood, the immune system and the bones.
In many papers describing these effects the extent of the exposure and the purity of the chloroprene are not stated. It is also likely that exposure to a variety of other chemicals occured.

Remark: Exposure to the dimer may be responsible for the occurrence of hair loss which is recognised in workers in chloroprene plants.

Remark: Reports of a study carried out in the USSR suggest that there is an increased incidence of cancers in chloroprene exposed workers while a more recent study in the USA has not found chloroprene to be a human carcinogen.
Remark: It is the opinion of the authors that the results of a recent case-control study and a cohort study suggested that chloroprene exposure increases the risk of developing cancer.  

(77)

Remark: One case of liver angiosarcoma has been reported in a worker who had extensive exposure to finished polychloroprene (no information about the amount of residual monomere in the polychloroprene).

(59)

Remark: An increase in the incidence of chromosomal aberrations in lymphocytes has been reported in several surveys of chloroprene workers in the U.S.S.R.  

(64) (65) (136) (152)

Remark: Reports from the U.S.S.R. have attributed infertility and a number of gynaecological conditions as well as premature births to chloroprene exposure. Long-term exposure of male workers has been described as affecting sexual function, semen volume and the morphological appearance of spermatozoa.  

(136) (144)

Remark: An evaluation of the biochemical and hematological status of active chloroprene workers at Du Pont Company plant does not indicate that the workers have biochemical and hematological alterations of medical significance.  

(50)

Remark: No increasing of sister chromatid exchange in workers chronically exposed to chloroprene was found.  

(51)
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