FOREWORD INTRODUCTION

2-BUTENE, 1,3-DICHLORO

CAS N°: 926-57-8

SIDS Initial Assessment Report

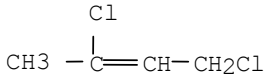
For

SIAM 22

Paris, France, 18-21 April 2006

1. Chemical Name:	2-BUTENE, 1,3-DICHLORO-
2. CAS Number:	926-57-8
3. Sponsor Country:	United States
4. Shared Partnership with:	DuPont Performance Elastomers, L.L.C., TOSOH Corporation, Polimeri Europa France, Bayer, AG, Denki Kagaku Kogyo
5. Roles/Responsibilities of the Partners:	
• Name of industry sponsor /consortium	International Institute of Synthetic Rubber Producers (IISRP) Houston, TX
• Process used	The IUCLID Data Set and SIAR were prepared by the Industry Consortium. Data were obtained from published scientific literature, databases, handbooks, unpublished industry files and testing.
6. Sponsorship History	
• How was the chemical or category brought into the OECD HPV Chemicals Programme?	The IISRP submitted a test plan and IUCLID to the United States Environmental Protection Agency (U.S. EPA) in April 2004 as part of the International Council of Chemical Associations' (ICCA) global initiative on High Production Volume (HPV) chemicals.
7. Review Process Prior to the SIAM:	Members of the IISRP conducted a comprehensive literature search. The SIDS Dossier was prepared and reviewed by industry toxicologists prior to submission to the U.S. EPA. The U.S. EPA reviewed the submitted data and offered comments to industry. The U.S. EPA submitted the documents to the OECD for consideration at SIAM 22.
8. Quality check process:	The quality of existing data was determined using guidance provided in the Manual for Investigation of HPV Chemicals, Chapter 3: Data Evaluation (OECD, 2002)
9. Date of Submission:	22 April 2004
10. Date of last Update:	10 May 2006
11. Comments:	

SIDS INITIAL ASSESSMENT PROFILE

CAS No.	926-57-8
Chemical Name	2-butene, 1,3-dichloro-
Structural Formula	

SUMMARY CONCLUSIONS OF THE SIAR

There are no studies available concerning the toxicokinetics, metabolism and distribution of 1,3-dichloro-2-butene (1,3-DCB). However, based on physicochemical properties, structural similarities and expected similar metabolic profiles, data for the analogue substance, 1,3-dichloropropene, typically containing 50% *cis* and 50% *trans*, (DCP; CAS No. 542-75-6;) have been included in the human health section. DCP is considered a suitable analogue for 1,3-dichloro-2-butene (1,3-DCB containing ~20% *cis*-1,3-dichloro-2-butene, CAS No. 10075-38-4, and ~80% *trans*-1,3-dichloro-2-butene, CAS No. 7415-31-8); its structural similarities to DCP suggest the utilisation of the same metabolic pathways.
Because 1,3-DCB is susceptible to hydrolysis, data generated with the major hydrolysis product 3-chloro-2-buten-1-ol (3C2B; CAS No. 40605-42-3) are presented for the ecotoxicity endpoints.

Human Health

1,3-DCB is acutely toxic via the oral and inhalation routes. There are no valid animal dermal LD_{50} studies available for 1,3-DCB. The oral LD_{50} for 1,3-DCB was 300 and 414 mg/kg bw in fasted male and female Wistar rats, respectively and 1368 mg/kg bw in the non-fasted male Cr1:CD rat. The inhalation 4-hour LC_{50} of 1,3-DCB in the male rat ranged from 546 to 756 ppm (2840 to 3930 mg/m^3) and the 2-hour LC_{50} in the mouse was 846 ppm (4400 mg/m^3). The structural analogue, DCP, is acutely toxic via the oral (LD50 in rats is 110-170 mg/kg in males and 110-250 mg/kg in females), dermal (LD_{50} in rats is 800-1300 mg/kg in males and 1300-2000 mg/kg in females) and inhalation [(4-hr LC_{50} values in rats range from 586 to 666 ppm (2700 to 3070 mg/m^3)] routes of exposure.

1,3-DCB is corrosive to the skin of rabbits. Occupational experience shows that1,3-DCB is also irritating and corrosive to the skin , and that 1,3-DCB vapour is irritating to the eyes and respiratory tract. No eye irritation studies were identified with 1,3-DCB but based on its corrosivity, 1,3-DCB is likely to be severely irritating to eyes. There is no skin sensitization data for 1,3-DCB. The *cis* isomer of DCP showed moderate skin sensitisation in guinea pigs.

Repeated dose inhalation studies in animals indicate that 1,3-DCB may affect the integrity of lung epithelium. Based on histopathological changes, the NOAEL's range from 2 ppm (10 mg/m^3) in rats and rabbits exposed over a 5 month period, to 10 ppm (52 mg/m^3) in rats exposed for two weeks. Data on the analogue substance, DCP, suggest primarily portal of entry effects with NOEL's being 10 ppm (45 mg/m^3) in rats and 30 ppm (136 mg/m^3) in mice. By the inhalation route of exposure, degenerative changes in nasal and pulmonary epithelium are potential outcomes of 1,3-DCB exposure. Data from less well documented studies have reported additional 1,3-DCB effects in adrenal tissue, liver, myocardium, kidney, and spleen.

1,3-DCB is not mutagenic in the bacterial reverse mutation assay (Ames test) in *Salmonella typhimurium* strains (TA 98 and TA 1537) but is mutagenic in Salmonella typhimurium strains (TA 100 and TA 1535) without metabolic activation and in (TA 100) with metabolic activation. 1,3-DCB gave equivocal results in *Saccharomyces cerevisiae*. *In vivo*, 1,3-DCB does not induce micronuclei in the rat bone marrow assay.

While no carcinogencity data exist for 1,3-DCB, studies in rats and mice on the analogue chemical indicate that chronic inhalation of DCP (containing epoxidized soya stabilizer) produces non-neoplastic nasal degeneration and changes in transitional epithelium of the bladder and benign bronchoalveolar adenomas in lungs of male mice.

Gavage dosing with technical grades of DCP containing 1% epichlorohydrin produced tumors at the site of application (forestomach adenoma/carcinoma in rats and mice) and remote sites, involving bronchoalveolar adenoma/carcinoma of the lungs and transitional cell carcinomas of the urinary bladder in female mice. Data from DCP suggest 1,3-DCB is a possible carcinogen. The International Agency for Research on Cancer (IARC) has classified DCP (technical grade containing 1% epichlorohydrin) as possibly carcinogenic to humans: Group 2B.

Available data for 1,3-DCB for reproductive toxicity are from acute and short term, repeated-dose inhalation toxicity studies. No toxic effects on the reproductive organs were observed. No data are available for developmental toxicity. A two-generation inhalation study in rats and developmental studies in rats and rabbits with DCP showed no effects on reproduction/development at the highest dose tested [90 ppm (409 mg/m^3)]. The NOEL for reproductive toxicity was 30 ppm (136 mg/m^3) based on body weight effects and histopathologic changes in the nose and stomach. For developmental toxicity, the maternal NOEL, based on reduced body weight gains was <20 ppm (<91 mg/m^3) in rats and 20 ppm (91 mg/m^3) in rabbits. No evidence of a teratogenic or embryotoxic response was observed in either species at any exposure level. Evidence for slight fetotoxicity was seen in rats at 120 ppm (545 mg/m^3), a level producing maternal toxicity. The NOEL for teratogenicity was greater than 120 ppm (545 mg/m^3) in both rats and rabbits.

Environment

The melting point of 1,3-DCB is – 75°C and the boiling point is 128-130°C. The vapor pressure is 13.3 hPa at 25°C. The water solubility of 1,3-DCB cannot be determined due to rapid hydrolysis. The density of 1,3-DCB is 1.161 g/mL at 4°C. The calculated log Kow is 2.84.

1,3-DCB is predicted to be photodegraded by reaction with hydroxyl radicals in the atmosphere with a half-life of approximately 27 hours (calculated). However, its major path of degradation is hydrolysis, with a measured half-life of 6.0 hrs; the major hydrolysis product being 3-chloro-2-buten-1-ol (3C2B). 3C2B water solubility exceeds 92 mg/L (40,000 mg/L, calculated). Distribution modeling using Mackay Level I for 1,3-DCB indicated that partitioning will occur to air (99.99%), water (0.003%), and soil (0.002%) phases. The fugacity model Mackay Level III predicts that 1,3-DCB will distribute primarily to water (72.4%) with much smaller distributions to air (20%), soil (7.0%) and sediment (0.58%). Based on the formation of 3C2B from the hydrolysis of 1,3-DCB in water, the estimated Mackay Level III fugacity model distribution, assuming emission to water, is almost entirely to water (99.7%) with lesser amounts in air (0.05%), soil (0.02%) and sediment (0.2%). 1,3-DCB is not readily biodegradable (0% degraded in 28 days). Based on an estimated BCF of 30 for 1,3-DCB and an estimated BCF of 1.5 for 3C2B, neither substance is likely to bioaccumulate.

Because 1,3-DCB is susceptible to hydrolysis, data for the major hydrolysis product, 3C2B, are used for the ecotoxicity endpoints. For 3C2B, the 96-hour LC_{50} for rainbow trout (*Pimephales promelas*) is 4.0 mg/L (measured: ECOSAR 96-hour LC_{50} 8.4 mg/L for allyl halide and 0.5 mg/L for allyl alcohol), the 48-hour EC_{50} for *Daphnia magna* is 11 mg/L (measured: ECOSAR 48-hour EC_{50} 980.4 mg/L) and the 72-hour cell count biomass and growth rate values for algae (*Pseudokirchneriella subcapitata*) are EbC_{50} equal to 650 mg/L (calculated by probit method) and ErC_{50} > 650 mg/L (nominal: ECOSAR 72-hour EC_{50} 104.6 mg/L), respectively

Exposure

There are only three countries producing 1,3-DCB globally (Japan, Germany and USA). Annual global production (2002) of 1,3-DCB totalled approximately 5,000 tonnes In the USA, 1,3-DCB is produced at one site. It is manufactured by the reaction of 2-chloro-1,3-butadiene with HCl in the presence of a copper chloride catalyst.

Among the producers, 1,3-DCB is produced and used only as a site limited intermediate used only to make 2,3-dichloro-1,3-butadiene, a co-monomer in some grades of polychloroprene synthetic rubber. Consequently, all 1,3-DCB is consumed in the production of polychloroprene. Laboratory scale quantities are available from some commercial specialty-chemical suppliers (e.g., Sigma-Aldrich) as a mixture of the cis and trans isomers.

Occupational exposure to 1,3-DCB may occur through inhalation and/or dermal contact with this compound at workplaces where 1,3-DCB is produced/or used. The total number of workers in manufacturing operations with potential 1,3-DCB exposure is estimated to be less than approximately 200, globally. Since production does not utilize any open vessels and engineering and administrative controls are used in conjunction with personal protective equipment, no significant occupational exposure occurs. .
There are no consumer uses of 1,3-DCB. Extensive sampling shows that the amount of residual 1,3-DCB in 2,3-dichloro-1,3-butadiene is less than 0.5 ppm.

The end product (polychloroprene rubber) will contain even lower levels of 1,3-DCB since the 2,3-dichloro-1,3-butadiene-containg grades of polychloroprene rubber contain 10% or less 2,3-dichloro-1,3-butadiene. Consequently, potential exposure to 1,3-DCB in consumer products is expected to be negligible (<<50 parts per billion, wt/wt) .

RECOMMENDATION AND RATIONALE FOR THE RECOMMENDATION AND NATURE OF FURTHER WORK RECOMMENDED

Human Health: The chemical possesses properties indicating a hazard to human health (acute toxicity, portal of entry repeated dose toxicity, corrosivity, mutagenicity, possible carcinogen). Based on data presented by the Sponsor country, relating to 50% of global production in a closed-system as a chemical intermediate, and use patterns in one country, exposure to humans is anticipated to be low, and therefore, this chemical is currently of low priority for further work. Countries may desire to investigate any exposure scenarios that were not presented by Sponsor countries.

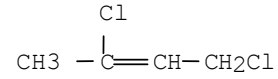
Environment: The chemical possesses properties indicating a hazard to the environment (acute toxicity to fish and invertebrates). Based on data presented by the Sponsor country, relating to 50% of global production in a closed-system as a chemical intermediate, emissions to the environment are expected to be negligible and therefore, this chemical is currently of low priority for further work.. Countries may desire to investigate any exposure scenarios that were not presented by the Sponsor Country.

SIDS Initial Assessment Report

1 IDENTITY

1.1 Identification of the Substance

CAS Number: 926-57-8
IUPAC Name: 2-Butene, 1,3-dichloro-
Molecular Formula: $C_4H_6C1_2$
Structural Formula:



Molecular Weight: 125.00
Synonyms: 1,3-Dichloro-2-butene
1,3-Dichlorobutylene
1,3-Dichlorobutene
1,3-Dichlorobutene-2
1,3-Dichloro-2-butene (cis and trans)
1,3-DCB

1,3-DCB (CAS No. 926-57-8) consists of a mixture of cis-1,3-dichloro-2-butene (CAS No. 10075-38-4) and trans-1,3-dichloro-2-butene (CAS No. 7415-31-8).

1.2 Purity/Impurities/Additives

1,3-DCB is produced as an isomeric mixture of cis- and trans- 1,3-DCB isomers. 1,3-DCB is typically

>98% 1,3-DCB (consisting of approximately 80% trans-1,3-dichloro-2-butene and approximately 20% cis-1,3-dichloro-2-butene) w/w

<2% Mixed chlorinated hydrocarbons w/w

<1% Hydrochloric acid (CAS No. 7647-01-0) w/w

1.3 Physico-Chemical properties

Data are presented below for the subject chemical, 1,3-dichlorobutene (1,3-DCB containing ~20% cis-1,3-dichloro-2-butene, CAS No. 10075-38-4, and ~80% trans-1,3-dichloro-2-butene, CAS No. 7415-31-8). Despite the presence of two isomers, 1,3-DCB as manufactured and used commercially, can be considered a single substance. As specific data do not exist for some HPV endpoints, the analog substance 1,3-dichloropropene (DCP; CAS 542-75-6) was cited.

Table 1: Summary of Physico-chemical Properties

Property	Value	Reference	Value	Reference	Value	Reference
	1,3-Dichlorobutene (1,3-DCB)		**1,3-Dichloropropene (DCP)**		**3-Chloro-2-buten-1-ol (3C2B)**	
CAS Number	926-57-8		542-75-6		40605-42-3	
Physical state	Liquid		Liquid		Liquid	
Melting point	-75ºC	Hatch and Ballin, 1949	-84ºC	Krijgsheld et al., 1986	-46.7ºC	MPBPWIN v.1.41
Boiling point	128-130ºC @ 1013 hPa (760 mm Hg)	DuPont, 1993; Lide, 1990-1991	108ºC	IPCS, 1993	148.9.5ºC @ 1013 hPa (760 mm Hg) (c)	STN, 2005
Vapour pressure	13.3 hPa @ 25ºC (9.98 mm Hg)	Bayer AG, 1973	24 hPa @ 20ºC (18 mm Hg)	IPCS, 1993	1.05 hPa @ 25ºC (0.784 mm Hg) (c)	STN, 2005
Water solubility	Cannot be determined due to hydrolysis; 363 mg/L* (c)	DuPont, 2005a WSKOW 1.41	2700 mg/L. Significant hydrolysis observed in water	Krijgsheld et al., 1986	>92 mg/L 40,000 mg/L (c)	DuPont, 2005b WSKOW 1.41
Partition coefficient n-octanol/water (log value)	2.84 (c)	Howard and Meylan, 1997	1.98	Krijgsheld et al., 1986	1.12 (c)	KOWWIN 1.67

(c) = calculated

* Calculated water solubility is not relevant due to observed rapid hydrolysis; value presented for comparison.

1.4 Analog Justification

The analog substance DCP has been used for some SIDS human health endpoints to fill data gaps for the sponsored substance; specifically repeated-dose and repro/developmental toxicity. DCP has an extensive dataset (IUCLID dataset 2000). Although toxicokinetic data are unavailable, based on physicochemical properties (Section 1.3: Table 1) and expected similar metabolic profiles (Section 3.1.1), DCP is considered an appropriate analog for 1,3 DCB. Where DCP data are cited, consideration was given first to studies which used cis/trans mixtures of DCP without stabilizer (often epichlorohydrin): otherwise data for specific endpoints were cited using the more volatile isomer in studies conducted according to Good Laboratory Practices (GLP). DCP was typically >90% pure, containing ~50% cis and ~50% trans 1,3-DCP isomers

Because 1,3-DCB is susceptible to hydrolysis, data generated with the major hydrolysis product 3-chloro-2-buten-1-ol (3C2B; CAS No. 40605-42-3) have also been presented for the ecotoxicity endpoints.

2 GENERAL INFORMATION ON EXPOSURE

Globally, 1,3-DCB is only used commercially as an isolated intermediate that is stored and consumed in on-site facilities for the manufacture of 2,3-dichlorobutadiene, a component of some polychloroprene synthetic rubbers. One manufacturer isolates 1,3-DCB from high boilers and still heels in the acetylene route for chloroprene manufacture and converts it to 2,3-dichlorobutadiene

for use as a co-monomer in chloroprene polymerization (Kirk-Othmer, 1979). 1,3-DCB may also be a low-level residual contaminant in 2,3-dichlorobutadiene manufactured from butadiene (Johnson, 1976). Historical uses of 1,3-DCB have included: preparation of the pesticide DDB (propane, 1,3-dichloro-2-methyl-, mixture with 1,3,dichloro-2-methyl-1-propene and 3,3-dichloro-2-methyl-1-propene) (Ekshtat, Matveyeva, and Kermis, 1971); use as an intermediate in the production of 19-nortestosterone steroids (Kirk-Othmer, 1979); and as a starting material for the synthesis of the chlorocrotyl ester of 2,4-dichlorophenoxy acetic acid herbicide, krotiline (Barsegyan, 1969). No information could be located regarding the production of 1,3-DCB for contemporary use other than synthetic rubber production.

2.1 Production Volumes and Use Pattern

There are only three countries producing 1,3-DCB globally (Japan, Germany and US). Annual global production of 1,3-DCB totalled approximately 5,000 tonnes for 2002 (International Institute of Synthetic Rubber Producers, 2002). In the US, which constitutes approximately 50% of global production, 1,3-DCB is produced only in Louisville, KY by DuPont Performance Elastomers. It is manufactured by the reaction of 2-chloro-1,3-butadiene with HCl in the presence of a copper chloride catalyst. Among these producers, 1,3-DCB is produced and used only as a site limited intermediate. 1,3-DCB is only used in the manufacture of 2,3-dichlorobutadiene. Consequently, all 1,3-DCB is consumed in the production of polychloroprene synthetic rubber. Laboratory scale quantities are available from some commercial specialty-chemical suppliers (e.g., Sigma-Aldrich) as a mixture of the cis and trans isomers.

Occupational exposure to 1,3-DCB may occur through inhalation and/or dermal contact with this compound at workplaces where 1,3-DCB is produced/used. Since production does not utilize any open vessels, no significant occupational exposure occurs. Some manufacturing personnel may be transiently exposed during sampling of product for quality control and during maintenance of production facilities (see section 2.3.1 for additional details). Similarly, environmental releases are expected only to occur during accidental spills. 1,3-DCB is not listed on the US EPA Toxic Release Inventory EPA. (2005).

2.2 Environmental Exposure and Fate

2.2.1 Photodegradation

If present in air, based on a measured vapor pressure of 13.3 hPa (9.98 mm Hg; Bayer AG, 1973), 1,3-DCB is expected to exist solely as a vapor in the ambient atmosphere (Bidleman, 1988). This vapor pressure value agrees with modelled data (9.57 mm Hg; using MPBPWIN 1.41). Vapor-phase 1,3-DCB is expected to degrade in the atmosphere by reaction with photochemically-produced hydroxyl radicals and ozone. The half-life for the reaction of 1,3-DCB in air with hydroxyl radicals is estimated to be 27 hours (24-hr day; 0.5E6 OH radicals/cm^3) and the reaction with ozone molecules is estimated to be about 8 days (at 7E11 molecules/cm^3; AOPWIN 1.91). The reaction with OH radicals is expected to be the primary degradation mechanism for 1,3-DCB in air. The estimated half-life for this reaction of 27 hours would indicate a low level of concern for persistence of 1,3-DCB in air.

The half-life for the reaction of 3-chloro-2-buten-1-ol (3C2B is the 1,3-DCB hydrolytic product), in air with hydroxyl radicals is estimated to be 18 hours (24-hr day; 0.5E6 OH radicals/cm^3) and the reaction with ozone molecules is estimated to be about 27 hours (at 7E11 molecules/cm^3; AOPWIN 1.91). The reaction with OH radicals is expected to be the primary degradation mechanism for

3C2B in air. The estimated half-life for this reaction of 18 hours would indicate a low level of concern for persistence of 3C2B in air.

2.2.2 Stability in Water

If present in water, 1,3-DCB is not expected to adsorb to suspended solids and sediment based upon the estimated Koc of 125 (PCKOCWIN 1.66). Volatilization from water surfaces is expected to be an important fate process based upon this compound's estimated Henry's Law constant. Estimated volatilization half-lives for a model river and model lake are 1 hour and 4.4 days, respectively (EPISUITE 3.12). This would indicate a low level of concern for persistence in water.

Based on experimental data, 1,3-DCB is unstable in water. The half-life for 1,3-DCB in 20ºC water (pH ~7) was 6.0 hours in capped vials without headspace (representing hydrolysis) and 2.4 hours in uncapped vials (representing hydrolysis and volatilisation) (DuPont, 2005a). Hydrolysis of 1,3-DCB (consisting of cis/trans-1,3-DCB isomers) was found to yield the corresponding cis/trans 3-chloro-2-buten-1-ol isomers (3C2B; identified as CAS No. 40605-42-3).

2.2.3 Transport between Environmental Compartments

The fugacity model (Mackay Level III run in EPISUITE 3.12 assuming equal emissions of 1,3-DCB to air, water, and soil) predicts that in a steady state, 1,3-DCB will distribute primarily to the water (72.4%) with much smaller distributions to air (20%), soil (7.03%), and sediment (0.58%) using the following input parameters: Henry's Law Constant: 3.84E-002 atm-m^3/mole (HENRYWIN 1.90), Vapor Pressure: 9.98 mm Hg (MPBPWIN program), Log Kow: 2.84 (KOWWIN 1.67), Soil Koc: 125 (PCKOCWIN 1.66). Distribution modeling using Mackay Level I for 1,3-DCB indicated that partitioning will occur to air (99.99%), water (0.003%), and soil (0.002%) phases (Mackay, 2001). The predicted half-lives of 1,3-DCB from the fugacity model for air (23.5 hrs), water (900 hrs), soil (1800 hrs) and sediment (8100 hrs) would indicate a low level of concern for persistence in air and water. However, due to the low levels predicted to partition to the soil and sediment, there is also low concern for persistence of 1,3-DCB in soil and sediment. (EPISUITE 3.12).

Based on the formation of 3C2B from the hydrolysis of 1,3-DCB in water, the estimated Level III fugacity model (Mackay Level III run in EPISUITE 3.12 assuming emission to water) distribution of 3C2B is almost entirely to water (99.7%) with lesser amounts in air (0.05%), soil (0.02%), and sediment (0.2%) using the following input parameters: Henry's Law Constant: 3.99E-006 atm-m^3/mole (HENRYWIN 1.90), Vapor Pressure: 1.44 mm Hg (MPBPWIN program), Log Kow: 1.12 (KOWWIN 1.67), Soil Koc: 3.78 (PCKOCWIN 1.66). This agrees with the finding that the 1,3-DCB hydrolysis product, 3C2B, will tend to remain in water rather than partition to other environmental media (Jawarska et al., 2002). However, the estimated steady state Level III fugacity model distribution (assuming equal emissions of 3C2B to air, water, and soil) predicts most of the 3C2B will partition to soil (54.4%) with lesser amounts in water (44.2%), air (1.38%), and sediment (0.088%) (EPISUITE 3.12). Based on a predicted Henry's Law Constant of 3.99E-006, 3C2B has volatilisation half-life estimates for a model river and model lake as 6.3 days and 73 days, respectively (EPISUITE 3.12). The predicted half-lives for 3C2B from the fugacity model for air (10.5 hrs), water (360 hrs), soil (720 hrs) and sediment (3240 hrs) would indicate a low level of concern for persistence in air, water and soil (EPISUITE 3.12). However, due to the low level predicted to distribute to sediment, there is also a low level of concern for persistence of 3C2B in sediment.

2.2.4 Biodegradation

1,3-DCB is not readily biodegradable (0% degraded in 28 days; Bayer AG, 1992).

2.2.5 Bioaccumulation

An estimated BCF of 30 suggests the potential for 1,3-DCB bioconcentration in aquatic organisms is low (BCFWIN 2.15; EPISUITE 3.12). 1,3-DCB is unlikely to be bioaccumulative.

The estimated BCF for 3C2B, the 1,3-DCB hydrolysis product, is 1.5 (BCFWIN 2.15; EPISUITE 3.12). 3C2B is unlikely to be bioaccumulative.

2.3 Human Exposure

2.3.1 Occupational Exposure

Only plants in Japan, Germany, and the US produce 1,3-DCB. At these sites, 1,3-DCB is handled as a site limited intermediate and is used solely in the manufacture of 2,3-dicholorobutadiene, which is a co-monomer used in polychloroprene manufacture. There are no sales or commercial uses of 1,3-DCB. Wastes generated from 1,3-DCB manufacture in the US are disposed in an approved and permitted thermal oxidizer.

Potential human exposure to 1,3-DCB in these plants is limited because the material is manufactured, purified, stored, and consumed on-site. Production does not utilize any open vessels hence no significant occupational exposure to 1,3-DCB occurs. Some exposure may occur during line breaks for equipment maintenance and sampling of product for quality control but air-monitoring data shows that actual exposures are very low. Although manufacturing sites can have up to several thousand total personnel (including construction, contractor, and non manufacturing plant employees), most of these individuals are not involved in 1,3-DCB operations. A far smaller cohort, involving production, maintenance and quality control personnel will have potential exposures to 1,3-DCB. The total number of workers in manufacturing operations with potential 1,3-DCB exposure is estimated to be less than approximately 200, globally.

Opportunities for occupational exposure are limited. During sampling of product for quality control, individuals wear full-face respirators and gloves, apron, boots, or whole bodysuit of impervious clothing to prevent contact. Based on its low vapor pressure (9.98 mm Hg at 25ºC), there is limited potential for inhalation exposure. Since protection provided by air purifying respirators is limited, use of a positive pressure air supplied respirator is used if there is any potential for an uncontrolled release or any other circumstances where air purifying respirators may not provide adequate protection.

The sites have effective safety, health, and environmental practices, training and procedures in addition to engineering controls, environmental controls, and personal protective equipment to control exposure. Adequate safety equipment, such as safety showers, eyewash fountains, and washing facilities, as well as on-site medical facilities are available in the event of an occupational exposure.

The DuPont occupational Acceptable Exposure Limit (AEL) for 1,3-DCB is currently 0.3 ppm (8- and 12-hour TWA); this value was established based on observed genotoxicity in bacterial mutagenicity testing and changes in nasal epithelial cell proliferation indices in a two-week inhalation study. Air monitoring has been conducted on 1,3-DCB and results are shown in Tables 2 and 3; data are representative of exposure monitoring among manufacturers. At least 96% of all

samples ever taken indicate exposures were below workplace action limit of 0.15 ppm (set at ½ of the AEL) and at least 98% of all samples are below the recommended AEL of 0.3 ppm. Performance in recent years has improved with exposure data showing a clear trend towards lower exposures. The sampling method was based on gas chromatographic (flame ionisation) analyses of carbon disulfide extracts of activated carbon containing air sampling tubes.

EXPOSURE DATA

Table 2: Available Human Exposure Data, Maydown, Ireland (former DuPont Performance Elastomers manufacturing site) from 1983 to 1998: Location - Monomer area

	No. of Results	Avg. of TWA (ppm)	Minimum (ppm)	Maximum (ppm)
All results	5091	0.007	0.001	1.86
Detection Limit: 0.001 ppm 98.9% of results were ≤ 0.15 ppm (1/2 of current AEL) 99.49% of results were ≤ 0.3 ppm (current AEL)				

Table 3: Available Human Exposure Data, Louisville, Kentucky (DuPont Performance Elastomers manufacturing facility from 1970 to 1993: Location - Monomer area

	No. of Results	Avg. of TWA (ppm)	Minimum (ppm)	Maximum (ppm)
All results	2629	0.001	0.001	36
Detection Limit: 0.001 ppm 96.54% of results were ≤ 0.15 ppm (1/2 of current AEL) 98.59% of results were ≤ 0.3 ppm (current AEL) A total of 8 samples ever measured exceeded the 1 ppm 1,3-DCB internal control limit that was established in 1988; all of these samples were reported in the late 1970's. The AEL was subsequently reduced to 0.3 ppm in 1993. From 1988 to 1993, 3 of the 34 samples taken exceeded the 0.3 ppm AEL (0.51, 0.60 and 0.64 ppm).				

Japan

Air monitoring studies in 1,3-DCB and neoprene production facilities (monomer area, and neoprene polymerization and finishing sections) at two different facilities show that no 1,3-DCB was found over an 8-hour sampling period with detection limits of 0.020 ppm or better. The analytical method involved gas chromatography of 1,3-DCB in solvent extracts of activated carbon containing air sampling tubes.

2.3.2 Consumer Exposure

There are no consumer uses of 1,3-DCB. The only commercial use of 1,3-DCB is for the production of 2,3-dichloro-1,3-butadiene, which is used to make some grades of polychloroprene rubber. Extensive sampling shows that the amount of residual 1,3-DCB in 2,3-dichloro-1,3-butadiene is less than 0.5 ppm. The end product (polychloroprene rubber) will contain even lower levels of 1,3-DCB since the 2,3-dichloro-1,3-butadiene-containing grades of polychloroprene rubber contain 10% or less 2,3-dichloro-1,3-butadiene. Consequently, potential exposure to 1,3-DCB in consumer products is expected to be negligible (<<50 parts per billion wt/wt).

Conclusion:

Level III fugacity model calculations, assuming an equal release to air, water and soil show that in a steady state, 1,3-DCB will be distributed primarily to water. Following fugitive discharges to air, 1,3-DCB is expected to degrade via atmospheric reactions (e.g., OH radical, ozone, hydrolysis, etc) with an estimated half-life of approximately 23.5 hrs. Fugitive discharges of 1,3-DCB to water will likely involve rapid hydrolysis to 3C2B. The predicted half-lives of 1,3-DCB from the fugacity model are: air (23.5 hrs), water (900 hrs), soil (1800 hrs) and sediment (8100 hrs). It is also likely that 1,3-DCB will undergo hydrolysis in moist soil. These observations and modelling estimates suggest that 1,3-DCB will be rapidly transformed in the environment. The available biodegradation data for 1,3-DCB and the modelling estimates suggest that 1,3-DCB does not biodegrade quickly but undergoes primary degradation in days to weeks and ultimate biodegradation in weeks to months.

If present in air, 3C2B, the likely 1,3-DCB hydrolysis product, would have an estimated half-life of air (10.5 hrs), water (360 hrs), soil (720 hrs) and sediment (3240 hrs). The oxidative and hydrolytic transformation products of 1,3-DCB are expected to be more polar than the parent compound. This results in products expected to have a low tendency to bioaccumulate, which correspond to the estimated values. In summary, there is low concern for persistence or bioaccumulation of 1,3-DCB or for 3C2B, its hydrolytic product.

Given that 1,3-DCB is a site limited intermediate, human exposure potential is minimal and restricted to product sampling for quality assurance purposes and facility maintenance. Personal protective equipment is used in these activities to minimize exposures. Workplace air monitoring shows that exposures are well controlled with at least 96% of all workplace exposures below the current DuPont Performance Elastomers action limit of 0.15 ppm. No exposure to 1,3-DCB in consumer end products is expected.

3 HUMAN HEALTH HAZARDS

3.1 Effects on Human Health

3.1.1 Toxicokinetics, Metabolism and Distribution

There are no studies available concerning toxicokinetics, metabolism and distribution of 1,3-DCB. Based on the results from various toxicity studies, 1,3-DCB can be absorbed following inhalation, oral or dermal exposure.

While no experimental biotransformation data are available for 1,3-DCB, both 1,3-DCB and its chemical analogue, DCP (1,3-dichloro-1-propene), contain chlorine in the allylic position, a feature that should allow these structural analogues to be metabolized similarly *in vivo*.

Figure 1 shows the proposed metabolic pathway for DCP that is based on *in vivo* administration and identification of excreted metabolites. The metabolism of DCP is analogous to allyl chloride (De Rooij et al., 1996) for which the primary route is expected to be direct conjugation of the allylic position with glutathione and displacement of the chlorine atom. Following *in vivo* administration of allyl chloride or DCP, a significant fraction of radioactive label is excreted in urine as glutathione derived mercapturates (De Rooij et al., 1996; Bartels et al., 2004). 1,3-DCB is also likely to be metabolized by this pathway (Figure 2). However, it should be noted that the extent to which the chlorine in the C3 vinylic position of 1,3-DCB may alter GSH conjugation is not known because its electron withdrawing effect on the pi-electrons of the C=C bond. The next most important pathway predicted for the biotransformation of 1,3-DCB is oxidative dechlorination at the allylic C1

position. This reaction occurs with allyl chloride and DCP. For DCP, oxidative dechlorination eventually leads to exhalation of CO_2 and additional mercapturates in urine (De Rooij et al., 1996). Epoxidation of the double bond is a minor pathway for DCP since it has only been shown to be present at very high doses administered to mice by intraperitoneal injection (Schneider, Quistad, and Casida, 1998; Bartels et al., 2000). While electronic factors may favor epoxidation of 1,3-DCB because of the presence of the vinylic chlorine at C3 (Bartels et al., 2004), steric factors imposed by the presence of the C4 methyl group may mitigate this effect. Since the epoxidation reaction is not predicted to be an important route of metabolism, this pathway is not shown in Figure 2. Another reaction predicted for 1,3-DCB is methyl hydroxylation which is not possible with DCP due to the lack of the terminal C4 group. In summary, the biotransformation of 1,3-DCB is predicted to be qualitatively similar to DCP.

Figure 1. Proposed pathway for the metabolism of DCP (1,3-dichloro-1-propene; adapted from Bartels et al., 2004)

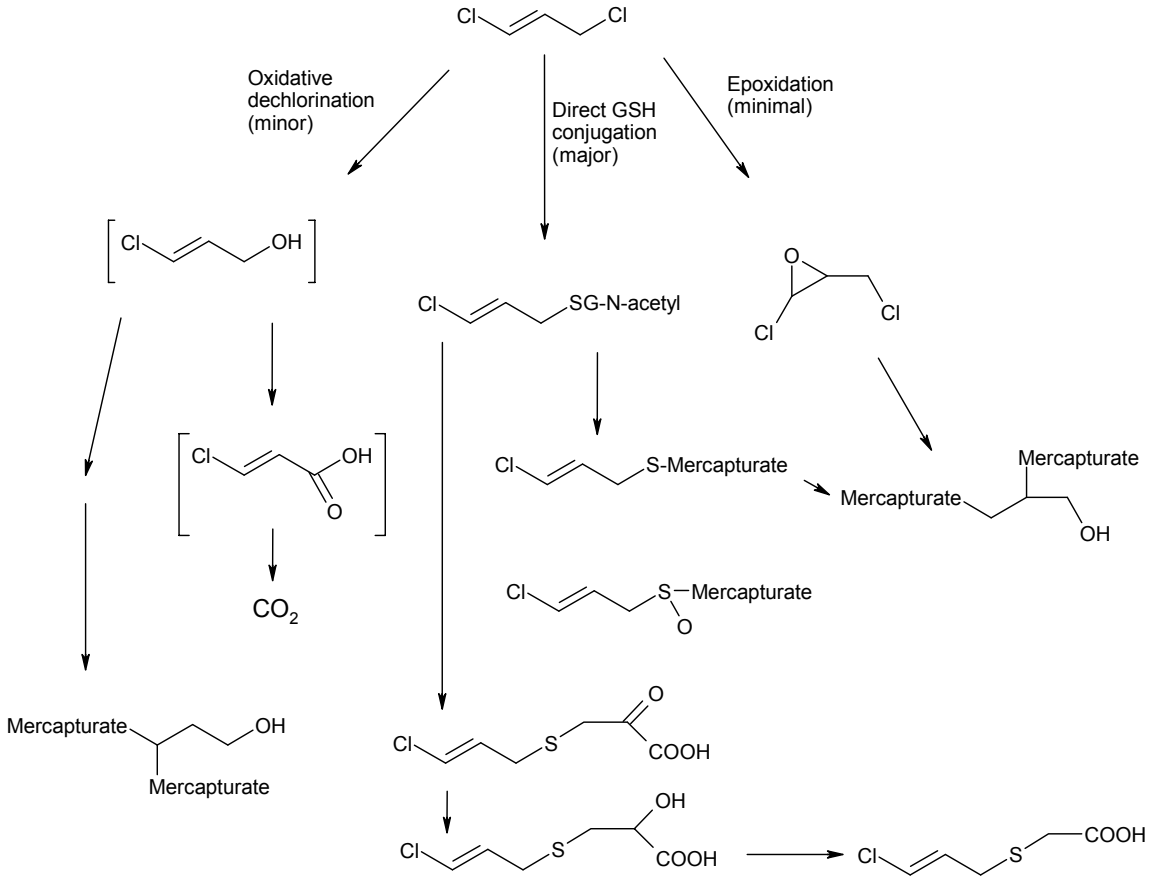
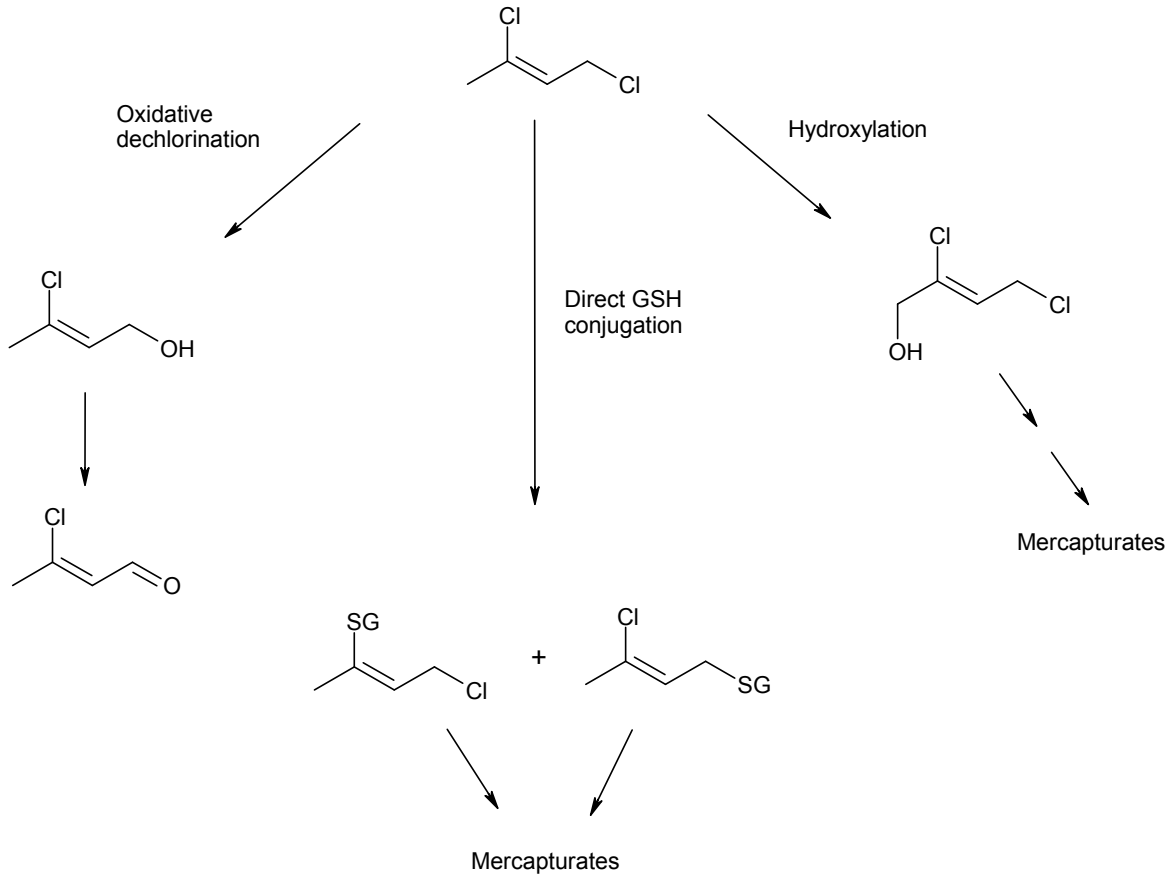


Figure 2. Predicted pathway for the metabolism of 1,3-DCB (1,3-dichloro-2-butene)



3.1.2 Acute Toxicity

Studies in Animals

Inhalation

The inhalation 4-hour LC_{50} of 1,3-DCB in the male rat ranged from 546 (Kwon and Waritz, 1968) to 756 ppm (2840 to 3930 mg/m^3) (Barsegyan, 1969). At lethal levels, 1,3-DCB caused irregular breathing, lacrimation, salivation, and hyperemia of the ears. Histopathologic examination revealed hemorrhage of lungs, tracheitis, and cell degeneration in the liver, spleen, thymus, and lymph nodes; no changes were observed in the testes. Tubular degeneration of the kidneys was also noted (Kwon and Waritz, 1968). The 2-hour LC_{50} in the mouse was 846 ppm (4400 mg/m^3) (Barsegyan, 1969)

For DCP, reported 4-hr LC_{50} values in rats range from 586 to 666 ppm (2700 to 3070 mg/m^3) (Dow Chemical Co., 1987a). Reported clinical signs in animals were partially closed eyes, reduced respiratory rate and irregular respiration, wet fur around the mouth, hunched posture, restless behavior and reddening of ears, tail and feet. At lethal exposure levels, fecal staining of the fur around the urogenital region and lung congestion were noted (Dow Chemical Co., 1987a).

Dermal

There are no rat or rabbit dermal LD_{50} studies available for 1,3-DCB.

Acute dermal LD_{50} for DCP in rats is reported to be 800-1300 mg/kg in males and 1300-2000 mg/kg in females. Lethargy, salivation, red/brown staining around mouth, eyes and snout, diarrhea, diuresis, decreased respiratory rate, lacrimation, ataxia, loss of righting reflex, hunched posture, and piloerection were reported. At lethal exposure levels, lung, liver and GI tract abnormalities were reported (Jones et al., 1986a).

Oral

The oral LD_{50} for 1,3-DCB was 300 and 414 mg/kg in fasted male and female rats, respectively (Bayer AG, 1991), and 1368 mg/kg in the non-fasted male rat (DuPont, 1982a). Clinical signs of toxicity included stained and wet fur, wet perineal area, diarrhea, weakness, hunched posture, alopecia, salivation, chromodacryorrhea, rough coat, sedation, and/or weight loss (Bayer AG, 1991; DuPont, 1982a). The pathology examinations of animals that died on study showed congested vessels of the stomach, reddened mucous membranes, reddened small intestine, and clear fluid in the stomach.

Acute oral LD_{50} values for DCP in rats are reported to be 110-170 mg/kg in males and 110-250 mg/kg in females. Signs of toxicity include hunched posture, piloerection, decreased respiratory rate, lethargy, ptosis, diarrhea, diuresis, ataxia, tip-toe gait, red/brown staining around the snout, tremors, emaciation, pallor of the extremities, increased salivation/lacrimation and body weight losses. At lethal exposure levels, hemorrhagic lungs, mottled/dark liver, patchy pallor of the liver, dark kidneys, hemorrhagic stomach, hemorrhage/congestion of the small intestine, injection of blood vessels around the stomach, and adherence of the stomach to abdominal wall and liver were observed (Jones et al., 1986b).

Studies in Humans

Inhalation

Exposure of workers to 1,3-DCB can cause dizziness and nausea (DuPont, 1993). Exposure details were not reported.

Conclusion

In rats, 1,3-DCB is acutely toxic via the inhalation and oral routes of exposure. Data from the structural analogue, DCP, suggest that 1,3-DCB is also acutely toxic via the dermal route of exposure in rats.

3.1.3 Irritation

Skin Irritation

Studies in Animals

1,3-DCB was not a corrosive substance in the *in vitro* International Corrositex™ assay (DuPont, 1999a). A follow-up *in vivo* study was conducted in one rabbit to confirm this result. Two sites were tested, one for 3 minutes and one for one hour. At the skin site treated for 3 minutes with 1,3-DCB, mild erythema, but no edema was noted. At 24 hours after test substance removal, moderate erythema and moderate edema were observed. At 48 and 72 hours after test substance removal, moderate erythema and severe edema were observed. After a 1-hour exposure, moderate erythema and severe edema were observed. Necrosis, severe erythema, severe edema, and a raw spot were observed at 24, 48, and 72 hours after test substance removal. Microscopic examination

of the 3-minute test site revealed multifocal minimal ulceration with degeneration of adjacent collagen and diffuse mild epidermal hyperplasia. Microscopic examination of the 1-hour test site revealed severe transmural necrosis with hemorrhage and edema (DuPont, 1999b). Similar results were observed in a 24-hour dermal irritation study with rabbits (DuPont, 1970).

Studies in Humans

On human epidermis, 1,3-DCB caused an itching and burning sensation in 3 minutes. At 6 minutes, the itching and burning sensation had vanished and there was no skin inflammation (Roubal and Pokorny, 1943). No information on the exposure conditions, number of individuals tested, or test substance purity were available. In contrast to this report, current plant site experience indicates that 1,3-DCB is irritating and corrosive to human skin.

Eye Irritation

No eye irritation studies were identified with 1,3-DCB but based on its corrosivity, 1,3-DCB is likely to be severely irritating to the eyes.

Respiratory Tract Irritation

Studies in Humans

In humans, the threshold for irritation of the mucous membranes of the upper airways and eyes is 4 ppm (20 mg/m^3) (Petrosyan and Gizhlaryan, 1985). In humans, the olfactory odor threshold is 2 ppm (10 mg/m^3) (Petrosyan and Gizhlaryan, 1985; Barsegyan, 1969).

Conclusion

1,3-DCB is corrosive to the skin of rabbits. Occupational experience shows that 1,3-DCB is also irritating and corrosive to the skin, and that 1,3-DCB vapour is irritating to the eyes and respiratory tract. No eye irritation studies were identified with 1,3-DCB but based on its corrosivity, 1,3-DCB is likely to be severely irritating to eyes.

3.1.4 Sensitisation

No dermal sensitization studies were identified for 1,3-DCB.

DCP, when tested as the cis isomer, was shown to be a moderate skin sensitizer in guinea pigs (Buehler test) (Shell, 1982).

3.1.5 Repeated Dose Toxicity

All available repeated dose studies for 1,3-DCB were reviewed. Some studies did not have a sufficient level of detail available to determine the scientific adequacy of the data. These studies are briefly summarized below. The DuPont, 1982b study was identified as the key study because it was well-conducted, had sufficient detail to determine the reliability of the data, and was the most recent repeat dose study conducted. Therefore, for the purpose of determining NOELs, the 2-week inhalation study in rats (DuPont, 1982b) was given the most credibility. By comparison, there is extensive toxicity information on DCP; well documented studies from the IUCLID dataset are summarized here.

Studies in Animals

Inhalation

A two-week inhalation study conducted with 1,3-DCB in male rats produced a NOAEL of 10 ppm (52 mg/m^3). At 100 ppm (520 mg/m^3), rats showed a significant weight depression through the exposure period, but experienced a rate of weight gain parallel to the controls throughout the 14-day recovery period. Clinical chemistry findings at the end of the exposure period included increased average erythrocyte counts, hemoglobin, and hematocrit in the 100 ppm (520 mg/m^3) group and decreased mean corpuscular hemoglobin concentration in both the 10 and 100 ppm (52 and 520 mg/m^3) groups. Serum protein concentration was increased in the 100 ppm (520 mg/m^3) group and urine pH and serum glucose was increased in the 10 and 100 ppm (52 and 520 mg/m^3) groups. These changes were considered either non-adverse or not concentration–related. No compound-related clinical chemistry effects were observed at the end of the recovery period. Pathological examination at the end of the exposure period showed mild lung congestion and mild, but diffuse, degeneration of alveolar lining cells at 100 ppm (520 mg/m^3); no histopathological changes were observed in reproductive organs. No compound-related changes were observed in organ to body weight ratios at this time period. Following the 14-day recovery period, lung weights were significantly heavier in rats in the 100 ppm (520 mg/m^3) group. The significance of this change was difficult to interpret since no microscopic lesions were observed at the end of the recovery period. A NOAEL of 10 ppm (52 mg/m^3) was reported based on histopathological changes in the lung and effects on red blood cell parameters in the 100 ppm (5201 mg/m^3) group (DuPont, 1982b).

In a separate rat inhalation study, repeat exposure (15 or 30 exposures) to 100 ppm (500 mg/m^3) of 1,3-DCB caused morphological changes in the adrenal cortex. These changes were not observed at 20 ppm (100 mg/m^3) (Mirzabekyan et al., 1971). When rats were exposed via inhalation for 92 exposures, slight morphological changes to the adrenal tissue were noted at 20 ppm (100 mg/m^3), but not at 2 ppm (10 mg/m^3). Necrosis of the glomerular capillaries and renal tubular epithelium was noted at 20 ppm (100 mg/m^3). Granular dystrophy of renal tubular epithelium and focal hemorrhage were noted at 2 ppm (10 mg/m^3) (Oganesyan and Akopdzhanyan, 1969). Based on the descriptions provided, many of the kidney changes reported can be attributed to artifact, probably arising from either tissue autolysis or fixation/processing techniques; since description of lesion incidence in controls was not reported, this possibility should not be excluded.

A NOAEL of 2 ppm (10 mg/m^3) was reported in a 4.5-5.5 month inhalation study in rats and rabbits with 1,3-DCB. At 20 ppm (100 mg/m^3), lung blood vessel capillary damage, necrobiotic changes in the myocardium, liver, kidney, and spleen, and pulmonary emphysema secondary to chronic ischemia and lung hemorrhage were observed (Barsegyan, 1969; Barsegyan, 1970; Gasparyan and Barsegyan, 1970).

A repeated dose inhalation study with 1,3-DCB in dogs produced biochemical changes and disturbances in the effects of insulin and adrenalin regulation of carbohydrate metabolism at 48 and 100 ppm (250 and 500 mg/m^3), but not at 20 ppm (100 mg/m^3) (Mkheyan, 1959). A 1-month repeated dose oral study in 1 dog administered approximately 1 mL/week produced limited effects (alopecia, weight loss, and acidic gastric juices) (Roubal and Pokorny, 1943).

A 28-day inhalation study with DCP in Fischer 344 rats and CD-1 mice was conducted at exposure concentrations of 0, 3.81, 10.1, and 29.5 ppm (0, 17, 45, 133 mg/m^3). In rats, all test substance exposed females had stained fur and high level male rats had increased body weights. Pale and granular liver was observed grossly in all treated male rats. In mice, high level groups showed stained fur and unkempt appearance. Gross examination revealed the incidence of pale liver was increased in all test substance exposed groups. The study LOAEL was 3.81 ppm (17 mg/m^3) in rats and mice (Dow Chemical Co., 1978).

A 90-day inhalation study was conducted with DCP at exposure concentrations of 0, 11.98, 32.14 and 93.0 ppm (0, 54, 145, 419 mg/m^3) in Fischer 344 rats and CD-1 mice. In rats, no mortality or clinical signs were observed but high level male and female rats had significantly decreased body weight gains. Gross examination showed discolored kidneys in all DCP exposed male rats. Compound related histopathologic changes were seen in the nasal cavity of all high level male and female rats and 9/10 intermediate level female rats; changes were reported as a decreased height of nasal epithelium due to apparent loss of cytoplasm, disorganized nuclei and necrotic cells. In mice, no mortality was noted. Body weights were significantly reduced in high level females. In 6/10 high level female mice, decreased height of nasal epithelium due to apparent loss of cytoplasm and necrotic cells was reported. The study NOAEL was 12.0 ppm (54 mg/m^3) in rats and 32.1 ppm (145 mg/m^3) in mice (Dow Chemical Co., 1979).

An additional 90-day inhalation study was reported with DCP at concentrations of 0, 10, 30, 90 and 150 ppm (0, 45, 136, 409, 681 mg/m^3) in Fischer 344 rats and B6C3F1 mice. Depressed growth was observed in rats and mice from the 90 and 150 ppm (409 and 681 mg/m^3) groups. The weight changes observed at these levels were associated with changes in several haematology (increased RBC count) or clinical chemistry parameters (reduced serum protein or serum BUN, increased serum ALT activities) or altered organ weights relative to controls; however, these changes were considered to be secondary effects of DCP exposure arising from the reductions in body weight. Concentration related degeneration of nasal olfactory epithelium or respiratory epithelial hyperplasia was noted in all animals exposed to 90 and 150 ppm (409 and 681 mg/m^3) and in 2/10 male rats exposed to 30 ppm (136 mg/m^3). Diffuse hyperplasia of transitional epithelium was found in the bladder of female mice exposed to 90 or 150 ppm (409 and 681 mg/m^3) DCP. The overall study NOEL was 10 ppm (45 mg/m^3), based on nasal degeneration observed in male rats (Stott et al., 1988).

Inhalation studies were also reported for rabbits, guinea pigs and dogs exposed to 0, 0.9 or 2.6 ppm (0, 4 or 12 mg/m^3) DCP for 7 hours/day for 6 months. Other than cloudy swelling of renal tubular epithelium in rats, no effects were reported in the test animals at any exposure level (Torkelson et al., 1977).

Conclusion

Repeated dose inhalation studies for DCP indicate that the study NOAEL/NOELs observed in rats for 1,3-DCB and DCP are comparable with both likely to cause portal of entry toxicity. For 1,3-DCB, a NOAEL of 10 ppm (52 mg/m^3) was observed in a well-conducted two-week inhalation study in rats, based on hematological effects and histopathological changes in the lung. Inhalation studies over 4.5-5.5 months, in rats and rabbits, produced effects at 20 ppm (100 mg/m^3) with a NOAEL of 2 ppm (10 mg/m^3). DCP exhibits portal of entry effects, with repeated dose NOAELs based on nasal olfactory epithelial degeneration; in a 90-day inhalation studies, the NOAEL was 12.0 ppm (54 mg/m^3) in rats and 32.1 ppm (145 mg/m^3) in mice. In a separate 90-day inhalation study in rats and mice, the overall study NOEL was 10 ppm (45 mg/m^3) based on nasal olfactory epithelial degeneration in rats.

3.1.6 Mutagenicity

Studies in Animals

In vitro Studies

1,3-DCB was negative when tested in *Salmonella typhimurium* (De Lorenzo et al., 1977; DuPont, 1974) and equivocal when tested in *Saccharomyces cerevisiae* (DuPont, 1974) mutation assays. However, when 1,3-DCB was tested for mutagenicity in *Salmonella typhimurium* utilizing the plate assay for volatile liquids, it produced positive results with metabolic activation, in the TA1535 and TA100 strains (DuPont, 1980). Appropriate tester strain specific positive control substances (2-aminoanthracene, 9-aminoacridine, N-methyl-N'-nitro-N-nitrosoguanidine, and 2-nitro-fluorene), and a gaseous positive control substance (chloroethene) were included in the studies and showed expected mutagenic responses. The Ames studies were well conducted, reliable, and broadly compliant with current test guidelines. No *in vitro* data with mammalian cell systems are available.

In vivo Studies

When tested in an *in vivo* inhalation rat micronucleus assay according to OECD TG 474, 1,3-DCB was negative (DuPont, 1995). The rats were exposed by the inhalation route to 10, 50, and 100 ppm for 6 hours/day, 5 days/week, for 2 weeks. A significant decrease in body weight gain occurred in all groups of exposed male rats after 10 days of exposure. No weight effects were seen in any female dose group, and no other significant clinical signs of toxicity were noted. No mortality occurred. There was no significant depression in the proportion of polychromatic erythrocytes (PCEs) among total erythrocytes. The positive control substance, 40 mg/kg body weight of cyclophosphamid, induced micronuclei in the PCEs at statistically significant levels ($p<0.05$). Although 1,3-DCB was reported to cause chromatid breaks when administered intraperitoneally to rats (Nersesyan, Kumkumadzhyan, and Zil'fyan, 1990), insufficient details were provided to interpret the study.

Conclusion

1,3-DCB is not mutagenic in the bacterial reverse mutation test (Ames test) in *Salmonella typhimurium* strains (TA 98 and TA 1537) but is mutagenic in Salmonella typhimurium strains (TA 100 and TA 1535) without metabolic activation and in (TA 100) with metabolic activation. 1,3-DCB gave equivocal results in *Saccharomyces cerevisiae.* *In vivo*, 1,3-DCB does not induce micronuclei in the rat bone marrow assay. 1,3-DCB is genotoxic *in vitro* in bacteria, but was not able to induce genotoxic effects *in vivo* in rats. These data indicate that 1,3-DCB might be mutagenic.

3.1.7 Carcinogenicity

Studies in Animals

No carcinogenicity studies were available with 1,3-DCB.

Long term gavage studies by the NTP were conducted with DCP containing 1.0% epichlorohydrin in groups of 104 Fischer 344 rats/dose level/sex that were administered daily doses of 0, 25 or 50 mg/kg for 3 days/week. Mean body weights were slightly (5%) decreased in high dose males. Primary organs affected were the forestomach and liver. Non-neoplastic lesions were basal cell or epithelial hyperplasia of the forestomach. The NTP authors concluded there was clear evidence for the carcinogenicity of DCP for male rats as indicated by a compound related increased incidence of squamous cell papillomas and carcinomas of the forestomach as well as a dose related increased incidence of neoplastic nodules of the liver. In female rats, some evidence of carcinogenicity was

indicated by a dose related increased incidence of squamous cell papillomas of the forestomach. An increased incidence of neoplastic nodules of the liver was found in the 50 mg/kg females only (NTP, 1985b). See Table 4.

Table 4: Neoplasm Incidence from NTP 2-yr Gavage Bioassay with DCP in Rats

	Exposure Level (mg/kg/d)			Historical Control Incidence
Males	0	25	50	
Forestomach				
Squamous Cell Papilloma	1/52	1/52	9/52	2/1114 (0.2%)
Squamous Cell Carcinoma	0/52	0/52	4/52	Not reported
Squamous Cell Papilloma or Carcinoma	1/52	1/52	13/52	6/1114 (0.5%)
Liver				
Neoplastic Nodule	1/52	6/52	7/52	31/1141(2.7%)
Hepatocellular Carcinoma	0/52	0/52	1/52	9/1141(0.8%)
Neoplastic Nodule or Hepatocellular Carcinoma	1/52	6/52	8/52	40/1141 (3.5%)
Females				
Forestomach				
Squamous Cell Papilloma	0/52	2/52	3/52	1/1125 (0.09%)
Squamous Cell Carcinoma	0/52	0/52	0/52	Not reported
Squamous Cell Papilloma or Carcinoma	0/52	2/52	3/52	5/1125 (0.4%)

Long term gavage studies were conducted by the NTP with DCP containing 1.0% epichlorohydrin in groups of 100 B6C3F1 mice/dose level/sex that were administered daily doses of 0, 50 or 100 mg/kg for 3 days/week. Initial body weights were lower in the treatment groups of male and female mice relative to controls by 6-22%; weight differences decreased to 5-9% by the end of the study. In the control group, 25 males in the control group had died from myocarditis during weeks 48-51. By the end of the study, survival rates were 8/50, 28/50, and 31-50/50 for the control, low and high dose males, respectively. Among female mice, survival rates were significantly reduced; 36/50 high dose females survived compared to 46/50 in controls. Primary organs affected were forestomach, urinary bladder and lungs. Compound related non-neoplastic lesions were basal cell or epithelial hyperplasia of the forestomach, epithelial hyperplasia of the urinary bladder, and kidney hydronephrosis. The NTP considered this study “inadequate” for determination of carcinogenicity in male mice due to their reduced survival. The NTP concluded there was clear evidence of carcinogenicity in female mice as indicated by a dose-related increase in transitional cell carcinomas of the urinary bladder, of alveolar/bronchiolar adenomas or carcinomas of the lung and of squamous cell papillomas or carcinomas of the forestomach in female mice (NTP, 1985b). See Table 5.

Table 5: Neoplasm Incidence from NTP 2-yr Gavage Bioassay with DCP in Mice

	Exposure Level (mg/kg/d)			Historical Control Incidence
Males	0	25	50	
Forestomach				
Squamous Cell Papilloma	0/50	2/50	3/50	Not reported
Squamous Cell Carcinoma	0/50	0/50	0/50	1/1055(0.09%)
Squamous Cell Papilloma or Carcinoma	0/50	2/50	3/50	Not reported
Lung				
Alveolar/bronchiolar Adenoma	1/50	11/50	9/50	99/1082 (9.1%)
Alveolar/bronchiolar Carcinoma	0/50	2/50	3/50	58/1082 (5.4%)
Alveolar/bronchiolar Adenoma or Carcinoma	1/50	13/50	12/50	155/1082 (14%)
Urinary Bladder				
Transitional Cell Carcinoma	0/50	0/50	2/50	0/1033
Females				
Forestomach				
Squamous Cell Papilloma	0/50	1/50	2/50	1/1077(0.09%)
Squamous Cell Carcinoma	0/50	0/50	2/50	Not reported
Squamous Cell Papilloma or Carcinoma	0/50	1/50	4/50	4/1077 (0.4%)
Lung				
Alveolar/bronchiolar Adenoma	0/50	3/50	8/50	36/1103 (3.3%)
Alveolar/bronchiolar Carcinoma	2/50	1/50	0/50	16/1103 (1.5%)
Alveolar/bronchiolar Adenoma or Carcinoma	2/50	4/50	8/50	52/1103 (4.7%)
Urinary Bladder				
Transitional Cell Carcinoma	0/50	8/50	21/48	0/1025

Chronic inhalation studies were conducted in groups of 70 Fischer 344 rats/dose level/sex that were exposed to 0, 5, 20 or 60 ppm (0, 23, 91, 272 mg/m^3) technical grade DCP (92.1% pure with epoxidized soya as stabilizer) daily for 6 hours/day, 5 days/week for 2 years. Body weights were significantly reduced in the high level animals in the first 425 days (males) and 327 days (females), and among intermediate level males during days 117-327. While no significant changes in gross lesions were observed, increased incidences of unilaterally/bilaterally decreased thickness of the olfactory epithelium, unilateral/bilateral erosions of olfactory epithelium and unilateral/bilateral submucosal fibrosis of the underlying olfactory mucosa were observed histopathologically in high dose males and females. Decreased thickness of olfactory epithelium with loss of olfactory cells was the prevalent microscopic change. In the high dose group rats, a slightly increased incidence of primary benign subcutaneous fibromas was noted (in 5/50 males and 3/50 females, compared to 3/50 and 1/50, respectively, in controls); both incidences were reported to be slightly above the historical control incidences of 5.7 and 1.8%, respectively (Lomax et al., 1989; Dow Chemical Co., 1987c).

A chronic inhalation bioassay was also conducted in groups of 70 B6C3F1 mice/dose level/sex that were exposed to 0, 5, 20 or 60 ppm (0, 23, 91, 272 mg/m^3) technical grade DCP (92.1% pure with epoxidized soya as stabilizer) daily for 6 hours/day, 5 days/week for 2 years. Body weights were significantly decreased during the whole study in males and during months 1-5 in females at the high dose level. Grossly, morphological alterations were noted in the urinary bladder (high level males and females and intermediate level females) and lung (high level males). Microscopically,

hyperplasia of the transitional epithelium of the urinary bladder was reported at high and intermediate levels, and degeneration of the olfactory epithelium was observed in high level animals. In the intermediate level females and high level males and females, hyperplasia of nasal respiratory epithelium was also noted. In high level males, an increased incidence of hyperplasia of the nonglandular stomach was observed. In high level female mice, increased incidences of decreased vacuolation of liver, dilatation/hypercellularity of the larynx and chronic inflammation of the urinary bladder were observed. With the exception of a statistically significant increase in the incidence of bronchoalveolar adenomas in high dose level males (22/50 compared to 9/50 in controls), no significant increases in tumors were reported in treated male or female mice (Lomax et al., 1989; Dow Chemical Co., 1987d).

Conclusion

While no carcinogencity data exist for 1,3-DCB, studies on the analog chemical indicate that chronic inhalation of DCP produces non-neoplastic nasal degeneration and changes in transitional epithelium of the urinary bladder. In addition, benign bronchoalveolar ademomas were observed in lungs of male mice exposed chronically to technical grade DCP containing epoxidized soya stabilizer; no tumors were observed in similarly treated rats. Chronic gavage of a technical grade of DCP containing epichlorohydrin stabilizer, produced tumors at both the site of contact (squamous cell papilloma or carcinoma of the forestomach in rats and mice) as well as tumors at remote sites, notably bronchoalveolar adenoma/carcinoma of the lungs and transitional cell carcinomas of the urinary bladder in female mice (NTP, 1985b). Data from DCP suggest 1,3-DCB is a possible carcinogen. The International Agency for Research on Cancer (IARC) has classified DCP (technical grade containing 1% epichlorohydrin) as possibly carcinogenic to humans: Group 2B.

3.1.8 Toxicity for Reproduction

Studies in Animals

Effects on Fertility

In a two-week inhalation repeated dose study with 1,3-DCB in rats exposed to 10 ppm (50 mg/m^3) and 100 ppm (500 mg/m^3), (DuPont, 1982b) microscopic pathological evaluations were conducted on the testes and epididymides after 10 exposures and following a 14-day recovery period. No compound-related effects were observed in these reproductive organs. No effects on reproductive organs were observed in rats in acute inhalation studies (Kwon and Waritz, 1968).

An inhalation, two-generation reproduction study was conducted with DCP at exposure concentrations of 0, 10, 30 and 90 ppm (0, 45, 136, 409 mg/m^3). Mean body weights of F0 and F1 males and females were decreased during the study. Body weights were slightly decreased in F1 females exposed to 90 ppm (409 mg/m^3) during gestation and slightly decreased in F0 and F1 females exposed to 90 ppm (409 mg/m^3) during lactation. Stomach ulcers were seen in 90 ppm (409 mg/m^3) F0 and F1 male and female rats. In the nasal cavity, subacute inflammation of respiratory mucosa (F0), slight focal hyperplasia of respiratory epithelium (F0 and F1) and slight degeneration of olfactory epithelium (F0 and F1) was noted at 90 ppm (409 mg/m^3) male and female rats. No adverse effects on reproductive performance were observed. Overall, the study NOEL was 30 ppm (136 mg/m^3) based on body weight effects and histopathologic changes in the nose and stomach (Dow Chemical Co., 1987e).

Developmental Toxicity

There are no developmental toxicity studies available for 1,3-DCB.

The developmental toxicity of DCP was evaluated in Fischer 344 rats and New Zealand White rabbits exposed by inhalation to 0, 20, 60 or 120 ppm (0, 91, 272, 545 mg/m^3) for 6 hours/day on gestational days 6-15 (rats) or 6-18 (rabbits) (Hanley et al., 1987). Concentration related decreases in maternal food consumption and body weight gains were observed in all DCP exposed groups of rats and in the 60 and 120 ppm (272 and 545 mg/m^3) groups of exposed rabbits. In rats, a slight, but significantly increased number of fetuses showing delayed ossification of vertebral centra were observed at 120 ppm (545 mg/m^3). In light of the maternal toxicity at this concentration, however, this change was not considered to represent selective toxicity to the fetus. In rabbits, delays in ossification of the metacarpals or phalanges were noted in a few fetuses at 60 or 120 ppm (272 or 545 mg/m^3). The delayed ossification was consistent with the substantially smaller size of these fetuses. The maternal NOEL, based on reduced body weight gains was <20 ppm (<91 mg/m^3) in rats and 20 ppm (91 mg/m^3) in rabbits. No evidence of a teratogenic or embryotoxic response was observed in either species at any exposure level. Evidence for slight fetotoxicity was seen in rats at 120 ppm (545 mg/m^3), a level producing maternal toxicity. The NOEL for teratogenicity was greater than 120 ppm (545 mg/m^3) in both rats and rabbits.

Conclusion

Studies with the analog chemical, DCP, indicate no effects on reproductive parameters; the study NOEL of 30 ppm (136 mg/m^3) being derived from portal of entry effects, principally nasal olfactory degeneration. In developmental toxicity testing with DCP, no evidence for teratogenicity or effects on reproductive parameters was observed in offspring. While some evidence for fetotoxicity, expressed as delayed ossification was observed, the changes occurred at levels where maternal toxicity was evident. DCP did not exhibit selective toxicity to the fetus: the NOEL in rats and rabbits being >120 ppm (545 mg/m^3). Based on the data for the chemical analog, DCP, 1,3-DCB is not likely to be a reproductive or developmental toxicant.

3.2 Initial Assessment for Human Health

Based on physicochemical properties, structural similarities and similar metabolic profiles, data for DCP have been included in the human health section. DCP is considered a suitable analog for 1,3-DCB.

There are no studies available concerning toxicokinetics, metabolism and distribution of 1,3-DCB but its structural similarities to DCP suggest the utilisation of the same metabolic pathways. 1,3-DCB is acutely toxic via the oral and inhalation routes. There are no valid animal dermal LD_{50} studies available for 1,3-DCB. The oral LD_{50} for 1,3-DCB was 300 and 414 mg/kg bw in fasted male and female Wistar rats, respectively and 1368 mg/kg bw in the non-fasted male Cr1:CD rat. The inhalation 4-hour LC_{50} of 1,3-DCB in the male rat ranged from 546 to 756 ppm (2840 to 3930 mg/m^3) and the 2-hour LC_{50} in the mouse was 846 ppm (4400 mg/m^3). The structural analogue, DCP, is acutely toxic via the oral (LD50 in rats is 110-170 mg/kg in males and 110-250 mg/kg in females), dermal (LD_{50} in rats is 800-1300 mg/kg in males and 1300-2000 mg/kg in females) and inhalation [(4-hr LC_{50} values in rats range from 586 to 666 ppm (2700 to 3070 mg/m^3)] routes of exposure.

1,3-DCB is corrosive to the skin of rabbits. Occupational experience shows that 1,3-DCB is also irritating and corrosive to the skin, and that 1,3-DCB vapour is irritating to the eyes and respiratory tract. No eye irritation studies were identified with 1,3-DCB but based on its corrosivity, 1,3-DCB is likely to be severely irritating to eyes.

There is no skin sensitization data for 1,3-DCB. The cis isomer of DCP showed moderate skin sensitisation in guinea pigs.

Repeated dose inhalation studies, in animals, indicate that 1,3-DCB may affect the integrity of lung epithelium. Based on histopathological changes, the NOAEL's range from 2 ppm (10 mg/m^3) in rats and rabbits exposed over a 5 month period, to 10 ppm (52 mg/m^3) in rats exposed for two weeks. Data on the analog substance, DCP, suggest primarily portal of entry effects with NOEL's being 10 ppm (45 mg/m^3) in rats and 30 ppm (136 mg/m^3) in mice. By the inhalation route of exposure, degenerative changes in nasal and pulmonary epithelium are potential outcomes of 1,3-DCB exposure. Data from less well documented studies have reported additional 1,3-DCB effects in adrenal tissue, liver, myocardium, kidney, and spleen.

1,3-DCB is not mutagenic in the bacterial reverse mutation assay (Ames test) in *Salmonella typhimurium* strains (TA 98 and TA 1537) but is mutagenic in Salmonella typhimurium strains (TA 100 and TA 1535) without metabolic activation and in (TA 100) with metabolic activation. 1,3-DCB gave equivocal results in *Saccharomyces cerevisiae.* *In vivo*, 1,3-DCB does not induce micronuclei in the rat bone marrow assay. While no carcinogencity data exist for 1,3-DCB, studies on the analog chemical indicate that chronic inhalation of DCP (containing epoxidized soya stabilizer) produces non-neoplastic nasal degeneration and changes in transitional epithelium of the bladder and benign bronchoalveolar adenomas in lungs of mice. Gavage dosing with technical grades of DCP containing 1% epichlorohydrin produced tumors at the site of application (forestomach adenoma/carcinoma in rats and mice) and remote sites, involving the bronchoalveolar adenoma/carcinoma of the lungs and transitional cell carcinomas of the urinary bladder in female mice. The International Agency for Research on Cancer (IARC) has classified DCP (technical grade containing 1% epichlorohydrin) as possibly carcinogenic to humans: Group 2B.

Available data for 1,3-DCB for reproductive toxicity are from acute and short term, repeated-dose inhalation toxicity studies. No toxic effects on the reproductive organs were observed. No data are available for developmental toxicity. A two-generation inhalation study in rats and developmental studies in rats and rabbits with the structural analog, DCP, showed no effects on reproduction/development at the highest dose tested [90 ppm (409 mg/m^3)]. The NOEL for reproductive toxicity was 30 ppm (136 mg/m^3) based on body weight effects and histopathologic changes in the nose and stomach. For developmental toxicity, the maternal NOEL, based on reduced body weight gains was <20 ppm (<91 mg/m^3) in rats and 20 ppm (91 mg/m^3) in rabbits. No evidence of a teratogenic or embryotoxic response was observed in either species at any exposure level. Evidence for slight fetotoxicity was seen in rats at 120 ppm (545 mg/m^3), a level producing maternal toxicity. The NOEL for teratogenicity was greater than 120 ppm (545 mg/m^3) in both rats and rabbits.

The chemical is of low priority for further work. The chemical possesses properties indicating a hazard to human health (acute toxicity, portal of entry repeated dose toxicity, corrosivity, mutagenicity, possible carcinogen). Based on data presented by the Sponsor country relating to 50% of global production in a closed-system as a chemical intermediate, and use patterns in one country, exposure to humans is anticipated to be low, and therefore, this chemical is currently of low priority for further work. Countries may desire to investigate any exposure scenarios that were not presented by the Sponsor country.

4 HAZARDS TO THE ENVIRONMENT

4.1 Aquatic Effects

Acute Toxicity Test Results

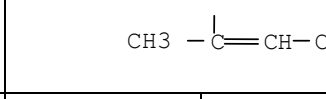
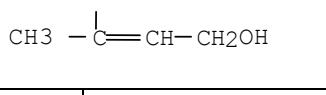
1,3-DCB was reported to have 96-hour LC_{50}'s in zebrafish of > 11 mg/L (Bayer AG, 1992) and a 96-hour TL_M in bluegill sunfish of 6.4 mg/L (DuPont, 1971). The endpoints in the Bayer study

were reported as being potentially affected by the hydrolysis of 1,3-DCB. In addition, the effects of volatilisation of 1,3-DCB and generation of hydrolysis product cannot be ignored. For these reasons, the zebrafish study was considered invalid. Similar problems may have been encountered in the bluegill sunfish study however, the documentation was insufficient for critical examination. Subsequent investigation to evaluate the stability of 1,3-DCB in water (including potential for volatilisation and/or hydrolysis) demonstrated that 1,3-DCB has a volatilisation/hydrolysis half-life of 2.4 hours and a hydrolysis half-life of 6 hours at approximately 20°C in well water (DuPont 2005a). Based on this information, a static, 48-hour daphnid study was conducted utilizing a zero headspace test design and with analytical monitoring of 1,3-DCB concentrations at test start and termination. Significant losses of 1,3-DCB occurred over the 48-hour study period with concurrent appearance of hydrolysis products. Recoveries of 1,3-DCB based on mean measured concentrations over the course of the study ranged from approximately 1 – 3 % of initial nominal test concentrations. These recoveries are in general agreement with the hydrolysis rate determined for 1,3-DCB (DuPont 2005a) for comparable duration.

The rapid degradation of 1,3-DCB suggested hydrolysis products, rather than the parent compound, might be a concern for potential effects on aquatic organisms. The principal hydrolysis products were identified as cis/trans 3-chloro-2-buten-1-ol (3C2B) (DuPont 2005a). Because 3C2B was observed to be more stable than the parent compound, 1,3-DCB, acute toxicity testing was conducted on 3C2B using algae, invertebrates and fish (DuPont 2005b; 2005c; 2005d).

The results of the acute toxicity testing with 3C2B demonstrated that fish were the most sensitive species with a static, 96-hour LC_{50} of 4.03 mg/L based on mean measured test concentrations from open test chambers. The daphnid 48-hour EC_{50} was 11 mg/L based on mean measured test concentrations while the 72-hour EC_{50} for *Pseudokirchneriella subcapitata* was 650 mg/L (biomass; calculated by probit method) and >650 mg/L (growth rate) based on nominal test concentrations. Recoveries of 3C2B during the static fish and daphnid studies, based on mean measured test concentrations, ranged from 61 – 98% of initial nominal test concentrations and were generally between 72 and 98% of nominal concentrations. These data are in reasonable agreement with the ECOSAR estimations of the acute aquatic toxicity of 3C2B with the notable exception that ECOSAR appears to under-predict the toxicity of 3C2B to daphnids (Table 6).

Table 6: Aquatic Toxicity Values

Endpoint	1,3-dichloro-2-butene (1,3-DCB); C4H6Cl2		3-chloro-2-buten-ol (3C2B); C4H7ClO	
CAS Number	926-57-8		40605-42-3	
Structural Formula				
	ECOSAR	Actual Value	ECOSAR	Actual Value
Log Kow (KOWWIN)	2.84		1.12	
Toxicity to Algae 72-h EC_{50}	5.7 mg/L* (96-h) Reliability = 2		104.6 mg/L* (96-h) Reliability = 2	EbC_{50} = 650 mg/L (N) ErC_{50} > 650 mg/L (N) *Pseudokirchneriella subcapitata* Reliability = 2
Toxicity to Invertebrates 48-h EC_{50}	9.2 mg/L* Reliability = 2		980.4 mg/L* Reliability = 2	11 mg/L (M) *Daphnia magna* Reliability = 1

Endpoint	1,3-dichloro-2-butene (1,3-DCB); C4H6Cl2		3-chloro-2-buten-ol (3C2B); C4H7ClO	
Toxicity to fish 96-h LC_{50}	0.7 mg/L* Reliability = 2		8.4 mg/L* 0.5 mg/L** Reliability = 2	4.03 mg/L (M) *Pimephales promelas* Reliability = 1

*- vinyl/allyl halides; ** - vinyl/allyl alcohols

N - nominal concentrations
M - measured concentrations

Chronic Toxicity Test Results

No data were available for the chronic toxicity of 3C2B to aquatic organisms.

Toxicity to Microorganisms

A test for 1,3-DCB inhibition of oxygen consumption by activated sludge was conducted at concentrations of 56, 100, 180, 320, and 560 mg/L. An EC_{50} of 152 mg/L was reported (Bayer AG, 1992).

4.2 Terrestrial Effects

No information was available.

4.3 Other Environmental Effects

No information was available.

4.4 Initial Assessment for the Environment

The melting point of 1,3-DCB is – 75°C and the boiling point is 128-130°C. The vapor pressure is 13.3 hPa at 25°C. The water solubility of 1,3-DCB cannot be determined due to rapid hydrolysis. The density of 1,3-DCB is 1.161 g/mL at 4°C. The log Kow is 2.84 calculated. 1,3-DCB is predicted to be photodegraded by reaction with hydroxyl radicals in the atmosphere with a half-life of approximately 27 hours (calculated). However, its major path of degradation is hydrolysis with a measured half-life of 6.0 hrs; the major hydrolysis product being 3-chloro-2-buten-1-ol (3C2B). 3C2B water solubility exceeds 92 mg/L (40,000 mg/L, calculated). Distribution modeling using Mackay Level I for 1,3-DCB indicated that partitioning will occur to air (99.99%), water (0.003%), and soil (0.002%) phases. The fugacity model Mackay Level III predicts that 1,3-DCB will distribute primarily to water (72.4%) with much smaller distributions to air (20%), soil (7.0%) and sediment (0.58%). Based on the formation of 3C2B from the hydrolysis of 1,3-DCB in water, the estimated Mackay Level III fugacity model distribution, assuming emission to water, is almost entirely to water (99.7%) with lesser amounts in air (0.05%), soil (0.02%) and sediment (0.2%). 1,3-DCB is not readily biodegradable (0% degraded in 28 days). Based on an estimated BCF of 30 for 1,3-DCB and an estimated BCF of 1.5 for 3C2B, neither substance is likely to bioaccumulate.

Because 1,3-DCB is susceptible to hydrolysis, data for the major hydrolysis product, 3C2B, are used for the ecotoxicity endpoints. For 3C2B, the 96-hour LC_{50} for rainbow trout (*Pimephales promelas*) is 4.0 mg/L (measured: ECOSAR 96-hour LC_{50} 8.4 mg/L for allyl halide and 0.5 mg/L for allyl alcohol), the 48-hour EC_{50} for *Daphnia magna* is 11 mg/L (measured: ECOSAR 48-hour

EC_{50} 980.4 mg/L) and the 72-hour cell count biomass and growth rate values for algae (*Pseudokirchneriella subcapitata*) are EbC_{50} equal to 650 mg/L (calculated by probit method) and ErC_{50} > 650 mg/L (nominal: ECOSAR 72-hour EC_{50} 104.6 mg/L), respectively. The ECOSAR estimations of the acute aquatic toxicity of 3C2B are in agreement with the experimental data with the exception that ECOSAR appears to under-predict the toxicity of 3C2B to daphnids.

5 RECOMMENDATIONS

Human Health: The chemical is of low priority for further work. The chemical possesses properties indicating a hazard to human health (acute toxicity, portal of entry repeated dose toxicity, corrosivity, mutagenicity, possible carcinogen). Based on data presented by the Sponsor country relating to 50% of global production in a closed-system as a chemical intermediate, and use patterns in one country, exposure to humans is anticipated to be low, and therefore, this chemical is currently of low priority for further work. Countries may desire to investigate any exposure scenarios that were not presented by the Sponsor country.

Environment: The chemical is of low priority for further work. The chemical possesses properties indicating a hazard to the environment (acute toxicity to fish and invertebrates). Based on data presented by the Sponsor country relating to 50% of global production in a closed-system as a chemical intermediate, emissions to the environment are expected to be negligible. Countries may desire to investigate any exposure scenarios that were not presented by the Sponsor Country."

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I U C L I D

Data Set

Existing Chemical	:	ID: 926-57-8
CAS No.	:	926-57-8
Substance name	:	2-Butene, 1,3-dichloro-
Synonym	:	1,3-DCB

Producer related part

Company	:	DuPont Performance Elastomers LLC
Creation date	:	02.05.2006

Substance related part

Company	:	DuPont Performance Elastomers LLC
Creation date	:	02.05.2006
Status	:	
Memo	:	
Printing date	:	11.05.2006
Revision date	:	
Date of last update	:	02.05.2006
Number of pages	:	100
Chapter (profile)	:	Chapter: 1, 2, 3, 4, 5, 6, 7, 8, 10
Reliability (profile)	:	Reliability: without reliability, 1, 2, 3, 4
Flags (profile)	:	Flags: without flag, confidential, non confidential, WGK (DE), TA-Luft (DE), Material Safety Dataset, Risk Assessment, Directive 67/548/EEC, SIDS

1.0.1 APPLICANT AND COMPANY INFORMATION

Type	:	manufacturer
Name	:	
Contact person	:	Michael A. Lynch
Date	:	
Street	:	560 Highway 44
Town	:	70068-6908 LaPlace, LA
Country	:	United States
Phone	:	985-536-5435
Telefax	:	985-536-5483
Telex	:	
Cedex	:	
Email	:	
Homepage	:	

28.04.2006

1.0.2 LOCATION OF PRODUCTION SITE, IMPORTER OR FORMULATOR

Type	:	manufacturer
Name of plant	:	DuPont Performance Elastomers - Louisville site
Street	:	4242 Campground Road
Town	:	40216 Louisville, KY
Country	:	United States
Phone	:	
Telefax	:	
Telex	:	
Cedex	:	
Email	:	
Homepage	:	

28.04.2006

1.0.3 IDENTITY OF RECIPIENTS

1.0.4 DETAILS ON CATEGORY/TEMPLATE

1.1.0 SUBSTANCE IDENTIFICATION

IUPAC Name	:	2-Butene, 1,3-dichloro-
Smiles Code	:	C(=CCCl)(C)Cl
Molecular formula	:	C4H6Cl2
Molecular weight	:	125.00
Petrol class	:	
Remark	:	1,3-DCB contains ~20% cis-1,3-dichloro-2-butene, CAS No. 10075-38-4, and ~80% trans-1,3-dichloro-2-butene, CAS No. 7415-31-8). Despite the presence of two isomers, 1,3-DCB as manufactured and used commercially, can be considered a single substance.

28.04.2006

1.1.1 GENERAL SUBSTANCE INFORMATION

Purity type :
Substance type : other: chlorinated alkene
Physical status : liquid
Purity : > 98 . % w/w
Colour : colorless
Odour : pungent

28.04.2006

1.1.2 SPECTRA

1.2 SYNONYMS AND TRADENAMES

1,3-DCB

25.10.2000

1,3-Dichloro-2-butene

25.10.2000

1,3-Dichloro-2-butene (cis and trans)

01.11.2005

1,3-Dichlorobutene

01.11.2005

1,3-Dichlorobutene-2

25.10.2000

1,3-Dichlorobutylene

01.11.2005

1.3 IMPURITIES

Purity : other: typical substance composition
CAS-No :
EC-No :
EINECS-Name :
Molecular formula :
Value :

Remark : Mixed chlorinated hydrocarbons ca. <2% w/w
28.04.2006

Purity : other: typical substance composition
CAS-No : 7647-01-0
EC-No : 231-595-7
EINECS-Name : hydrogen chloride
Molecular formula : HCl
Value : < 1 % w/w

28.04.2006

1.4 ADDITIVES

1.5 TOTAL QUANTITY

Quantity : ca. 5000 - tonnes produced in 2002

Remark : Globally, 1,3-DCB is only used commercially in a closed system as a chemical intermediate that is stored and consumed in on-site facilities for the manufacture of 2,3 dichlorobutadiene, a component of some polychloroprene synthetic rubbers. 1,3-DCB is manufactured at sites in the US, Germany and Japan. Annual global production of 1,3-DCB totaled approximately 5000 tonnes for 2002 of which ca. 2500 tonnes was produced in the US.

28.04.2006 (41)

1.6.1 LABELLING

Symbols : Xn, , ,
Nota : , ,
R-Phrases : (22) Harmful if swallowed
S-Phrases :

Remark : Denmark only
25.04.2006 (41)

1.6.2 CLASSIFICATION

1.6.3 PACKAGING

Memo : Not applicable

28.04.2006

1.7 USE PATTERN

Type of use : industrial
Category : Polymers industry

Remark : Among the global producers, 1,3-DCB is produced in a closed-system and used only as a site limited intermediate for the manufacture of 2,3-

dichlorobutadiene, a component of some polychloroprene synthetic rubbers. Consequently, all 1,3-DCB is consumed in the production of polychloroprene synthetic rubber. Laboratory scale quantities are available from some commercial specialty-chemical suppliers (e.g., Sigma-Aldrich) as a mixture of the cis and trans isomers.

Globally, 1,3-DCB is only used commercially as an isolated intermediate that is stored and consumed in on-site facilities for the manufacture of 2,3 dichlorobutadiene , a component of some polychloroprene synthetic rubbers. Globally, 1,3-DCB is only used commercially as an isolated intermediate that is stored and consumed in on-site facilities for the manufacture of 2,3 dichlorobutadiene, a component of some polychloroprene synthetic rubbers. In the US, 1,3-DCB is produced only in Louisville, KY by DuPont Performance Elastomers. Among the global producers, 1,3-DCB is produced and used only as a site limited intermediate. 1,3-DCB is only used in the manufacture of 2,3-dichlorobutadiene. Consequently, all 1,3-DCB is consumed in the production of polychloroprene synthetic rubber. Laboratory scale quantities are available from some commercial specialty-chemical suppliers (e.g., Sigma-Aldrich) as a mixture of the cis and trans isomers.

28.04.2006

1.7.1 DETAILED USE PATTERN

1.7.2 METHODS OF MANUFACTURE

Origin of substance : Monomer
Type : Production

Remark : 1,3-DCB is typically manufactured by the reaction of 2-chloro-1,3-butadiene with HCl in the presence of a copper chloride catalyst. One manufacturer isolates 1,3-DCB from high boilers and still heels in the acetylene route for chloroprene manufacture.

28.04.2006

1.8 REGULATORY MEASURES

1.8.1 OCCUPATIONAL EXPOSURE LIMIT VALUES

Type of limit : other: DuPont Acceptable Exposure Limit (8- and 12-hour TWA)
Limit value : .3 other: ppm

28.04.2006

1.8.2 ACCEPTABLE RESIDUES LEVELS

1.8.3 WATER POLLUTION

1.8.4 MAJOR ACCIDENT HAZARDS

1.8.5 AIR POLLUTION

1.8.6 LISTINGS E.G. CHEMICAL INVENTORIES

Type : TSCA
Additional information : Listed on January 2006 TSCA Inventory

25.04.2006 (14)

Type : NDSL
Additional information : Listed on Canada Gazette, Part I, January 31, 1998

25.04.2006 (14)

Type : EINECS
Additional information : Listed on Annex to Official Journal of the European Communities, 15 June 1990

25.04.2006 (14)

Type : ENCS
Additional information : Listed as: Unlisted chemical name. For ENCS chemical class or category name refer to ENCS No. 2-118

25.04.2006 (14)

Type : other: ASIA - PAC
Additional information :

25.04.2006 (14)

1.9.1 DEGRADATION/TRANSFORMATION PRODUCTS

Type : degradation product in water
CAS-No : 40605-42-3
EC-No :
EINECS-Name : 3-chloro-2-buten-1-ol
IUCLID Chapter :

25.04.2006

1.9.2 COMPONENTS

1.10 SOURCE OF EXPOSURE

1.11 ADDITIONAL REMARKS

Memo : 1,3-DCB hydrolytic product: 3-chloro-2-buten-1-ol (3C2B, CAS# 40605-42-3)

01.11.2005

Memo : Conversion factor for 1,3-DCB

Remark : 1 ppm = 5.20 mg/m3 at 20°C
19.12.2005 (12)

Memo : Conversion factor for 1,3-DCP

Remark : 1 ppm = 4.61 mg/m3 at 20°C
25.04.2006 (12)

Memo : Conversion factor for 3C2B

Remark : 1 ppm = 4.43 mg/m3 at 20°C (calculated)
19.12.2005

1.12 LAST LITERATURE SEARCH

Type of search : Internal and External
Chapters covered :
Date of search : 17.12.2002

25.04.2006

1.13 REVIEWS

2.1 MELTING POINT

Value : -75 °C
Sublimation :
Method :
Year :
GLP : no
Test substance : as prescribed by 1.1 - 1.4

Reliability : (2) valid with restrictions
Handbook value.
Flag : Critical study for SIDS endpoint
23.03.2005 (52)

Value : 127 - 128 °C
Sublimation :
Method :
Year :
GLP : no
Test substance : as prescribed by 1.1 - 1.4

Remark : at 760 mm Hg
Reliability : (3) invalid
Inadequate test substance characterization
26.10.2005 (96)

Value : -69.2 °C
Sublimation :
Method : other
Year :
GLP :
Test substance : as prescribed by 1.1 - 1.4

Method : Modeled MPBPWIN v1.41
Reliability : (2) valid with restrictions
Estimated value based on accepted model.
01.11.2005 (42)

Value : -84 °C
Sublimation :
Method :
Year : 1986
GLP : no data
Test substance : other TS: 1,3-DCP

Test substance : 1,3-DCP, purity not reported
Reliability : (2) valid with restrictions
Handbook value.
Flag : Critical study for SIDS endpoint
20.12.2005 (62)

Value : -46.7 °C
Sublimation :
Method : other
Year :
GLP :

Test substance : 3C2B

Method : Modeled. MPBPWIN v1.41
Estimated value based on accepted model.
Flag : Critical study for SIDS endpoint
22.03.2006 (42)

2.2 BOILING POINT

Value : 128 - 130 °C at 1013 hPa
Decomposition :
Method :
Year :
GLP : no data
Test substance : as prescribed by 1.1 - 1.4

Remark : 1013 hPa = 760 mm Hg
Reliability : (2) valid with restrictions
Handbook value.
Flag : Critical study for SIDS endpoint
23.03.2005 (31) (65)

Value : 34 °C at 26.7 hPa
Decomposition :
Method :
Year :
GLP : no
Test substance : as prescribed by 1.1 - 1.4

Reliability : (2) valid with restrictions
Handbook value.
06.04.2005 (52)

Value : 40 °C at 26.7 hPa
Decomposition :
Method :
Year :
GLP : no
Test substance : as prescribed by 1.1 - 1.4

Reliability : (2) valid with restrictions
Handbook value.
06.04.2005 (51)

Value : 133 °C at 995.8 hPa
Decomposition :
Method :
Year :
GLP : no
Test substance : as prescribed by 1.1 - 1.4

Reliability : (2) valid with restrictions
Handbook value.
06.04.2005 (51)

Value : 125 - 129 °C at
Decomposition :

Method :
Year :
GLP : no data
Test substance : other TS: 1,3-DCB, purity 95% (mixture of cis and trans)

Reliability : (4) not assignable
06.04.2005 (2)

Value : 127 - 129 °C at
Decomposition :
Method :
Year :
GLP : no data
Test substance : as prescribed by 1.1 - 1.4

Reliability : (2) valid with restrictions
22.03.2006 (47)

Value : 129.9 °C at 993 hPa
Decomposition :
Method :
Year :
GLP : no data
Test substance : as prescribed by 1.1 - 1.4

Reliability : (2) valid with restrictions
06.04.2005 (49) (52)

Value : 131 °C at
Decomposition :
Method :
Year :
GLP : no data
Test substance : as prescribed by 1.1 - 1.4

Reliability : (2) valid with restrictions
Handbook value.
22.03.2006 (66)

Value : 131 °C at 1013 hPa
Decomposition :
Method :
Year :
GLP : no data
Test substance : as prescribed by 1.1 - 1.4

Reliability : (2) valid with restrictions
Handbook value.
06.04.2005 (44)

Value : 108 °C at
Decomposition :
Method :
Year :
GLP : no data
Test substance : other TS: 1,3-DCP

Test substance : mixture of isomers

Reliability : (2) valid with restrictions
Handbook value.
Flag : Critical study for SIDS endpoint
20.12.2005 (57)

Value : 148.9 °C at 1013 hPa
Decomposition :
Method : other: MPBPWIN v1.41
Year :
GLP : no
Test substance : other TS: 3-chloro-2-buten-1-ol

Method : Adapted Stein and Brown method
Reliability : (2) valid with restrictions
Estimated value based on accepted model.
Flag : Critical study for SIDS endpoint
22.03.2006 (42) (103)

2.3 DENSITY

Type :
Value : 1.1605 at 4 °C
Method :
Year :
GLP : no data
Test substance : as prescribed by 1.1 - 1.4

Remark : Value is for liquid density.
Vapor density = 4.31
Reliability : (2) valid with restrictions
Flag : Critical study for SIDS endpoint
23.03.2005 (31) (52) (65) (85) (98)

Type :
Value : 1.1573 at 20 °C
Method :
Year :
GLP : no data
Test substance : as prescribed by 1.1 - 1.4

Remark : Value is for liquid density.
Reliability : (2) valid with restrictions
06.04.2005 (47)

Type :
Value : 1.1542 at 25 °C
Method :
Year :
GLP : no
Test substance : as prescribed by 1.1 - 1.4

Remark : Value is for liquid density.
Reliability : (2) valid with restrictions
Handbook value.
06.04.2005 (52)

Type :

Value : 1.162 at 25 °C
Method :
Year :
GLP : no
Test substance : as prescribed by 1.1 - 1.4

Remark : Value is for liquid density.
Reliability : (2) valid with restrictions
Handbook value.
06.04.2005 (51)

Type :
Value : 1.1473 at 30 °C
Method :
Year :
GLP : no
Test substance : as prescribed by 1.1 - 1.4

Remark : Value is for liquid density.
Reliability : (2) valid with restrictions
Handbook value.
06.04.2005 (52)

Type : bulk density
Value : 1.159 at °C
Method :
Year :
GLP :
Test substance : as prescribed by 1.1 - 1.4

Remark : Specific gravity
Reliability : (3) invalid
Inadequate test substance characterization
26.10.2005 (96)

Type :
Value : 1.161 at °C
Method :
Year :
GLP : no data
Test substance : other TS: 1,3-DCB, purity 95% (mixture of cis and trans)

Remark : Value is for specific gravity.
Reliability : (4) not assignable
Handbook value.
06.04.2005 (1) (2)

Type :
Value : 1.112 g/cm³ at 20 °C
Method :
Year :
GLP : no
Test substance : other TS: 3-chloro-2-buten-1-ol

Test substance : 3C2B, purity not reported
Reliability : (2) valid with restrictions
Handbook value.
Flag : Critical study for SIDS endpoint

20.12.2005 (53)

2.3.1 GRANULOMETRY

2.4 VAPOUR PRESSURE

Value : 12.76 hPa at 25 °C
Decomposition :
Method : other (calculated): Modeled
Year :
GLP :
Test substance : as prescribed by 1.1 - 1.4

Method : Mean of Antoine & Grain methods. Modeled MPBPWIN v1.41
Remark : Value = 9.57 mm Hg
Reliability : (2) valid with restrictions
Estimated value based on accepted model.
22.03.2006 (42) (69) (86)

Value : 13.3 hPa at 25 °C
Decomposition :
Method : other (measured): DIN 51794
Year :
GLP : no data
Test substance : as prescribed by 1.1 - 1.4

Reliability : (2) valid with restrictions
Test procedure in accordance with standard methods with acceptable restrictions
Flag : Critical study for SIDS endpoint
06.04.2005 (8)

Value : 13.33 hPa at 25 °C
Decomposition :
Method :
Year :
GLP : no data
Test substance : as prescribed by 1.1 - 1.4

Reliability : (2) valid with restrictions
Test procedure in accordance with standard methods with acceptable restrictions
06.04.2005 (31)

Value : 16.8 hPa at °C
Decomposition :
Method : other (calculated): Estimated
Year :
GLP :
Test substance : as prescribed by 1.1 - 1.4

Method : fragment constant method (Neely W. B. and Blau G. E. (1985). Environmental Exposure from Chemicals, Volume I, CRC Press).
Remark : Value = 12.6 mm Hg
Reliability : (2) valid with restrictions
Estimated value based on accepted model.

06.04.2005 (102)

Value : 24 hPa at 20 °C
Decomposition :
Method :
Year :
GLP : no data
Test substance : other TS: 1,3-DCP

Test substance : mixture of isomers
Reliability : (2) valid with restrictions
Handbook value.
Flag : Critical study for SIDS endpoint
22.03.2006 (57)

Value : 1.05 hPa at 25 °C
Decomposition :
Method : other (calculated)
Year :
GLP : no
Test substance : other TS: 3-chloro-2-buten-1-ol

Method : Calculated using Advanced Chemistry Development (ACD/Labs) Software V8.14.
Reliability : (2) valid with restrictions
Estimated value based on accepted model.
Flag : Critical study for SIDS endpoint
20.12.2005 (104)

2.5 PARTITION COEFFICIENT

Partition coefficient : octanol-water
Log pow : 2.84 at °C
pH value :
Method : other (calculated): Estimated
Year :
GLP :
Test substance : as prescribed by 1.1 - 1.4

Reliability : (2) valid with restrictions
Estimated value based on accepted model.
Flag : Critical study for SIDS endpoint
06.04.2005 (56)

Partition coefficient : octanol-water
Log pow : 1.12 at °C
pH value :
Method : other (calculated): KOWWIN 1.67
Year :
GLP : no
Test substance : other TS: 3-chloro-2-buten-1-ol

Reliability : (2) valid with restrictions
Estimated value based on accepted model.
Flag : Critical study for SIDS endpoint
20.12.2005 (42)

Partition coefficient	:	octanol-water
Log pow	:	1.98 at °C
pH value	:	
Method	:	
Year	:	1986
GLP	:	no data
Test substance	:	other TS: 1,3-DCP
Test substance	:	mixture of isomers
Reliability	:	(2) valid with restrictions Handbook value.
Flag	:	Critical study for SIDS endpoint

20.12.2005 (62)

2.6.1 SOLUBILITY IN DIFFERENT MEDIA

Solubility in	:	Water
Value	:	at °C
pH value	:	
concentration	:	at °C
Temperature effects	:	
Examine different pol.	:	
pKa	:	at 25 °C
Description	:	
Stable	:	
Deg. product	:	
Method	:	other: water solubility column method
Year	:	
GLP	:	yes
Test substance	:	other TS: 1,3-DCB, purity 99.1%
Remark	:	A determination of water solubility was not possible for the following reasons. 1. When preliminary tests were performed, diappearance of the 2 phases was observed on prolonged standing. 2. A reduction of the stirring time to 4 hours and immediate analysis of the content showed that 1,3-DCB content decreased by 26% between the first and eighth injections. 3. In a subsequent main experiment using 10 times the originally weighed-in amount of test material, the mixture was homogeneous after half of the presecribed stirring time, which indicated hydrolysis and solubilization.
Reliability	:	(2) valid with restrictions Quantitative data not obtained

01.11.2005 (11)

Solubility in	:	Water
Value	:	363.1 mg/l at 25 °C
pH value	:	
concentration	:	at °C
Temperature effects	:	
Examine different pol.	:	
pKa	:	at 25 °C
Description	:	
Stable	:	
Deg. product	:	
Method	:	other: Modeled

Year :
GLP :
Test substance : as prescribed by 1.1 - 1.4

Method : Modeled: WSKOW v1.41
Reliability : (3) invalid
Water reactive material. Calculated water solubility is not relevant due to observed rapid hydrolysis; value presented for comparison.
22.03.2006 (42) (72) (73) (80)

Solubility in : Water
Value : < .01 other: mol/L at °C
pH value : 7
concentration : at °C
Temperature effects :
Examine different pol. :
pKa : at 25 °C
Description :
Stable :
Deg. product :
Method : other: Modeled
Year :
GLP :
Test substance : as prescribed by 1.1 - 1.4

Method : Modeled: Advanced Chemistry Development (ACD) Software Solaris V4.67 ((C) 1994-2003 ACD)
Remark : Molar Solubility (SLB.MOL)
Equivalent to < 1250 mg/L
Reliability : (3) invalid
Water reactive material.
06.04.2005

Solubility in : Water
Value : at °C
pH value :
concentration : at °C
Temperature effects :
Examine different pol. :
pKa : at 25 °C
Description :
Stable :

Result : Insoluble
Reliability : (4) not assignable
22.03.2006 (44) (49) (63)

Solubility in : Water
Value : at °C
pH value :
concentration : at °C
Temperature effects :
Examine different pol. :
pKa : at 25 °C
Description :
Stable :

Remark : rapid hydrolysis
Reliability : (4) not assignable

22.03.2006 (9)

Solubility in	:	Water
Value	:	at °C
pH value	:	
concentration	:	at °C
Temperature effects	:	
Examine different pol.	:	
pKa	:	at 25 °C
Description	:	
Stable	:	
Deg. product	:	
Method	:	
Year	:	2005
GLP	:	
Test substance	:	other TS: 1,3-DCB, purity 95.6%

Method : Solubility:
The solubility limit of 1,3-Dichloro-2-butene over a period of 25 hours of stirring, and at a temperature of approximately 20ºC as prepared in solutions of well water containing 0.01% dimethyl formamide (DMF - added to assist with dispersion), was investigated using gas chromatography with electron capture detection (GC/ECD).

Triplicate 1,3-DCB standards were prepared by weighing 323 µL (approx. 0.37 grams) of the 1,3-DCB standard into HPLC vials containing 178 µL DMF. A graduated cylinder was used to add 175 mL of HLWW into nine 150-mL centrifuge tubes containing stir bars. A 50-µL syringe was used to add 49.3 µL from each of the triplicate 1,3-DCB standards, into three of the 150-mL glass centrifuge tubes and the tubes capped immediately with aluminum foil, parafilm, and a screw cap leaving minimal headspace. The three resulting centrifuge tube samples were identified as the 1-hour, 24-hour, and 25-hour samples for one of the triplicate 1,3-DCB standards. The remaining two 1,3-DCB in DMF standards were processed to prepare the total of nine 1,3-DCB centrifuge tube samples with approximately 200 ppm 1,3-DCB in well water containing 0.01% DMF.

The nine 150-mL centrifuge tubes were placed in a water bath/stirrer, kept at a temperature of 20°C and stirred for approximately 25 hours. An aliquot was removed from each flask at 1, 24, and 25 hours. Each aliquot was centrifuged for 30 minutes at 20 °C and 10,500 xg relative centrifuge force. After centrifugation a 100 µL aliquot was removed and diluted 10x with acetonitrile. The diluted samples were prepared for analysis by diluting an additional 10x (100x total dilution) into a final matrix that contained 10% (0.01%DMF in well water) and 90% acetonitrile. The samples were analyzed for 1,3-DCB content by gas chromatography/electron capture detection (GC/ECD) using calibration standards that bracketed the sample concentrations.

Result : It was not possible to determine the solubility limit for 1,3-DCB in well water with 0.01% DMF due to non-equilibrium concentrations over the 25-hour test period. However, the average of triplicate 1-hour solubility results suggests that the solubility limit is at least 101 mg/L before dropping due to hydrolysis.

Reliability : (1) valid without restriction
Flag : Critical study for SIDS endpoint
10.10.2005 (36)

Solubility in	:	Water
Value	:	2700 mg/l at 20 °C

pH value :
concentration : at °C
Temperature effects :
Examine different pol. :
pKa : at 25 °C
Description :
Stable :
Deg. product :
Method :
Year : 1986
GLP : no data
Test substance : other TS: 1,3-DCP

Test substance : cis isomer
Reliability : (2) valid with restrictions
Handbook value.
Flag : Critical study for SIDS endpoint
20.12.2005 (62)

Solubility in : Water
Value : 40070 mg/l at °C
pH value :
concentration : at °C
Temperature effects :
Examine different pol. :
pKa : at 25 °C
Description :
Stable :
Deg. product :
Method : other: WSKOW v1.41
Year :
GLP : no
Test substance : other TS: 3-chloro-2-buten-1-ol

Reliability : (2) valid with restrictions
Estimated value based on accepted model.
Flag : Critical study for SIDS endpoint
20.12.2005 (42) (80)

Solubility in : Water
Value : > 92.7 mg/l at 22.4 °C
pH value :
concentration : at °C
Temperature effects :
Examine different pol. :
pKa : at 25 °C
Description :
Stable :
Deg. product :
Method :
Year : 2005
GLP :
Test substance : other TS: 3C2B

Method : The solubility and stability of 3C2B were evaluated under actual aquatic toxicity test conditions. The test substance solutions were prepared by direct addition of 3C2B to Haskell Laboratory well water. Test solutions were prepared by adding the appropriate volume of 3C2B to the appropriate volume of Haskell Laboratory well water (final volume of

approximately 9 L) and stirring for approximately 10 minutes. Five nominal concentrations (1.0, 3.0, 10, 30, and 100 mg/L) and a dilution water control were used in the study. Concentrations of 3C2B were measured by high performance liquid chromatography with ultraviolet absorbance detection (HPLC/UV).

Result : Solubility in Haskell Laboratory well water, based on the mean, measured test concentration over the course of the study for the nominal 100 mg/L test concentration, was demonstrated to be greater than 92 mg/L at the mean study temperature of 22.4°C. The mean measured concentrations ranged from 94-97% and 61-72% of initial nominal concentrations after 72 and 96 hours, respectively.

Reliability : (2) valid with restrictions
Limited information available but acceptable method was used.

17.01.2006 (38)

2.6.2 SURFACE TENSION

2.7 FLASH POINT

Value : 27.2 °C
Type : closed cup
Method :
Year :
GLP : no data
Test substance : as prescribed by 1.1 - 1.4

Reliability : (2) valid with restrictions
Handbook value.
Flag : Critical study for SIDS endpoint
06.04.2005 (88) (97)

Value : 26.7 °C
Type : closed cup
Method :
Year :
GLP : no data
Test substance : as prescribed by 1.1 - 1.4

Reliability : (2) valid with restrictions
Handbook value.
06.04.2005 (44)

Value : 33 °C
Type :
Method :
Year :
GLP : no data
Test substance : as prescribed by 1.1 - 1.4

Reliability : (2) valid with restrictions
06.04.2005 (101)

Value : 33.9 °C
Type :
Method :
Year :

GLP : no data
Test substance : other TS: 1,3-DCB, purity 95% (mixture of cis and trans)

Reliability : (4) not assignable
06.04.2005 (2)

Value : 36 °C
Type :
Method : other: DIN 51755
Year :
GLP : no data
Test substance : as prescribed by 1.1 - 1.4

Reliability : (2) valid with restrictions
Limited information available but guideline method was used.
06.04.2005 (7)

Value : 42.5 °C
Type :
Method :
Year :
GLP : no
Test substance : other TS: 3-chloro-2-buten-1-ol

Remark : 42.5±20.4°C
Reliability : (2) valid with restrictions
Estimated value based on accepted model.
Flag : Critical study for SIDS endpoint
20.12.2005 (104)

2.8 AUTO FLAMMABILITY

2.9 FLAMMABILITY

2.10 EXPLOSIVE PROPERTIES

Result : other: explosive limits: 2-13%
Method :
Year :
GLP : no data
Test substance : as prescribed by 1.1 - 1.4

Reliability : (2) valid with restrictions
23.03.2005 (31)

2.11 OXIDIZING PROPERTIES

2.12 DISSOCIATION CONSTANT

Acid-base constant : Not expected to dissociate in water
Method : other: Modeled

Year	:	
GLP	:	
Test substance	:	as prescribed by 1.1 - 1.4
Method	:	Modeled: Advanced Chemistry Development (ACD) Software Solaris V4.67 ((C) 1994-2003 ACD)
Reliability	:	(3) invalid Water reactive material.
21.10.2005		
Acid-base constant	:	13.4 at 25 deg C
Method	:	other: calculated
Year	:	
GLP	:	no
Test substance	:	other TS: 3-chloro-2-buten-1-ol
Reliability	:	(2) valid with restrictions Estimated value based on accepted model.
20.12.2005		(104)

2.13 VISCOSITY

2.14 ADDITIONAL REMARKS

3.1.1 PHOTODEGRADATION

Deg. product	:	
Method	:	other (calculated): AOPWIN 1.91
Year	:	
GLP	:	
Test substance	:	as prescribed by 1.1 - 1.4
Result	:	The half-life reaction in air with hydroxyl radicals is estimated to be 27 hours (24-hour day; 0.5E6 OH radicals/cm3) and the reaction with ozone molecules (7E11 molecules/cm3) is about 8 days.
Reliability	:	(2) valid with restrictions Estimated value based on accepted model.
Flag	:	Critical study for SIDS endpoint
01.11.2005		(3)
Type	:	other
Light source	:	
Light spectrum	:	nm
Relative intensity	:	based on intensity of sunlight
Deg. product	:	
Method	:	other (calculated): modeled
Year	:	
GLP	:	
Test substance	:	as prescribed by 1.1 - 1.4
Result	:	According to a model of gas/particle partitioning of semivolatile organic compounds in the atmosphere (Bidleman, 1988), 1,3-DCB which has an estimated vapor pressure of 12.6 mm Hg at 25ºC (SRC, n.d.), determined from a fragment constant method (Lyman, 1985), is expected to exist solely as a vapor in the ambient atmosphere. Vapor-phase 1,3-DCB is expected to degrade in the atmosphere by reaction with photochemically-produced hydroxyl radicals and ozone (SRC, n.d.). The half-life for the reaction in air with hydroxyl radicals is estimated to be 27 hours (SRC, n.d.), calculated from its rate constant of 1.4E-11 cu cm/molecule-sec at 25ºC (SRC, n.d.) that was derived using a structure estimation method (Meylan and Howard, 1993). The half-life for the reaction in air with ozone is estimated to be 8 days (SRC, n.d.), calculated from its rate constants 1.4E-18 cu cm/molecule-sec at 25ºC (SRC, n.d.) that was derived using a structure estimation method (Meylan and Howard, 1993).
Reliability	:	(2) valid with restrictions Estimated value based on accepted model.
Flag	:	Critical study for SIDS endpoint
01.11.2005		(13) (70) (74) (102)
Deg. product	:	
Method	:	other (calculated): AOPWIN 1.91
Year	:	
GLP	:	
Test substance	:	other TS: 3C2B
Result	:	If present in air, the half-life reaction of 3C2B with hydroxyl radicals is estimated to be 18 hours (24-hour day; 0.5E6 OH radicals/cm3) calculated from its rate constant of 2.18E-11 cm3/molecule-sec at 25ºC (AOPWIN) and the reaction with ozone molecules is about 27 hours (at 7E11

molecules/cm3) calculated from its rate constant of 1.06E-17 cm3/molecule-sec at 25ºC (AOPWIN) that was derived using a structure estimation method (Meylan and Howard, 1993).

Reliability : (2) valid with restrictions
Estimated value based on accepted model.

01.11.2005 (3)

3.1.2 STABILITY IN WATER

Deg. product :
Method :
Year : 2005
GLP :
Test substance : other TS: 1,3-DCB, purity 95.6%

Method : Stability:
The stability of 1,3-DCB at an initial concentration of 11.1 mg/L as prepared in solutions of well water containing 0.01% DMF, was investigated for up to 72 hours at temperatures of approximately 4ºC and 20ºC using GC/ECD. Recoveries were measured at 24-hour intervals.

1,3-DCB Half-life Study:
The 1,3-DCB half-life study was performed using HPLC with UV detection, because the technique was best suited to detect and quantify the lower level hydrolysis products. A graduated cylinder was used to add 120 mL of well water into one 100-mL glass septum vial (i.e., no headspace). A 10-µL syringe was used to add 10 µL of 1,3-DCB test substance and the vial capped with a foil-lined cap. This sample contained 94.0 mg/L 1,3-DCB in well water. The vial was sonicated for 10 minutes and then allowed to stand for 10 minutes to allow undissolved 1,3-DCB to settle on the bottom. Approximately 80 mL of the prepared sample was decanted into a beaker, leaving undissolved 1,3-DCB on the bottom of the vial. Aliquots of the 1,3-DCB sample in the beaker were removed to prepare three sets of approximately 20 HPLC vials each as follows: Set 1 contained 800 µL sample in open HPLC vials (no caps). Set 2 contained 800 µL sample and was capped (i.e. approximately 800 µL headspace). Set 3 was completely filled with sample and capped (no headspace). The samples were analyzed at different time intervals by HPLC/UV with the autosampler tray set at a temperature of 20 °C.
The qualitative identification of hydrolysis products was performed using GC/MS, because this technique was best suited to ionize and fragment the 1,3-DCB and hydrolysis products for qualitative identification. For the qualitative identification of the 1,3-DCB hydrolysis products, the following standards were prepared from purchased standards at the approximate 100 ppm level; a) 1,3-DCB in acetonitrile, b) 1,3-DCB in well water, c) 3C2B in acetonitrile, and d) 3C2B in well water. The samples were analyzed at different time intervals using HPLC/UV and GC/MSD techniques.

Remark : Although the pH was not measured in this study, the well water pH is typically ~ 7.5.

Result : The stability results indicated that 1,3-DCB is not stable in well water containing 0.01% DMF over the 72-hour test period.

1,3-DCB has two peaks from the cis and trans isomers. The major peak is 86.3% by peak area while the minor peak is 13.7%. The analysis of a 1,3-DCB test sample in well water via UV detection was able to correlate the loss of the 1,3-DCB with the concurrent formation of two hydrolytic peaks. The half-life of 1,3-DCB in well water at 20 ºC was determined to be 6.0

hours in capped HPLC vials without headspace, 7.1 hours in capped HPLC vials containing approximately 800 uL sample and 800 uL headspace, and 2.4 hours in HPLC vials containing 800 uL sample, but not capped (open headspace). The two hydrolytic peaks appear to be stable based on the results for the vials that were capped (no headspace). However, the results for the vials that were not capped (open headspace) suggests that the major hydrolytic peak is not volatile while the minor hydrolysis peak is volatile.

The identities of the two peaks observed using HPLC/UV were confirmed to be the corresponding 1,3-DCB alcohols, cis and trans 3-chloro-2-buten-ol (3C2B) isomers formed from the hydrolysis of the cis and trans 1,3-DCB isomers that are present in the test substance. The 3C2B identities were confirmed based on matching retention times and electron impact (EI) fragmentation spectra obtained from an authentic 3C2B standard (purity, 98.5%) to that of a hydrolyzed 1,3-DCB test sample.

Reliability : (1) valid without restriction
Flag : Critical study for SIDS endpoint
19.12.2005 (36)

Deg. product :
Method : other: water solubility column method
Year :
GLP : yes
Test substance : other TS: 1,3-DCB, purity not reported

Remark : A determination of water solubility was not possible due to rapid hydrolysis. When preliminary tests were performed, disappearance of the 2 phases was observed on prolonged standing. A reduction in the stirring time to 4 hours and immediate analysis of the content showed that the content decreased by 26% between the first and eighth injections. In a subsequent main experiment using 10 times the originally weighed-in amount of test material, the mixture was homogeneous after half of the prescribed stirring time, which indicated hydrolysis and solubilization.
Reliability : (2) valid with restrictions
Quantitative data not obtained
01.11.2005 (11)

Deg. product :
Method : other: modeled
Year :
GLP :
Test substance : as prescribed by 1.1 - 1.4

Result : Based on a classification scheme (Swann et al., 1983), an estimated Koc value of 125 (SRC, n.d.), determined from a structure estimation method (Meylan et al., 1992), indicates that 1,3-DCB is not expected to absorb to suspended soilds and sediment (SRC, n.d.). Volitization from water surfaces is expected (Lyman et al., 1990) based upon an estimated Henry's Law constant of 3.8E-2 atm-cu m/mole (SRC, n.d.), developed using a fragment constant estimation method (Meylan and Howard, 1991). Using this Henry's Law constant and an estimation method (Lyman et al., 1990), volitization half-lifes for a model river and model lake are 1 hour and 4.4 days, respectively (SRC, n.d.).

1,3-DCB is unstable in water with half-times of 6 hours in capped vials without headspace (representing hydrolysis) and 2.4 hours in uncapped vials (representing hydrolysis and volatilisation (DuPont, 2005).
Reliability : (2) valid with restrictions

Estimated value based on accepted model.
01.11.2005 (36) (46) (56) (69) (75) (77) (78) (102) (106)

3.1.3 STABILITY IN SOIL

Type	:	other
Radiolabel	:	
Concentration	:	
Soil temperature	:	°C
Soil humidity	:	
Soil classification	:	
Year	:	
Deg. product	:	
Method	:	other: Modeled
Year	:	
GLP	:	
Test substance	:	as prescribed by 1.1 - 1.4
Result	:	Based on a classification system (Swann et al., 1983), an estimated Koc value of 125 (SRC, n.d.), determined from a structure estimation method (Meylan et al., 1992), indicates that 1,3-DCB is expected to have high mobility in soil (SRC, n.d.). Volitization of 1,3-DCB from moist soil surfaces is expected to be an important fate process (SRC, n.d.) given an estimated Henry's law constant of 3.8E-2 atm-cu m/mole (SRC, n.d.), using a fragment constant estimation method (Meylan and Howard, 1991). The potential for volatization of 1,3-DCB from dry soil surfaces may exist (SRC, n.d.) based upon an estimated vapor pressure of 12.6 mm Hg (SRC, n.d.), determined from a fragment constant method (Lyman, 1985). 1,3-DCB is unstable in water with half-times of 6 hours in capped vials without headspace (representing hydrolysis) and 2.4 hours in uncapped vials (representing hydrolysis and volatilisation (DuPont, 2005). This suggests that 1,3-DCB may undergo hydrolysis in moist soil.
Reliability	:	(2) valid with restrictions Estimated value based on accepted model.
Flag	:	Critical study for SIDS endpoint

01.11.2005 (36) (70) (75) (77) (92) (102) (106)

Type	:	other
Radiolabel	:	
Concentration	:	
Soil temperature	:	°C
Soil humidity	:	
Soil classification	:	
Year	:	
Deg. product	:	
Method	:	other: modeled
Year	:	
GLP	:	
Test substance	:	other TS: 3C2B
Result	:	3C2B has an estimated Koc value of 3.78 (PCKOCWIN) determined from a structure estimation method (Meylan et al., 1992). This indicates a moderate to strong sorption to soil with a negligible to slow migration potential to groundwater. An estimate Henry's law constant of 3.99E-006 atm-m3/mole (HENRYWIN) indicates only a slight volatility from moist soil.
Reliability	:	(2) valid with restrictions Estimated value based on accepted model.
Flag	:	Critical study for SIDS endpoint

01.11.2005 (54) (76) (77) (92)

3.2.1 MONITORING DATA

3.2.2 FIELD STUDIES

3.3.1 TRANSPORT BETWEEN ENVIRONMENTAL COMPARTMENTS

Type : fugacity model level III
Media : other: air, water, soil, sediment
Air : % (Fugacity Model Level I)
Water : % (Fugacity Model Level I)
Soil : % (Fugacity Model Level I)
Biota : % (Fugacity Model Level II/III)
Soil : % (Fugacity Model Level II/III)
Method : other: Modeled
Year :

Method : Calculated according to MacKay Level III as part of Syracuse Research Corporation EPIWIN Version 3.12 (USEPA EPISuite®) using the following physical chemical input values:
Chem Name : 2-Butene, 1,3-dichloro-
Molecular Wt: 125
Henry's LC : 0.0384 atm-m3/mole (HENRYWIN program)
Vapor Press : 9.98 mm Hg (User entered)
Log Kow : 2.84 (KOWWIN program)
Soil Koc : 125 (PCKOCWIN program)

And assuming a Level III emmissions scenario of equal emmisions to air, water and soil.

Result : Mass Amount (percent)

Air	18.5
Water	67.1
Soil	13.3
Sediment	1.08

Test substance : 1,3-DCB
Reliability : (2) valid with restrictions
Estimated value based on accepted model.
Flag : Critical study for SIDS endpoint
01.11.2005 (43) (55) (61) (93)

Type : fugacity model level III
Media : other: air, water, soil, sediment
Air : % (Fugacity Model Level I)
Water : % (Fugacity Model Level I)
Soil : % (Fugacity Model Level I)
Biota : % (Fugacity Model Level II/III)
Soil : % (Fugacity Model Level II/III)
Method : other: Modeled
Year :

Method : Calculated according to MacKay Level III as part of Syracuse Research Corporation EPIWIN Version 3.12 (USEPA EPISuite®) using the following

physical chemical input values:
Chem Name : 3-Chloro-2-buten-1-ol
Molecular Wt: 106.55
Henry's LC : 3.99E-006 atm-m3/mole (HENRYWIN program)
Vapor Press : 1.44 mm Hg (MPBPWIN program)
Log Kow : 1.12 (KOWWIN program)
Soil Koc : 3.78 (PCKOCWIN program)

And assuming a Level III emmissions scenario of equal emmisions to air, water and soil.

Result : Mass Amount

	(percent)
Air	1.35
Water	42.8
Soil	54.4
Sediment	0.088

Test substance : 3C2B
Reliability : (2) valid with restrictions
Estimated value based on accepted model.
01.11.2005 (43) (55) (61) (84) (93)

Type : fugacity model level I
Media : other: air, water, soil, sediment
Air : % (Fugacity Model Level I)
Water : % (Fugacity Model Level I)
Soil : % (Fugacity Model Level I)
Biota : % (Fugacity Model Level II/III)
Soil : % (Fugacity Model Level II/III)
Method : other: modeled
Year :

Method : Calculated according to MacKay Level I fugacity using the following physical chemical input values:

Data Temperature:	25°C (298.15 K)
Water Solubility:	1.01g/m³ (0.00808 mol/m³)
Vapour Pressure:	1330 Pa
Melting Point:	-75°C (198.15 K)
Henry's Law Constant:	164604 Pa.m³/mol
Log Kow:	2.84

Result :

	Mass Amount (%)
Air	99.99509
Water	3.01E-03
Soil	1.85E-03
Sediment	4.10E-05

Test substance : 1,3-DCB
Reliability : (2) valid with restrictions
Estimated value based on accepted model.
Flag : Critical study for SIDS endpoint
19.12.2005 (71)

Type : fugacity model level III
Media :
Air : % (Fugacity Model Level I)
Water : % (Fugacity Model Level I)
Soil : % (Fugacity Model Level I)
Biota : % (Fugacity Model Level II/III)
Soil : % (Fugacity Model Level II/III)
Method : other: modeled

Year :

Method : Calculated according to MacKay Level III as part of Syracuse Research Corporation EPIWIN Version 3.12 (USEPA EPISuite®) using the following physical chemical input values:

Chem Name : 3-Chloro-2-buten-1-ol
Molecular Wt: 106.55
Henry's LC : 3.99E-006 atm-m3/mole (HENRYWIN program)
Vapor Press : 1.44 mm Hg (MPBPWIN program)
Log Kow : 1.12 (KOWWIN program)
Soil Koc : 3.78 (PCKOCWIN program)

And assuming a Level III emmissions scenario to water.

Result : Mass Amount
(percent)
Air 0.052
Water 99.7
Soil 0.0183
Sediment 0.198

Test substance : 3C2B
Reliability : (2) valid with restrictions
Estimated value based on accepted model.

01.11.2005 (43) (55) (61) (84) (93)

Type :
Media :
Air : % (Fugacity Model Level I)
Water : % (Fugacity Model Level I)
Soil : % (Fugacity Model Level I)
Biota : % (Fugacity Model Level II/III)
Soil : % (Fugacity Model Level II/III)
Method : other: modeled
Year :

Result : Based on the formation of 3C2B from the hydrolysis of 1,3-DCB in water, the estimated Level III fugacity model distribution (emission to water) of 3C2B is air (0.05%), water (99.7%), soil (0.02%), and sediment (0.2%) (EPISUITE 3.12). This agrees with the study that 3C2B will tend to remain in water rather than partition to other environmental media (Jawarska et al., 2002) The estimated Level III fugacity model distribution (assuming equal emissions to air, water, and soil) of 3C2B is air (1.38%), water (44.2%), soil (54.4%) and sediment (0.88%) (EPISUITE 3.12). The fugacity model predicts that the overall half-life in water to be 15 days (EPISUITE 3.12). 3C2B has predicted to have volatilisation half-life estimates for a model river and model lake as 6.3 days and 73 days, respectively (EPISUITE 3.12).

Test substance : other TS: 3C2B
Reliability : (2) valid with restrictions
Estimated value based on accepted model.

22.03.2006 (42) (58)

3.3.2 DISTRIBUTION

Media :
Method : other (calculation): Modeled
Year :

Method : Calculated according to the WVOLNT program in EPISUITE 3.12 using the following physical chemical input values:

Molecular Weight : 125.00 g/mole
Henry's Law Constant: 0.0384 atm-m3/mole (estimated by Bond SAR Method)

	RIVER	LAKE
Water Depth (meters):	1	1
Wind Velocity (m/sec):	5	0.5
Current Velocity (m/sec):	1	0.05

Result :

	RIVER	LAKE
HALF-LIFE (hours) :	1.158	106.4

Test substance : 1,3-DCB
Reliability : (2) valid with restrictions
Estimated value based on accepted model.
01.11.2005 (42)

Media :
Method : other (calculation): Modeled
Year :

Method : Calculated according to the WVOLNT program in EPISUITE 3.12 using the following physical chemical input values:

Molecular Weight : 106.55
Henry's Law Constant: 3.99E-006 atm-m3/mole

	RIVER	LAKE
Water Depth (meters):	1	1
Wind Velocity (m/sec):	5	0.5
Current Velocity (m/sec):	1	0.05

Result :

	RIVER	LAKE
HALF-LIFE (hours) :	152.5	1750

Test substance : 3C2B
Reliability : (2) valid with restrictions
Estimated value based on accepted model.
01.11.2005 (42)

Media :
Method : other (calculation): Modeled
Year :

Method : Calculated according to the STP program in EPISUITE 3.12 using the following physical chemical input values:

Molecular weight (g/mol): 125
Vapor pressure (mm Hg): 9.98
Henry 's law constant (Atm-m3/mol): 0.0384
Air-water partition coefficient: 1.57045
Log Kow: 2.84
Biomass to water partition coefficient: 139.166
Temperature [deg C]: 25
Biodeg rate constants (h^-1),half life in biomass (h) and in 2000 mg/L

MLSS (h):

Primary tank	0.00	2177.31	10000.00
Aeration tank	0.00	2177.31	10000.00
Settling tank	0.00	2177.31	10000.00

Result : % of influent mass

Primary sludge	1.83
Waste sludge	0.17
Primary volatilization	1.27
Settling volatilization	0.23
Aeration off gas	90.25
Primary biodegradation	0.02
Settling biodegradation	0.00
Aeration biodegradation	0.01
Final water effluent	6.22
Total removal	93.78
Total biodegradation	0.03

Test substance : 1,3-DCB
Reliability : (2) valid with restrictions
Estimated value based on accepted model.
01.11.2005 (42)

Media :
Method : other (calculation): Modeled
Year :

Method : Calculated according to the STP program in EPISUITE 3.12 using the following physical chemical input values:

Molecular weight (g/mol): 106.55
Henry 's law constant (Atm-m3/mol): 3.99E-006
Air-water partition coefficient: 1.63179E-004
Log Kow: 1.12
Biomass to water partition coefficient: 3.43651
Temperature [deg C]: 25
Biodeg rate constants (h^-1),half life in biomass (h) and in 2000 mg/L
MLSS (h):

Primary tank	0.01	68.26	10000.00
Aeration tank	0.01	68.26	10000.00
Settling tank	0.01	68.26	10000.00

Result : % of influent mass

Primary sludge	0.28
Waste sludge	1.52
Primary volatilization	0.02
Settling volatilization	0.06
Aeration off gas	0.15
Primary biodegradation	0.02
Settling biodegradation	0.02
Aeration biodegradation	0.07
Final water effluent	97.88
Total removal	2.12
Total biodegradation	0.09

Test substance : 3C2B
Reliability : (2) valid with restrictions

Estimated value based on accepted model.

01.11.2005 (42)

3.4 MODE OF DEGRADATION IN ACTUAL USE

3.5 BIODEGRADATION

Type	:	aerobic
Inoculum	:	domestic sewage
Concentration	:	20 mg/l related to DOC (Dissolved Organic Carbon) related to
Contact time	:	
Degradation	:	0 (±) % after 28
Result	:	
Deg. product	:	
Method	:	other: OECD Screening Test
Year	:	
GLP	:	yes
Test substance	:	other TS: 1,3-DCB, purity 99.1%

Method :

The test method was biological degradability - modified OECD screening test. The procedure was devised based on Appendix V C.3 Degradability: Modified OECD Screening Test, Guideline of the Commission 84/449/EWG (Official Journal of the EEC No. L 251 of 19 September 1984).

The test material was dissolved in a mineral medium which was inoculated with a mixed population of aquatic microorganisms (activated sludge) and incubated for 28 days under aerobic conditions, in the dark, at 20-25 deg C. The biological degradation of the test material was determined during htis time based on the decrease in DOC.

The test concentration was 20 mg/L DOC. The concentration of the inoculation material was 0.5 mL/900 mL.

Result : DOC Value, Stock solution of the test substance: 52 mg/L

Time (days)	Test Material DOC net* (mg/L)	% Degradation
0	18	0
7	18	0
14	14	22
21	18	0
27	16	11
28	18	0

* blank DOC value of 2 mg/L was subtracted from the measured DOC value to get the DOC net value.

An additional flask of test material, without the inoculating material, was prepared for purposes of determining the volatility of 1,3-DCB. The DOC analyses did not show any reduction in the DOC concentration during the test period of 28 days.

1,3-DCB was classified as "Not Readily Biodegradable"

Reliability : (2) valid with restrictions
Uncertainty about hydrolysis behavior.

Flag : Critical study for SIDS endpoint
01.11.2005 (11)

3.6 BOD5, COD OR BOD5/COD RATIO

3.7 BIOACCUMULATION

BCF : 30
Elimination :
Method : other: Modeled BCFWIN 2.15
Year :
GLP :
Test substance : as prescribed by 1.1 - 1.4

Method : The BCF was estimated using an estimated log Kow of 2.84 (Howard and Meylan, 1997) and a regression-derived equation (Meylan et al., 1999).
Result : According to a classification scheme (Franke et al., 1994), this BCF suggests the potential for bioconcentration in aquatic organisms is low.
Reliability : (2) valid with restrictions
Estimated value based on accepted model.
25.10.2005 (46) (56) (78)

BCF : 1.5
Elimination :
Method : other: Modeled BCFWIN 2.15
Year :
GLP :
Test substance : other TS: 3C2B

Reliability : (2) valid with restrictions
Estimated value based on accepted model.
25.10.2005 (79)

3.8 ADDITIONAL REMARKS

4.1 ACUTE/PROLONGED TOXICITY TO FISH

Type	:	static
Species	:	Brachydanio rerio (Fish, fresh water)
Exposure period	:	96 hour(s)
Unit	:	mg/l
LC50	:	> 11
Limit test	:	
Analytical monitoring	:	no
Method	:	other: similar to OECD Guideline 203
Year	:	
GLP	:	yes
Test substance	:	other TS: 1,3-DCB, purity 99.1%

Method : The test procedure followed was the procedure from the Federal Office for Environment Protection, Berlin of May 1984 (which largely corresponds to the OECD 203 test method).

The test species, Zebra barbel, were 2.5-3.5 cm in body length. The test aquariums were 300 x 135 x 200 mm. The procedure was static and 5 1 test medium, aerated was used. There were 10 fish tested in each test concentration.

Nominal test concentrations for the test were 1.0, 1.4, 2.0, 2.8, 3.9, 5.5, 7.8, and 11.0 mg/L. The control and dilution water was synthetic fresh water per ISO with a water hardness of 7.3 'dH.

The test material weighed into the water was treated for 60 seconds with the Ultra-Turrax at 8000 revolutions.

Remark : In a preliminary test, an LC0 value of 1 mg/L and an LC100 value of 10 mg/L were obtained. In the main test, no mortality was observed with the highest test concentration (11 mg/L). The main test was repeated (results were not reported in the test report), a mortality effect of 100% was observed with a test concentration of 7.8 mg/L. The report states that the explanation of these non-uniform test results was possibly ascribable to the fact that the test material is subject to hydrolysis and that the chemical nature and the % concentrations of the corresponding hydrolysis products are unknown.

Result : The following Abiotic parameters were reported:

Temperature ranges (in deg C) were 20.3-21.5 throughout the 96-hour exposure period. Oxygen (in mg/L) ranged from 8.2-9.8 throughout the 96-hour exposure period. Oxygen (% saturation) ranged from 95.1-112.9 throughout the 96-hour exposure period. pH values ranged from 7.3-8.2 throughout the 96-hour exposure period.

There was no mortality reported at any dose level tested.

Reliability : (3) invalid
Only nominal concentrations were used. Significant methodological deficiences.

19.12.2005 (11)

Type	:	
Species	:	Lepomis macrochirus (Fish, fresh water)
Exposure period	:	96 hour(s)
Unit	:	
TLM	:	6.4

Method :
Year :
GLP : no
Test substance : other TS: 1,3-DCB, purity 100%

Remark : Units = ppm
Reliability : (4) not assignable
23.03.2005 (26)

Type : static
Species : Pimephales promelas (Fish, fresh water)
Exposure period : 96 hour(s)
Unit : mg/l
LC50 : 4
Limit test :
Analytical monitoring : yes
Method : OECD Guide-line 203 "Fish, Acute Toxicity Test"
Year : 2005
GLP : yes
Test substance : other TS: 3-chloro-2-buten-1-ol, purity 98.5%

Method : The acute toxicity of 3-chloro-2-buten-1-ol (3C2B) to unfed juvenile fathead minnow was determined in an unaerated, 96-hour, toxicity test. The study was conducted with five concentrations of 3C2B (1.0, 3.0, 10, 30, and 100 mg/L) and a dilution water control. Nominal concentrations were not adjusted for 98.5% purity during preparation.

One test chamber was used per test concentration with 10 fish in each chamber (10 fish per concentration).

Test substance solutions were prepared by direct addition of 3C2B to well water in the open test chambers; no attempt was made to control for volatilization. Test solutions were prepared by adding the appropriate volume of 3C2B to the appropriate volume of well water (final volume of approximately 9 mL) and stirring for approximately 10 minutes.

Addition of fish to the test solutions was initiated 26 minutes after mixing of the solutions was completed. Mortality and sublethal effect observations were made at test start, every 24 hours thereafter, and at test end.

A circulating water bath was used to maintain mean temperature in teh test chambers at approximately 22.4°C. A photoperiod of 16 hours light and 8 hours darkness was employed. Dissolved oxygen concentration, pH, and temperature were measured in each chamber of the dilution water control and test substance concentrations. These measurements were taken at test start, every 24 hours thereafter, and at test end or at total mortality in a concentration. Total alkalinity, EDTA hardness, and conductivity of the dilution water control and highest test substance concentration were measured on samples collected at the beginning of the test.

Test solution concentrations were analyzed for 3C2B via high performance liquid chromatography with ultraviolet absorbance detection (HPLC/UV).

The 24, 48, and 72-hour LC50 values and 95% confidence limits were calculated by the moving-average-angle method and the 96-hour LC50 value and fiducial limits were calculated by probit analysis based on mean, measured 3C2B concentrations and mortality. The highest mean, measured concentration causing no mortality at test end and the lowest mean, measured concentration causing 100% mortality at test end were

assessed by visual observation.

Result : Nominal concentrations (not adjusted for 98.5% purity during preparation) were 1.0, 3.0, 10, 30, and 100 mg/L. Mean, measured concentrations of 3C2B were 0.6, 1.83, 7.08, 28.7, and 92.7 mg/L, respectively. The dilution water control solution showed no detectable concentrations of 3C2B. The water solubility, based on measured test concentrations, was > 92 mg/L.

Total alkalinity, EDTA hardness, and conductivity of the dilution water control and highest test substance concentration at test start ranged from 48 to 50 mg/L as CaCO3, 125 to 127 mg/L as CaCO3, and 265 to 280 mmhos/cm, respectively. During the test, dissolved oxygen concentrations ranged from 6.2 to 8.2 mg/L, pH ranged from 7.3 to 7.6, and mean temperature was 22.4°C with a range of 22.0 to 22.6°C.

At test conclusion, fish from the dilution water control ranged from 1.9 to 2.2 cm in standard length (mean 2.0 cm) and 0.0836 to 0.1302 g in wet weight, blotted dry (mean 0.1073 g). Standard length of the longest fish was not more than twice the length of the shortest fish in the control. Loading in the dilution water control was 0.1073 g/L at test conclusion.

Test organism survival in the dilution water control was 90% at test end. Exposure of fathead minnow to mean, measured 3C2B concentrations of 0.6, 1.83, 7.08, 28.7, and 92.7 mg/L resulted in 0, 30, 70, 100, and 100% mortality respectively, at the end of 96 hours. No sublethal effects were observed in the surviving fish in the dilution water control or the 0.6 mg/L mean, measured test concentration at the end of 96 hours. Sublethal effects observed at the end of 96 hours in the 1.83 mg/L mean, measured concentration included lethargy, partial loss of equilibrium and rapid respiration. Sublethal effects observed at the end of the 96 hours in the 7.08 mg/L mean, measured concentration included the same effects observed at 1.83 mg/L as well as erratic swimming.

The LC50 values, based on mean, measured concentrations and mortality, were:
96-hour LC50 = 4.0 mg/L (95% fiducial limits of 2.0 to 7.7 mg/L).
72-hour LC50 = 9.0 mg/L (95% fiducial limits of 4.1 to 13.3 mg/L).
48-hour LC50 = 19.0 mg/L (95% fiducial limits of 11.3 to 34.8 mg/L).
24-hour LC50 = 68.9 mg/L (95% fiducial limits of 41.6 to 124.5 mg/L).

The highest mean, measured concentration causing no mortality at test end was 0.6 mg/L.

The lowest mean, measured concentration causing 100% mortality at test end was 28.7 mg/L.

Reliability : (1) valid without restriction
Flag : Critical study for SIDS endpoint
22.03.2006 (38)

Type :
Species : other: fish
Exposure period : 96 hour(s)
Unit : mg/l
LC50 : .7
Method : other: ECOSAR
Year : 2005
GLP : no
Test substance : other TS: 1,3-DCB

Method : LogKow = 2.84 (KOWWIN)

Modeled as a vinyl/allyl halide.
Reliability : (2) valid with restrictions
Estimated value based on accepted model.
19.12.2005 (42)

Type :
Species : other: fish
Exposure period : 96 hour(s)
Unit : mg/l
LC50 : 8.4
Method : other: ECOSAR
Year : 2005
GLP : no
Test substance : other TS: 3-chloro-2-buten-1-ol

Method : LogKow: 1.12 (KOWWIN)

Modeled as a vinyl/allyl halide and as a vinyl/allyl alcohol.
Result : 96-hour LC50 (vinyl/allyl halide) = 8.4 mg/L
96-hour LC50 (vinyl/allyl alcohol) = 0.5 mg/L
Reliability : (2) valid with restrictions
Estimated value based on accepted model.
19.12.2005 (42)

4.2 ACUTE TOXICITY TO AQUATIC INVERTEBRATES

Type : static
Species : Daphnia magna (Crustacea)
Exposure period : 48 hour(s)
Unit : mg/l
EC50 : .32
Analytical monitoring : yes
Method : OECD Guide-line 202
Year : 2005
GLP : yes
Test substance : other TS: 1,3-DCB, purity 95.7%

Method : The objective of this study was to assess the acute toxicity of 1-3-dichloro-2-butene (1,3-DCB) to unfed Daphnia magna neonates, less than 24 hours old at test start, during an unaerated, static, 48-hour test.

Test substance solutions were prepared by dilution from a stock solution of 1,3-DCB in well water. A 100 mg/L stock solution was prepared by adding approximately 0.2 grams of test material to a 2-L glass beaker, bringing it to volume with well water, and sonicating for approximately 40 minutes. Test solutions for the study were prepared by adding the appropriate volume of stock solution to the appropriate volume of well water (final volume of 1 L) and stirring for approximately 20 minutes. A 100 mg/L stock (and test) solution was prepared in a similar manner for the verification study and sonicated for 30 minutes with no subsequent stirring.

Five nominal concentrations (6.3, 12.5, 25, 50, 100 mg/L) and a dilution water control were used in this study. Nominal concentrations of 1,3-DCB were not adjusted for 95.7% purity during preparation.

Wheaton bottles (approximately 0.155 L) containing approximately 0.155 L of test solution (approximately 12-cm test solution depth) were used as test

chambers. Two replicate test chambers were used per test concentration with 10 daphnids in each chamber (20 daphnids per concentration). The test chambers were completely filled with test solution and capped during the test (i.e., no headspace). An additional verification study was conducted in a similar manner for 24 hours using a single test chamber containing 10 daphnids at a nominal test concentration of 100 mg/L.

Addition of daphnids to test solutions was initiated about 57 minutes after mixing of the test solutions was completed in the definitive study and approximately 31 minutes after sonication was completed in the verification study. Observations of test organisms were made daily.

A recirculating waterbath was used to maintain mean temperature in the test chambers during the 48-hour test In addition, a continuously-recording thermometer was used to check for temperature variation in the waterbath. A photoperiod of 16 hours light and 8 hours darkness was employed. The verification study was conducted in a waterbath under the same lighting regime although no measurements of light intensity were made during the verification study.

Dissolved oxygen concentration, pH, and temperature were measured in the dilution water control and test substance concentrations. Measurements were taken at test start from test solutions prior to allocation to the test chambers and at test end or at total immobility in a test concentration from either the two replicate test chambers (definitive study) or the single test chamber (verification study). Total alkalinity, EDTA hardness, and conductivity of the dilution water control and highest test substance concentration were measured only at the beginning of the 48-hour definitive test from the test solutions prior to allocation to the test chambers.

Test solution concentration were analyzed via high performance liquid chromatography with ultraviolet absorbance detection (HPLC/UV).

The 24- and 48-hour EC50 values were calculated by the binomial and moving average angle methods, respectively, based on nominal and mean, measured concentrations of 1,3-DCB and immobility. The highest mean, measured concentration causing no immobility at test end and the lowest mean, measured concentration causing 100% immobility at test end were assessed by visual observation.

Remark : Concentrations of 3C2B were not measured in the study.

Result : Mean, measured concentrations ranged from 1 to 3% of the nominal concentrations adjusted for 95.7% purity by analysis. These recoveries are in agreement with theoretical calculations based on the observed volatilization and hydrolysis of the test substance.

Dilution water quality was acceptable based on OECD and ASTM dilution water criteria. All chemical and physical parameters for the definitive test were within expected ranges. Total alkalinity, EDTA hardness, and conductivity of the dilution water control and highest test substance concentration at test start ranged from 49 mg/L as CaCO3, 121 to 123 mg/L as CaCO3, and 260 mmhos/cm, respectively. During the definitive test and the 24-hour verification study, dissolved oxygen concentrations ranged from 7.2 to 8.3 mg/L, pH ranged from 7.1 to 7.7, and mean temperature was 20.1°C with a range of 19.9 to 20.4°C.

Nominal Concentration	Mean Measured Concentration	% Recovery	24-Hour Immobility	48-Hour Immobility

(in mg/L)	(in mg/L)			
0	0		0/20	0/20
6.3	0.2	80	0/20	0/20
12.5	0.2	91	0/20	1/20
25	0.4	96	20/20	20/20
50	0.7	97	20/20	20/20
100	0.7	98	20/20	20/20

No sublethal effects were seen in the dilution water control or test substance solutions.

The 24-hour and 48-hour EC50 values, based on nominal test concentrations and immobility, were 17.7 and 16.7 mg/L, respectively. The 24-hour EC50, based on mean, measured concentrations of 1,3-DCB and immobility, was 0.28 mg/L.

The 48-hour EC50, based on mean, measured concentrations of 1,3-DCB and immobility, was 0.32 mg/L with 95% confidence intervals of 0.28 to 0.35 mg/L.

The highest mean, measured concentration causing no immobility at test end was 0.2 mg/L.

The lowest mean, measured concentration causing 100% immobility at test end was 0.4 mg/L.

Reliability : (4) not assignable
Inadequate assessment of hydrolysis products

Flag : Critical study for SIDS endpoint

22.03.2006 (37)

Type : static
Species : Daphnia magna (Crustacea)
Exposure period : 48 hour(s)
Unit : mg/l
EC50 : 11
Analytical monitoring : yes
Method :
Year : 2005
GLP : no
Test substance : other TS: 3-chloro-2-buten-1-ol, purity 98.5%

Method : The acute toxicity of 3-chloro-2-buten-1-ol (3C2B) to the water flea, Daphnia magna (less than 24 hours old) was determined in an unaerated, 48-hour, static test.
The study was conducted with five concentrations of 3C2B (1.0, 3.0, 10, 30, 100 mg/L) and a dilution water control.

Test substance solutions were prepared by dilution from a stock solution of 3C2B in well water. The stock solution (100 mg/L) was prepared by adding approximately 100 mg of 3C2B to 1 L of well water in a 1-L glass beaker and stirring for approximately 5 minutes. Test solutions were prepared by adding the appropriate volume of the stock solution to well water in 1 L glass beakers and stirring for approximately 11 minutes.

Based on visual observations, the dilution water control and the 1.0, 3.0, 10, 30, and 100 mg/L nominal 3C2B test concentrations were clear and colorless with no visible precipitate at test start.

Pyrex® beakers (250-mL) containing 200 mL of test solution

(approximately 6.5-cm test solution depth) were used as test chambers. One replicate test chamber was used per test concentration with 10 daphnids in each chamber. The test chambers were covered with a glass plate during the test.

Daphnia magna neonates were not fed during the test. Addition of daphnids to test solutions was initiated after mixing of the test solutions was completed. Immobility and behavioral observations were made daily.

A recirculating waterbath was used to maintain mean temperature in the test chambers during the 48-hour test. A photoperiod of 16 hours light and 8 hours darkness was employed.

Dissolved oxygen concentration, pH, and temperature were measured in all replicates of the dilution water control and test substance concentrations. These measurements were taken before daphnids were added at test start and at test end.

Test solution concentrations were analyzed via high performance liquid chromatography with ultraviolet absorbance detection (HPLC/UV).

Result : Mean, measured concentrations of 3C2B ranged from 80 to 98% of the targeted nominal test concentrations adjusted for test substance purity of 98.5%.

All water quality parameters were within acceptable ranges during the test. Dissolved oxygen concentrations ranged from 8.0 to 8.4 mg/L, pH ranged from 6.4 to 7.8, and mean temperature was 20.3°C with a range of 20.0 to 20.6°C.

Nominal Concentration (in mg/L)	Measured Concentration (in mg/L)	24-Hour Immobility	48-Hour Immobility	Recovery (%)
0	0	0/10	0/10	
1	0.787	0/10	0/10	79
3	2.68	0/10	0/10	89
10	9.49	0/10	3/10	95
30	28.8	0/10	10/10	96
100	96.8	5/10	10/10	97

No sublethal effects were seen in the dilution water control test organisms. Lethargy was observed in 4 of the remaining 7 daphnids in the 10 mg/L nominal 3C2B test concentration at the end of the study.

The highest nominal concentration causing no immobility at test end was 3.0 mg/L.

The lowest nominal concentration causing 100% immobility at test end was 30 mg/L.

Nominal and mean measured 3C2B concentrations and immobility were used to calculate EC50 values by the moving average angle method.

The 48-hour EC50 for 3C2B, based on nominal concentrations and immobility, was 11.7 mg/L with 95% confidence limits of 6.6 to 18 mg/L. The 48-hour EC50, based on mean measured concentrations and immobility, was 11 mg/L with 95% confidence limits of 6.1 to 17.5 mg/L.

Reliability : (1) valid without restriction
Flag : Critical study for SIDS endpoint
19.12.2005 (39)

Type	:	
Species	:	other: daphnid
Exposure period	:	48 hour(s)
Unit	:	mg/l
EC50	:	9.2
Method	:	other: ECOSAR
Year	:	2005
GLP	:	no
Test substance	:	other TS: 1,3-DCB
Method	:	LogKow = 2.84 (KOWWIN) Modeled as a vinyl/allyl halide.
Reliability	:	(2) valid with restrictions Estimated value based on accepted model.

19.12.2005 (42)

Type	:	
Species	:	other: daphnid
Exposure period	:	48 hour(s)
Unit	:	mg/l
EC50	:	980.4
Method	:	other: ECOSAR
Year	:	2005
GLP	:	no
Test substance	:	other TS: 3-chloro-2-buten-1-ol
Method	:	LogKow: 1.12 (KOWWIN) Modeled as a vinyl/allyl halide.
Reliability	:	(2) valid with restrictions Estimated value based on accepted model.

19.12.2005 (42)

4.3 TOXICITY TO AQUATIC PLANTS E.G. ALGAE

Species	:	other algae: diatoms
Endpoint	:	other: 50% reduction concentration bioassay
Exposure period	:	7 day(s)
Unit	:	
EC50	:	6.6
Method	:	
Year	:	
GLP	:	no
Test substance	:	other TS: 1,3-DCB, purity 100%
Method	:	Test was performed on diatom in soft dilution water using batch diatom tests. The tests were conducted in sterile 125 mL Erlenmeyer flasks. In each of the specific concentrations of sample in dilution water, there was a total of 50 mLs of liquid. This provided a relatively large surface to volume ratio, and thus allowed full exchange or gases in the air. Temperature: 18 +/- 1 deg C Closed system
Remark	:	units = ppm
Reliability	:	(4) not assignable

01.04.2004 (26)

Species	:	other algae: Pseudokirchneriella subcapitata
Endpoint	:	biomass
Exposure period	:	72 hour(s)
Unit	:	mg/l
NOEC	:	9
LOEC	:	13
EC50	:	650
Limit test	:	
Analytical monitoring	:	no
Method	:	
Year	:	2005
GLP	:	no
Test substance	:	other TS: 3-chloro-2-buten-ol, purity 98.5%

Method : Test substance solutions were prepared by dilution from a stock solution of 3C2B in filter-sterilized AAP nutrient medium. The stock solution with a nominal concentration of 100 mg/L was prepared by adding approximately 20 mg of 3C2B to 200 mL of filter-sterilized AAP nutrient medium and stirring for approximately 5 minutes. Test solutions were prepared by adding the appropriate volume of the stock solution to filter-sterilized AAP nutrient medium to make nominal concentrations of 1, 3, 10, 30, and 100 mg/L and stirring each for approximately 5 minutes. Aliquots of the filter-sterilized AAP nutrient medium were used for the blank control solution. Test substance solutions were clear and colorless with no visible precipitate.

Test chambers were sterilized 250-mL Erlenmeyer flasks containing 50 mL of test solution. Flasks were fitted with sterilized foam stoppers to permit gas exchange. The blank control and each test concentration were each tested as 2 replicates.

An approximate 0.2-mL aliquot of algal inoculum from a logarithmically growing stock culture was aseptically transferred to each flask to achieve the desired nominal concentration of approximately 10,000 P. subcapitata cells/mL at test initiation. P. subcapitata growth was determined by visually counting the number of cells taken from an approximate 0.2-mL sample from each flask at approximately 72 hours after test initiation. The counts were conducted using a hemacytometer and a compound microscope. An aliquot of each sample was loaded into the 2 grid areas of the hemacytometer and 8 squares from each grid area (16 total squares) were selected for counting.

All healthy cells located in the 16 squares were counted and recorded. The total number of cells counted was multiplied by 10,000 to determine the number of cells per milliliter. Cells outside these 16 squares were not counted nor included in the total number. Counts were made at approximately the same time as the day 0 inoculation.

Test flasks were maintained at 24 ± 2°C in an environmental chamber on a shaker table in a non-systematic design with a shaking speed of 103 rpm. Flasks were repositioned each working day. The pH measurements were taken at test start in an aliquot taken from the mixing vessel and at 72 hours in an aliquot taken after pooling all replicates of each control and test concentration. Air temperature in the environmental chamber was recorded with a continuous temperature recorder. The flasks were illuminated continuously using cool-white fluorescent tubes.

The 72-hour mean healthy cell count for each test concentration was expressed relative to the blank control. All calculations were based on the nominal test substance concentrations.

Levene's test was used to compare the variances of the control and treatment groups to determine whether an equal- or unequal-variance t-test was used.

The percent growth inhibition, % I, was calculated.

Result : All environmental parameters were within acceptable limits during the exposure. Test solution pH measurements ranged from 7.32 to 7.57 at test start and from 7.21 to 7.48 at 72 hours. The temperature from the digital readout of the temperature chart recorder ranged from 23.7 to 24.0ºC for the duration of the study. The light intensity for the areas used in the chamber ranged from 7440 to 7860 lux. The mean light intensity was 7692 lux.

Nominal Concentration (in mg/L)	0-Hour Healthy Cell Count (cells/mL)	72-Hour Healthy Cell Count (cells/mL)
0: Replicate 1	10,000	2,550,000
0: Replicate 2	10,000	3,130,000
1: Replicate 1	10,000	2,460,000
1: Replicate 2	10,000	3,320,000
3: Replicate 1	10,000	2,930,000
3: Replicate 2	10,000	2,590,000
10: Replicate 1	10,000	2,590,000
10: Replicate 2	10,000	2,600,000
30: Replicate 1	10,000	2,340,000
30: Replicate 2	10,000	2,610,000
100: Replicate 1	10,000	2,110,000
100: Replicate 2	10,000	2,220,000

Exposure of algae to nominal concentrations of 1, 3, 10, 30, and 100 mg/L 3C2B in nutrient medium resulted in -2, 3, 9, 13, and 24% inhibition based on healthy cell count (cell density), respectively, at the end of 72 hours. The effect was expressed as percent inhibition in growth based on healthy cell count relative to the blank control for the 72-hour (3-day) interval of the test. Nominal concentrations of 3C2B were used for the calculation of the EC50 value, i.e. the "effective concentration" producing a 50% inhibition of growth relative to the control. Similarly, exposure to nominal concentrations of 1, 3, 10, 30, and 100 mg/L resulted in 0, 0, 2, 2, and 5% inhibition of growth rate, respectively, at the end of 72 hours.

72 h EbC50 = 650 mg/L (calculated by probit method)

72 h EbC10 = 14 mg/L
72 h LOEC = 13 mg/L
72 h NOEC = 9 mg/L

The 72 h EbC50 = 650 mg/L and the 72h ErC50 > 650 mg/L.

Reliability : (2) valid with restrictions
Nominal concentrations only were used.

Flag : Critical study for SIDS endpoint

27.04.2006 (40) (107)

Species : other algae: green algae
Endpoint :
Exposure period : 96 hour(s)

Unit	:	mg/l
EC50	:	5.7
Method	:	other: ECOSAR
Year	:	2005
GLP	:	no
Test substance	:	other TS: 1,3-DCB
Method	:	LogKow = 2.84 (KOWWIN) Modeled as a vinyl/allyl halide.
Reliability	:	(2) valid with restrictions Estimated value based on accepted model.
19.12.2005		(42)
Species	:	other algae: green algae
Endpoint	:	
Exposure period	:	96 hour(s)
Unit	:	mg/l
EC50	:	104.6
Method	:	other: ECOSAR
Year	:	2005
GLP	:	no
Test substance	:	other TS: 3-chloro-2-buten-1-ol
Method	:	LogKow: 1.12 (KOWWIN) Modeled as a vinyl/allyl halide.
Reliability	:	(2) valid with restrictions Estimated value based on accepted model.
19.12.2005		(42)

4.4 TOXICITY TO MICROORGANISMS E.G. BACTERIA

Type	:	aquatic
Species	:	activated sludge
Exposure period	:	3 hour(s)
Unit	:	mg/l
EC50	:	152
Analytical monitoring	:	no
Method	:	ISO 8192 "Test for inhibition of oxygen consumption by activated sludge"
Year	:	
GLP	:	yes
Test substance	:	other TS: 1,3-DCB, purity 99.1%
Method	:	A given quantity of activated sludge was mixed with a synthetic nutrient solution and the respiration rate was measured. The respiration rate was compared with those measured in test preparations with different concentrations of the test material. The sensitivity of the activated sludge that was employed was tested with 3,5-dichlorophenol as a reference material. Test concentrations were 56, 100, 180, 320, and 560 mg/L. The autoxidation was 10,000 mg/L. The application method was via direct weighing. The concentration of the inoculation material was 6 g/L TS.
Result	:	Concentration (mg/L) Respiration Rate (mg/Lh) % Inhibition

56	19.2	16.5
100	13.5	41.3
180	10.0	56.5
320	6.0	73.9
560	3.6	84.3

The test concentrations were the amounts employed in preparing the test formulations and were not determined analytically.

EC10 = 32.5 mg/L
EC25 = 67.4 mg/L
EC50 = 152 mg/L
EC75 = 341 mg/L
EC90 = 707 mg/L
EC99 = 2480 mg/L

Reliability : (2) valid with restrictions
Flag : Critical study for SIDS endpoint
22.03.2006 (11)

5.0 TOXICOKINETICS, METABOLISM AND DISTRIBUTION

Method	:	
Year	:	
GLP	:	
Test substance	:	as prescribed by 1.1 - 1.4

Remark : Both 1,3-DCB and its chemical analogue DCP (1,3-dichloro-1-propene) contain chlorine in the allylic position, a feature that should allow these structural analogs to be metabolized similarly in vivo.

The accompanying figure (Figure 1) shows the proposed metabolic pathway for DCP that is based on in vivo administration and identification of excreted metabolites. The metabolism of DCP is analogous to allyl chloride (De Rooij et al., 1996) for which the primary route is expected to be direct conjugation of the allylic position with glutathione and displacement of the chlorine atom. Following in vivo administration of allyl chloride or DCP, a significant fraction of radioactive label is excreted in urine as glutathione derived mercapturates (De Rooij et al., 1996; Bartels et al., 2004). 1,3-DCB is also likely to be metabolized by this pathway (see Figure 2). However, it should be noted that the extent to which the chlorine in the C3 vinylic position of 1,3-DCB may alter GSH conjugation is not known because its electron withdrawing effect on the pi-electrons of the C=C bond. The next most important pathway predicted for the biotransformation of 1,3-DCB is oxidative dechlorination at the allylic C1 position. This reaction occurs with allyl chloride and DCP. For DCP, oxidative dechlorination eventually leads to exhalation of CO2 and additional mercapturates in urine (De Rooij et al., 1996). Epoxidation of the double bond is a minor pathway for DCP since it has only been shown to be present at very high doses administered to mice by intraperitoneal injection (Schneider, Quistad, and Casida, 1998; Bartels et al., 2000). While electronic factors may favor epoxidation of 1,3-DCB because of the presence of the vinylic chlorine at C3 (Bartels et al., 2004), steric factors imposed by the presence of the C4 methyl group may mitigate this effect. Since the epoxidation reaction is not predicted to be an important route of metabolism, this pathway is not shown in Figure 2. Another reaction predicted for 1,3-DCB is methyl hydroxylation which is not possible with DCP due to the lack of the terminal C4 group. In summary, the biotransformation of 1,3-DCB is predicted to be qualitatively similar to DCP.

Attached document : figures1and2.doc
03.01.2006 (6) (16) (99)

5.1.1 ACUTE ORAL TOXICITY

Type	:	LD50
Value	:	1368 mg/kg bw
Species	:	rat
Strain	:	other: Crl:CD(R)
Sex	:	male
Number of animals	:	50
Vehicle	:	
Doses	:	700, 1200, 1600, 1800, 2000 mg/kg
Method	:	other
Year	:	
GLP	:	no
Test substance	:	other TS: 1,3-DCB, purity 99.5% (mixture of cis and trans)

Method : No specific test guideline was reported; however, a scientifically defensible approach was used to conduct the study.

The test material, as a solution in corn oil, was administered by intragastric intubation in single doses to 5 groups of 10 unfasted young adult male rats. The surviving rats were weighed and observed during a 14-day recovery period and then sacrificed. The LD50 value was calculated from the mortality data using the method of Finney, 1971. Necropsies were not performed.

Result : Mortality ratios of 0/10, 4/10, 6/10, 8/10, and 10/10 were observed for the 700, 1200, 1600, 1800, and 2000 mg/kg groups, respectively.

Stained face, stained and wet perineal area, diarrhea, weakness, and weight loss were observed at all levels. Humped-posture and alopecia were observed at 1600 mg/kg. Stained and wet underside was noted at 2000 mg/kg. Salivation occurred in the 700 and 2000 mg/kg groups. Chromodacryorrhea was observed at all levels except 1800 mg/kg. Lethargy was noted at 1200, 1600, and 1800 mg/kg. Deaths occurred up to 12 days after dosing.

The 95% confidence limits on the LD50 value were 1114 - 1543 mg/kg.

Reliability : (1) valid without restriction
Comparable to guideline study.

Flag : Critical study for SIDS endpoint

11.01.2006 (30) (45)

Type : LD50
Value : 300 - 414 mg/kg bw
Species : rat
Strain : Wistar
Sex : male/female
Number of animals :
Vehicle : other: 1,2-propanediol
Doses : 90, 200, 448, 1000 mg/kg
Method : Directive 84/449/EEC, B.1 "Acute toxicity (oral)"
Year :
GLP : yes
Test substance : other TS: E/Z-1,3-DCB, purity 99.1%

Method : From about 16 hours before to 4 hours after administration, food was withheld. At all other times during the test, food was available ad libitum. Water was available ad libitum throughout the test.

The test material was dissolved in 1,2-propanediol and administered intragastric intubation to five male and five female rats per group. Clinical observations and body weights were recorded periodically throughout the test period. All animals that died or were sacrificed at the end of the experiment were evaluated by pathological-anatomic examination.

The calcuation of the LD50 was performed according to Spearman-Karer, the algorithm was taken from Sachs, L (1984) (Applied Statistics), 6th ed., p. 178.

Result : The LD50 for male rats = 414 mg/kg. The LD50 for female rats = 300 mg/kg.

In male rats, mortality ratios of 0/5, 0/5, 3/5, and 5/5 were observed for the 90, 200, 448, and 1000 mg/kg groups, respectively. In female rats, mortality ratios of 0/5, 0/5, 5/5, and 5/5 were observed for the 90, 200, 448,

and 1000 mg/kg groups, respectively. Deaths occurred between 1 hour post dose and 1 day post dose.

The symptoms after dosing with 200 to 1000 mg/kg were ruffled fur and sedation. At 1000 mg/kg, all animals showed salivation. At the dose of 90 mg/kg, there were no symptoms in either male or female rats.

Three rats in the 200 mg/kg group and 1 male in the 448 mg/kg group had a small weight loss during the first week.

The pathology of animals that died during the experiment showed very congested blood vessels in the stomach as well as highly reddened mucous membranes. The small intestine was also highly reddened.

After the 1000 mg/kg dose, the stomach was filled with a clear, flocculated fluid, and after the 448 mg/kg dose it was filled with a thin slurry of food.

The pathology of the animals at the end of the experiment showed that the liver of both males in the 448 mg/kg group had grown together with the stomach and peritoneum. All of the other animals were normal. No pathologic changes were observed in reproductive organs.

Reliability : (1) valid without restriction
Flag : Critical study for SIDS endpoint
01.04.2004 (10)

Type : LD50
Value : 110 - 250 mg/kg bw
Species : rat
Strain :
Sex :
Number of animals :
Vehicle :
Doses :
Method : OECD Guide-line 401 "Acute Oral Toxicity"
Year : 1986
GLP : yes
Test substance : other TS: 1,3-DCP

Result : LD50: 110-170 mg/kg (male)
LD50: 110-250 mg/kg (female)

Symptoms: hunched posture, piloerection, decreased respiratory rate, lethargy, ptosis, diarrhea, diuresis, ataxia, tip-toe gait, red/brown staining around the snout, tremors, emaciation and pallor of the extremities, increased salivation/lacrimation, body weight loss. By day 11, all surviving animals had recovered.

At necropsy, hemorrhagic lungs, mottled/dark liver, patchy pallor of the liver, dark kidneys, hemorrhagic stomach and hemoorhage/congestion of small intestine, injection of blood vessels around stomach and adherence of stomach to abdominal wall and liver were observed in animals who died during the study. In surviving animals, white raised areas scattered over the non-glandualr part of the stomach, and congestion of the lungs were commonly observed.

Test substance : Telone II, purity not reported
Reliability : (1) valid without restriction
GLP guideline study
Flag : Critical study for SIDS endpoint
13.12.2005 (60)

Type	:	
Value	:	
Species	:	rat
Strain	:	
Sex	:	
Number of animals	:	
Vehicle	:	
Doses	:	100, 300 mg/kg
Method	:	
Year	:	
GLP	:	no data
Test substance	:	other TS: 1,3-DCB, purity not reported
Result	:	After 72 hours, rats exposed to "enteral" administration of 0.25 and 0.75 of 1,3-DCB's LD50 and loading with water (2.5% of body weight), showed above normal urinary chloride. The biochemical data as well as histopathological observations indicated renal tubular damage. The necrotic nephrosis is apparently due to the inhibition of renal tubular SH-group containing enzymes.
Reliability	:	(3) invalid Documentation insufficient for assessment

17.10.2005 (89) (94)

5.1.2 ACUTE INHALATION TOXICITY

Type	:	LC50
Value	:	546 ppm
Species	:	rat
Strain	:	other: ChR-CD
Sex	:	male
Number of animals	:	
Vehicle	:	
Doses	:	not specified
Exposure time	:	4 hour(s)
Method	:	other
Year	:	
GLP	:	no
Test substance	:	other TS: 1,3-DCB, purity 92%
Method	:	The test material was metered into a glass U-tube immersed in a silicone oil bath at 120-125ºC. The resulting vapor was carried by a stream of air into an 18-L glass chamber containing 10 rats (initial body weight 250-286 g). Each exposure lasted 4 hours. The chamber atmospheric concentration was analyzed 8-10 times per exposure via gas chromotagraphy. Body weights of the surviving rats were measured daily for 14 days. For calculation of the LC50, the Litchfield and Wilcoxon method was used on the 14-day mortality data.
Result	:	LC50 = 546 ppm (2840 mg/m3). The 95% confidence limits for the LC50 value were 506-590 ppm (2639-3068 mg/m3). Several DCB isomers (3,4-DCB, 1,3-DCB, and 1,4-DCB) were tested. All deaths occurred post-exposure. Animals died between one day and 14 days post-exposure (no specific data presented for the individual isomers). At lethal levels, the isomers caused irregular breathing, lacrimation,

salivation, and hyperemia of the ears during exposure (no specific data presented on individual isomers). Initial body weight loss by rats caused by all isomers was approximately 10%. Only 4 of 21 survivors exposed to 1,3-DCB regained their pre-exposure weight loss within 14 days.

Histologic examination of tissues revealed lesions and hemorrhage of lungs, tracheitis, and cell degeneration in liver, spleen, thymus, and lymph nodes. Tubular degeneration of the kidneys was also noted.

Reliability : (2) valid with restrictions
Individual test concentrations not specified.

Flag : Critical study for SIDS endpoint

19.12.2005 (64) (67)

Type : LC50
Value : 756 ppm
Species : rat
Strain :
Sex : male/female
Number of animals :
Vehicle :
Doses : 576-1060 ppm (3000-5500 mg/m3)
Exposure time : 4 hour(s)
Method :
Year :
GLP : no
Test substance : other TS: 1,3-DCB, purity not reported

Method : Albino rats of both sexes (weighing 170-240 g) were tested in a 100-L chamber (2 rats in each chamber) for 4 hours. The rats were subjected to the inhalation effect of the test substance in concentrations ranging from 3 - 5.5 mg/L with intervals of 0.5 mg/L. Each concentration was tested on 8 animals. The concentrations tested were verified by the nephelometric technique proposed by L. P. Senderikhinya.

The results of the experiment were processed by the method of least squares.

Result : The picture of intoxication was initially characterized by an irritating and finally a suppressive effect.

The 4-hour LC50 with confidence limits in rats was found to be 3.93 (4.225-3.65) mg/L. When converted to ppm, the LC50 = 756 ppm (3930 mg/m3).

The macroscopic study of the internal organs of the sacrificed animals revealed plethora and hemorrhaging in the parenchymatous organs. Upon microscopic examination of the liver of the experimental animals, fatty dystrophy was found as well as dilation of the vessels and symptoms of hemostasis. Degenerative changes were noted in the other parenchymatous organs as well. The study was conducted with both rats and mice. The report did not specify whether the pathology findings noted above occurred in both species or in a specific species.

Reliability : (2) valid with restrictions
Limited methological information available.

19.12.2005 (4)

Type : LC50
Value : 586 - 666 ppm
Species : rat
Strain :
Sex :

Number of animals	:	
Vehicle	:	
Doses	:	
Exposure time	:	4 hour(s)
Method	:	OECD Guide-line 403 "Acute Inhalation Toxicity"
Year	:	1987
GLP	:	yes
Test substance	:	other TS: 1,3-DCP
Result	:	LC50 = 2.7-3.07 mg/L LC50 = 586-660 ppm (2700-3070 mg/m3) Symptoms: partial closing of the eyes, lacrymation, reduced respiratory rate, irregular respiratory movements and wet fur around the mouth, hunched posture, restless behavior and reddening of the ears, tail and feet. Also decreased body weight gain was observed. By day 6 most symptoms had disappeared. At necropsy, the animals that died showed brown staining of the fur, fecal material staining the urogenital region and lung congestion. In surviving rats, pale and swollen lungs were observed, with small gray depressed or red areas.
Test substance	:	Telone II, purity not reported
Reliability	:	(1) valid without restriction GLP guideline study
Flag	:	Critical study for SIDS endpoint

19.12.2005 (21)

Type	:	
Value	:	
Species	:	rat
Strain	:	
Sex	:	
Number of animals	:	
Vehicle	:	
Doses	:	0, 0.5, 5 mg/L (0, 96, 960 ppm)
Exposure time	:	4 hour(s)
Method	:	other
Year	:	
GLP	:	no
Test substance	:	other TS: 1,3-DCB, purity not reported
Method	:	Six white rats/group were exposed to 1,3-DCB in stationary chambers with a capacity of 760 L. At the end of the 4-hour experiment, the animals were sacrificed and dissected. Their adrenal glands were separated and fixed in neutral formalin, in Orth's and Wiesel's fluids. After preliminary treatment, the adrenal glands were immersed in paraffin and a series of sections were cut. The preparations were stained with hematoxylin-eosin, hematoxylin green after Heidenhain, picrofuchsin after Van Gieson and Wiesel. Some of the material was processed for lipids with scarlet red staining of the nuclei with Erlich's hematoxylin. Both kidneys were fixed in 10% formalin solution and in Ort's liquid; pieces were cast with paraffin. Sections were stained with hematoxylin-eosin, iron hematoxylin according to Heidenhain and picrofusion according to Van Gieson.

Result	:	The concentration of 5 mg/L caused damage mostly to the epithelium of the proximal compartments of the nephron, disruption of permeability of the vessels, and hemolysis of blood. In addition, 5 mg/L caused clear destructive changes in the tissues of the cortex and myeloid substance of the adrenal gland. Exposure to 0.5 mg/L caused pronounced spaces in the renal corpuscles and dystrophic changes in the epithelium of the tubules. Partial morphological changes in the adrenal cortex were observed, but no significant changes in the myeloid substance.
Reliability	:	(3) invalid Focus of study was not acute LC50 determination. Documentation insufficient for assessment.

19.12.2005 (82) (91)

Type	:	
Value	:	
Species	:	rat
Strain	:	
Sex	:	
Number of animals	:	
Vehicle	:	
Doses	:	1100 mg/m3
Exposure time	:	1 minute(s)
Method	:	
Year	:	
GLP	:	no data
Test substance	:	other TS: 1,3-DCB, purity not reported
Result	:	1,3-DCB was neurotoxic and affected the parenchymatous organs, and greatly affected the liver parenchyma, digestive tract organs, and to a lesser degree the kidneys. 1,3-DCB also had a polytropic action.
Reliability	:	(3) invalid Focus of study was not acute LC50 determination. Documentation insufficient for assessment.

21.10.2005 (95)

Type	:	
Value	:	
Species	:	rat
Strain	:	
Sex	:	
Number of animals	:	
Vehicle	:	
Doses	:	
Exposure time	:	
Method	:	
Year	:	
GLP	:	
Test substance	:	other TS: 1,3-DCB, purity not reported
Result	:	Dystrophic and necrobiotic changes were noted in liver parenchymatous cells of rats which inhaled 1,3-DCB. Hemodynamic changes including extravasation, hyperemia and plasmorrhagia, disturbances in glycogen and fat metabolism, and alkaline phosphatase activity also occurred.
Reliability	:	(3) invalid Focus of study was not acute LC50 determination. Documentation insufficient for assessment.

21.10.2005 (109)

Type	:	LC50
Value	:	846 ppm
Species	:	mouse
Strain	:	
Sex	:	male/female
Number of animals	:	
Vehicle	:	
Doses	:	576-1050 ppm
Exposure time	:	2 hour(s)
Method	:	
Year	:	
GLP	:	no
Test substance	:	other TS: 1,3-DCB, purity not reported
Method	:	Albino mice of both sexes (weighing 18-25 g) were tested in 20-L glass bottles (2 mice in each bottle) for 2 hours. The mice were subjected to the inhalation effect of the test substance in concentrations ranging from 3 - 5.5 mg/L with intervals of 0.5 mg/L. Each concentration was tested on 8 animals. The concentrations tested were verified by the nephelometric technique proposed by L. P. Senderikhinya. The results of the experiment were processed by the method of least squares.
Result	:	The picture of intoxication was initially characterized by an irritating and finally a suppressive effect. The 2-hour LC50 with confidence limits in mice was found to be 4.4 (4.8508-3.9422) mg/L. When converted to ppm, the LC50 = 846 ppm. The 2-hour EC50 (narcosis) was 10.60 (11.448-9.81) mg/L. When converted to ppm, the narcosis EC50 was 2040 ppm. The macroscopic study of the internal organs of the sacrificed animals revealed plethora and hemorrhaging in the parenchymatous organs. Upon microscopic examination of the liver of the experimental animals, fatty dystrophy was found as well as dilation of the vessels and symptoms of hemostasis. Degenerative changes were noted in the other parenchymatous organs as well. The study was conducted with both rats and mice. The report did not specify whether the pathology findings noted above occurred in both species or in a specific species.
Reliability	:	(2) valid with restrictions Limited methodology information was available.
Flag	:	Critical study for SIDS endpoint

19.12.2005 (4)

Type	:	
Value	:	
Species	:	mouse
Strain	:	
Sex	:	
Number of animals	:	
Vehicle	:	
Doses	:	3, 5, 10 mg/L (600, 1000, 2000 ppm)
Exposure time	:	
Method	:	
Year	:	
GLP	:	no
Test substance	:	other TS: 1,3-DCB, purity not reported

Result	:	Minimum concentration causing lateral position = 5 mg/L (1000 ppm) Minimum concentration causing narcosis = 10 mg/L (2000 ppm) Minimum concentration causing death = 3 mg/L (600 ppm)
Reliability	:	(3) invalid Focus of study was not acute LC50 determination. Documentation insufficient for assessment.

19.12.2005 (110)

Type	:	other: threshold concentration for respiratory rate
Value	:	150 ppm
Species	:	rabbit
Strain	:	
Sex	:	
Number of animals	:	
Vehicle	:	
Doses	:	
Exposure time	:	40 minute(s)
Method	:	
Year	:	
GLP	:	no
Test substance	:	other TS: 1,3-DCB, purity not reported

Result	:	The threshold concentration which altered the respiration rate was within the limits of 0.8 and 1.6 mg/L - usually 0.8 mg/L. When converted to ppm, 0.8 mg/L = 150 ppm.
Reliability	:	(2) valid with restrictions Limited methodology information was available.

19.12.2005 (4)

Type	:	
Value	:	
Species	:	rabbit
Strain	:	
Sex	:	
Number of animals	:	
Vehicle	:	
Doses	:	5, 10, 15 mg/L (1000, 2000, 3000 ppm)
Exposure time	:	
Method	:	
Year	:	
GLP	:	no
Test substance	:	other TS: 1,3-DCB, purity not reported

Result	:	Minimum concentration causing lateral position = 10 mg/L (2000 ppm) Minimum concentration causing narcosis = 15 mg/L (3000 ppm) Minimum concentration causing death = 5 mg/L (1000 ppm)
Reliability	:	(3) invalid Focus of study was not acute LC50 determination. Documentation insufficient for assessment.

19.12.2005 (110)

Type	:	
Value	:	
Species	:	rabbit
Strain	:	
Sex	:	
Number of animals	:	
Vehicle	:	
Doses	:	

Exposure time : 3.5 minute(s)
Method : other
Year :
GLP : no
Test substance : other TS: 1,3-DCB, purity not reported

Method : A rabbit weighing 2100 g was given urethane narcotic (20% urethane g/K intraveneously and subcutaneously). At the same time inhalation was begun by means of a mask from which poured about 7 cc DC.
Result : Blood pressure increased from 58 mm to 78 mm. Respiration became at first superficial and later even deeper than before the test. Respiration and blood pressure became normal after the end of the experiment.

1,3-DCB did not produce momentarily functional changes but its action being of long duration manifested itself several days later as a histological effect.
Reliability : (3) invalid
Focus of study was not acute LC50 determination. Documentation insufficient for assessment.
Inadequate test substance characterization.

26.10.2005 (96)

Type :
Value :
Species : cat
Strain :
Sex :
Number of animals :
Vehicle :
Doses : 5, 10, 15 mg/L (1000, 2000, 3000 ppm)
Exposure time :
Method :
Year :
GLP : no
Test substance : other TS: 1,3-DCB, purity not reported

Result : Minimum concentration causing lateral position = 10 mg/L (2000 ppm)
Minimum concentration causing narcosis = 15 mg/L (3000 ppm)
Minimum concentration causing death = 5 mg/L (1000 ppm)
Reliability : (3) invalid
Focus of study was not acute LC50 determination. Documentation insufficient for assessment.

19.12.2005 (110)

Type :
Value :
Species : cat
Strain :
Sex :
Number of animals : 1
Vehicle :
Doses : 12.27 mg/L (2360 ppm)
Exposure time : 30 minute(s)
Method : other
Year :
GLP : no
Test substance : other TS: 1,3-DCB, purity not reported

Method : 1,3-DCB was heated on a water bath at 35ºC at 741.4 mm Hg. The

temperature of the air in the chamber was 17ºC.

Result : The cat in the chamber had dyspnoea, and thick and stringy saliva. The cat survived the experiment. The cat weighed 1650 g at the time of the experiment and weighed 2250 g 5 months after the experiment.

Reliability : (3) invalid
Focus of study was not acute LC50 determination. Documentation insufficient for assessment.
Inadequate test substance characterization.

19.12.2005 (96)

5.1.3 ACUTE DERMAL TOXICITY

Type : LD50
Value : 800 - 2000 mg/kg bw
Species : rat
Strain :
Sex :
Number of animals :
Vehicle :
Doses :
Method : OECD Guide-line 402 "Acute dermal Toxicity"
Year : 1986
GLP : yes
Test substance : other TS: 1,3-DCP

Result : LD50: 800-1300 mg/kg (male)
LD50: 1300-2000 mg/kg (female)

Symptoms: lethargy, salivation, red/brown staining around mouth, eyes and snout, diarrhea, diuresis, decreased respiratory rate, lacrimation, salivation, ataxia, loss of righting reflex, hunched posture, piloerection.

At necropsy, common abnormalities seen in animals dying during the study were associated with lungs, liver, gastrointentinal tract and subcutaneous tissue at the application site.

In surviving animals, frquently adhesion of the skin to the underlying tissues at the site of application and congested lungs were observed.

Test substance : Telone II, purity not reported
Reliability : (1) valid without restriction
GLP guideline study
Flag : Critical study for SIDS endpoint
13.12.2005 (59)

Type : other: Skin absorption study
Value :
Species : mouse
Strain :
Sex :
Number of animals :
Vehicle :
Doses :
Method :
Year :
GLP : no
Test substance : as prescribed by 1.1 - 1.4

Method : Albino mice (12 treated and 12 control) were tested for the potential of the

test substance to absorb through the skin.

Result : On the second day of the experiment 1/12 experimental mice died, while in the surviving animals, necrosis of the tip of the tail developed with subsequent sloughling off of the necrotic parts.

Reliability : (3) invalid
Documentation insufficient for assessment

17.10.2005 (4)

Type :
Value :
Species : dog
Strain :
Sex :
Number of animals : 2
Vehicle :
Doses :
Method :
Year :
GLP : no
Test substance : other TS: 1,3-DCB, purity not reported

Result : Dogs dermally treated with 1,3-DCB lost 42-45% of their initial body weight and, in addition to local effects, exhibited marked hemodynamic and histological changes in the brain, lungs, liver, kidney, pancreas, and thyroid. In the central nervous system, hemodynamic disorders and weak histopatholgical changes were noted. The histological changes, localized mainly in the cerebral cortex, included: wrinkling of cells, signs of hyperchromatolysis, and swelling of the cells, with indications of vacuolization of the chromatolysis. Ameboid cells were also encountered devoid of appendages. The lungs showed evidence of bronchial pneumonia, manifested in blood-filling and blood effusion. The liver showed signs of hemodynamic changes and parenchymatous dystrophy. The kidneys exhibited weak hemodynamic changes and granularity of the protoplasm of the cells of the convoluted tubules. The pancreas showed foci of blood effusions, and the thyroid gland showed the majoritiy of the follicles devoid of colloid.

Reliability : (3) invalid
Documentation insufficient for assessment

17.10.2005 (83)

5.1.4 ACUTE TOXICITY, OTHER ROUTES

Type :
Value :
Species : rabbit
Strain :
Sex :
Number of animals : 6
Vehicle : other: olive oil or water
Doses :
Route of admin. : s.c.
Exposure time :
Method :
Year :
GLP : no
Test substance : other TS: 1,3-DCB, purity not reported

Result : Rabbit (cc/k) Died in

1	.397	24 hours
2	.15	60 hours
3	.09	survived
4	.09	survived
5	.07	survived
6	.03	survived

Histological effects:
Lungs: In rabbits, a pronounced bronchopneumonia stratum was found.

Liver: In rabbits, which survived, the cells appeared wrinkled, full-bloodedness of them was particularly enhanced.

Reliability : (3) invalid
Documentation insufficient for assessment
Inadequate test substance characterization

26.10.2005 (96)

Type :
Value :
Species : guinea pig
Strain :
Sex :
Number of animals : 6
Vehicle : other: olive oil or water
Doses :
Route of admin. : s.c.
Exposure time :
Method :
Year :
GLP : no
Test substance : other TS: 1,3-DCB, purity not reported

Result :

Guinea pig	(cc/k)	Died after
1	.8	17 hours
2	.638	19 hours
3	.435	19 hours
4	.142	20 hours
5	.0476	5 days
6	.0125	9 days

Animals after the injections became torpid and gradually, as though in a state of coma, perished, usually without convulsions.

Histological effects:
Lungs: In guinea pigs which were given smaller doses, the changes in the lungs spread to alveoli around the bronchi, and the blood vessels exuded. Authors note that these changes were probably due to exhaling of the test substance.

Liver: In guinea pigs, when they were given greater doses, degeneration of parencyhmatosis type, without hyperoemia, took place. With small doses, the results were reversed.

Kidneys: The guinea pigs at the higher doses had a considerable parenchymatosis degeneration.

Reliability : (3) invalid
Documentation insufficient for assessment
Inadequate test substance characterization

26.10.2005 (96)

5.2.1 SKIN IRRITATION

Species	:	
Concentration	:	
Exposure	:	
Exposure time	:	
Number of animals	:	
Vehicle	:	
PDII	:	
Result	:	
Classification	:	
Method	:	In-vitro test
Year	:	
GLP	:	no
Test substance	:	other TS: 1,3-DCB, purity 98.088%

Method : No specific test guideline was reported; however, a scientifically defensible approach was used to conduct the study.

1,3-DCB was evaluated for skin corrosion potential using the In Vitro International CorrositexTM assay. The test model is based on the time required for the test substance to pass through a biobarrier membrane and produce a change in a chemical detection system.

The biobarrier membrane discs were prepared the day before the assay was conducted. The test substance was first tested to determine if the sample was compatible with the CorrositexTM system. Approximately 150 uL of the test substance was added to the Qualify test tube, shaken, and allowed to stand for 1 minute. A change in color or consistency was observed so Step 2 for categorization was initiated. Approximately 150 uL was added to the test tube labeled A (yellow solution) and B (clear solution). The test tubes were capped and shaken. No color change was observed in either tube. Two drops of confirm agent was added to Tube 3. The tube was then capped and shaken until mixed. The color change corresponded to Category 2. Step 3 for classification was then started.

A membrane disc containing the biobarrier matrix was placed into a chemical detection system (CDS) vial. Approximately 500 uL was applied to the top of the disc. The vial was then observed for a color change in the CDS. This procedure was followed for each of the 4 test vials (Vials 1-4). Vial 5 was similarly treated with a positive control (95-98% sulfuric acid), and Vial 6 was similarly treated with a negative control (10% citric acid). Vials 1-4 were observed for > 60 minutes.

Result : The test substance did not pass through any of the membranes. No breakthrough occurred in Vials 1-4 and 6. Breakthrough of the biobarrier for Vial 5 (positive control) occurred in 58 seconds.

The test substance was not a corrosive substance.

Reliability : (1) valid without restriction
Flag : Critical study for SIDS endpoint
12.02.2004 (34)

Species	:	rabbit
Concentration	:	.5 other: mL
Exposure	:	Semiocclusive
Exposure time	:	1 hour(s)
Number of animals	:	1

Vehicle	:	
PDII	:	
Result	:	corrosive
Classification	:	
Method	:	other
Year	:	
GLP	:	no
Test substance	:	other TS: 1,3-DCB, purity 98.088%

Method : No specific test guideline was reported; however, a scientifically defensible approach was used to conduct the study.

Two aliquots of 0.5 mL of test substance were administered to 2 separate test sites on the back of the rabbit. One test site was designated for a 3-minute exposure period and the other for a 1-hour exposure period. The test sites were covered with a semi-occlusive dressing to ensure contact between the skin and test substance.

The test sites were evaluated and scored according to the Draize scale after patch removal and approximately 24, 48, and 72 hours after the end of the exposure periods. The adjacent areas of untreated skin were used for comparison.

The rabbit was examined for clinical signs of toxicity at each observation period. The rabbit was weighed on the day of treatment and at the last dermal evaluation.

The rabbit was sacrificed after the 72-hour evaluation. Microscopic evaluation was made of skin sections from the 2 test sites.

Result : The test substance produced mild erythema but no edema after a 3-minute exposure period. At 24 hours after test substance removal, moderate erythema and moderate edema were observed. At 48 and 72 hours, moderate erythema and severe edema were observed.

Moderate erythema and severe edema were observed after the 1 hour of exposure to the test substance. Necrosis was observed at 24, 48, and 72 hours after test substance removal. The rabbit also exhibited severe erythema, severe edema, or a raw area during the study.

Microscopic examination of the 3-minute test site revealed multifocal minimal epidermal ulceration with degeneration of adjacent collagen and diffuse mild epidermal hyperplasia. Microscopic examination of the 1-hour test site revealed severe transmural (epidermis and dermis) necrosis with hemorrhage and edema.

No significant weight loss or clincial signs were observed during the study.

Reliability : (1) valid without restriction
Flag : Critical study for SIDS endpoint
19.02.2004 (35)

Species	:	rabbit
Concentration	:	.5 other: mL
Exposure	:	Occlusive
Exposure time	:	24 hour(s)
Number of animals	:	13
Vehicle	:	
PDII	:	
Result	:	highly irritating

Classification	:	
Method	:	other
Year	:	
GLP	:	no
Test substance	:	other TS: 1,3-DCB, purity 92%
Method	:	Seven albino rabbits, previously clipped over the dorsal area, were restrained in wooden stocks. 0.5 mL of each of two undiluted samples (TDC and MDC)* was applied to intact and abraded skin of each animal. Treated areas were covered with squares of double thickness gauze fasted with adhesive tape and then covered with impervious film. The trunks were wrapped with rubberized cloth. After 24 hours, the rabbits were taken out of stocks and wrappings were removed. The treated areas were washed and then dried. Six additional rabbits were similarly treated with MDC alone. Animals were observed up to 15 days and then sacrificed. Necropsies were done at 2 days and 11 tissues were saved for histological examination on 3 of the rabbits treated with MDC and 1 rabbit treated with both TDC and MDC. * TDC = 1,3-DCB, Topped MDC = 1,3-DCB, Middle
Result	:	Exposure sites showed injuries in depth (generally light purple cast to skin) at one day. Reactions became more intense by 3 days with dilation of blood vessels. Strong irritation with increased edema persisted through 8 days. After removal from the stocks, all animals appeared to be unsteady and drowsy. These effects were more pronounced than usually observed in rabbits stocked for a 24-hour period and were believed to be attributed to the test material. In addition, all animals showed considerable weight loss following dosing and no subsequent weight gain. Histologic examination revealed an inflammatory response of intact skin and more extensive necrosis of abraded skin. No abnormalities were detected in the other organs examined in the rabbits treated with MDC only. However, the rabbit treated with both MDC and TDC had treatment-related changes in the kidney (tubular degeneration and necrosis), liver (lipid-like vacuolation), and thymus (thymocyte degeneration).
Test substance	:	Test substance also contained 4% toluene and 4% chlorobutanone.
Reliability	:	(2) valid with restrictions Current standards for a skin irritation study is a 4-hour test.

02.03.2004 (25)

Species	:	rabbit
Concentration	:	
Exposure	:	
Exposure time	:	
Number of animals	:	
Vehicle	:	
PDII	:	
Result	:	
Classification	:	
Method	:	other
Year	:	
GLP	:	no
Test substance	:	other TS: 1,3-DCB, purity not reported

Method	:	Three drops of 1,3-DCB was put on the side of a rabbit. The hair had been cut off previously. The skin of the rabbit before the experiment was not pigmented.
Result	:	Immediately after the drops were applied, the skin began to shiver. In 2 minutes, the skin became red. In 5 minutes, swelling began, redness continued, and small hairs bristled up. After 2 hours, the local swelling spread in the direction of the stomach. After 1 day, the skin was red where the drops flowed. The swelling moved more onto the stomach and the skin became less red. On the 4th day, the swelling disappeared and the spots where the drops flowed were brick red. After 10 days, the inflammation of the skin diminished. Small peeling of the skin began and there was a remarkable blackening of the skin.
Reliability	:	(3) invalid Documentation insufficient for assessment Inadequate test substance characterization

26.10.2005 (96)

Species	:	human
Concentration	:	
Exposure	:	
Exposure time	:	
Number of animals	:	
Vehicle	:	
PDII	:	
Result	:	
Classification	:	
Method	:	other
Year	:	
GLP	:	no
Test substance	:	other TS: 1,3-DCB, purity not reported

Result	:	On human epidermis, 1,3-DCB caused itching and burning sensation in 3 minutes. At 6 minutes, itching and burning sensation had vanished and there was no skin inflammation.
Reliability	:	(3) invalid Documentation insufficient for assessment Inadequate test substance characterization

26.10.2005 (96)

Species	:	rabbit
Concentration	:	
Exposure	:	
Exposure time	:	4 hour(s)
Number of animals	:	6
Vehicle	:	
PDII	:	
Result	:	moderately irritating
Classification	:	
Method	:	
Year	:	1987
GLP	:	no data
Test substance	:	other TS: 1,3-DCP

Method	:	6 New Zealand white rabbits (2 males/4 females) were patch tested on intact skins. Observations after 24, 48, and 72 hours, and 7 and 14 days.
Result	:	Slight-moderate erythema and severe edema were observed after 30 minutes. After 24 hours, well-defined moderate erythema and edema were observed. Effects diminished to slight or well-defined after 48 and 72 hours.

After 7 and 14 days, some animals still showed slight well-defined erythem and edema. Exfoliation was present in 2 animals after 7 days and in 4 animals after 14 days.

Pr. Irr. Index: 3.94 (MAX 8)

Test substance : Telone II, undiluted (0.5 mL, 4 hours)
Reliability : (2) valid with restrictions
Similar to guideline study with acceptable restrictions.
Flag : Critical study for SIDS endpoint
20.12.2005 (22)

Species : rabbit
Concentration :
Exposure :
Exposure time :
Number of animals :
Vehicle :
PDII :
Result : corrosive
Classification :
Method :
Year : 1982
GLP : no data
Test substance : other TS: 1,3-DCP

Result : The product is reported to be extremely irritant to occluded rabbit skin; resulting in exteremely severe eschar, intense edema, and black necrotic tissue.
Reliability : (4) not assignable
Documentation insufficient for assessment
13.12.2005 (100)

Species : rabbit
Concentration :
Exposure :
Exposure time :
Number of animals :
Vehicle :
PDII :
Result : corrosive
Classification :
Method :
Year : 1980
GLP : no data
Test substance : other TS: 1,3-DCP

Result : Intact skin with > 2 minute exposure produced definite injury; > 1 hour exposure produced edema and necrosis.
Test substance : Telone, purity not reported
Reliability : (4) not assignable
Documentation insufficient for assessment
20.12.2005 (19)

5.2.2 EYE IRRITATION

5.3 SENSITIZATION

Type	:	Buehler Test
Species	:	guinea pig
Number of animals	:	
Vehicle	:	
Result	:	sensitizing
Classification	:	
Method	:	
Year	:	1982
GLP	:	no data
Test substance	:	other TS: 1,3-DCP
Result	:	DCP, when tested as the cis isomer, was shown to be a moderate skin sensitizer in guinea pigs.
Test substance	:	cis 1,3-DCP, purity >= 90% (impurity ether)
Reliability	:	(2) valid with restrictions Similar to guideline study with acceptable restrictions.
Flag	:	Critical study for SIDS endpoint

19.12.2005 (100)

5.4 REPEATED DOSE TOXICITY

Type	:	Sub-acute
Species	:	rat
Sex	:	male
Strain	:	other: Crl:CD(R)
Route of admin.	:	inhalation
Exposure period	:	2 weeks
Frequency of treatm.	:	6 hours/day, 5 days/week
Post exposure period	:	14 days
Doses	:	0, 10, 100 ppm (0, 52, 530 mg/m3)
Control group	:	yes
NOAEL	:	10 ppm
Method	:	other
Year	:	
GLP	:	no
Test substance	:	other TS: 1,3-DCB, purity 99.5% (cis and trans mixture)

Method : No specific test guideline was reported; however, a scientifically defenisble approach was used to conduct the study.

Each test groups consisted of 10 rats, 8-10 weeks in age and weighing between 220 and 260 grams. All rats were weighed and observed daily (excluding weekends) through the exposure period and for 14 days post-exposure.

Atmospheres were generated by passing nitrogen through midget impingers containing the test material. Dilution air carried the resulting vapors into 20-L glass exposure chambers. Atmospheric concentrations were analyzed via gas chromatography. Chambers were analyzed at 30-minute intervals. Chamber temperature and oxygen were monitored with a thermometer and an oxygen analyzer, respectively.

Clinical laboratory measurements were made on urine samples collected overnight following the 9th exposure and the 13th day of recovery.

Analysis included quantitative measures of the volume, osmolality, and pH, and semi-quantitative tests for occult blood, protein, sugar, bilirubin, acetone, and urobilinogen. Each specimen was noted for color and appearance and the sediment from pooled specimens examined microscopically.

Blood samples were taken from the rats' tails after the 10th and 14th day of recovery. Twenty blood chemistry and hematology parameters were measured or calculated.

After the 10th exposure, 5 rats from each group were selected at random and sacrificed for gross and histopathological examination. Remaining rats were sacrificed on the 14th day of recovery for identical examinations. Twenty-three organs or tissues were examined. Heart, liver, lungs, kidneys, spleen, testes, and thymus were weighed.

Result : For all exposures, chamber oxygen was >= 20% and temperature was maintained at <= 30ºC. The mean measured exposure concentrations were 10.0±1.20 (52±6.2 mg/m3) and 100±8.5 (520±44 mg/m3) for the 10 and 100 ppm exposure groups, respectively.

During exposure, clinical observations of rats in both exposed groups included salivation, clear nasal discharge, hyperemia, and ruffled fur.

Rats exposed to 10 ppm (52 mg/m3) had body weights indistinguishable from controls throughout the study. Rats exposed to 100 ppm (520 mg/m3) showed a significant weight depression throughout the exposure period and a rate of gain parallel to controls during the recovery period.

Clinical chemistry measurements after the last exposure showed that the average erythrocyte count, hemoglobin, and hematocrit were higher in rats exposed to 100 ppm (520 mg/m3) of 1,3-DCB when compared to controls. Mean corpuscular hemoglobin was lower in these rats, and mean corpuscular hemoglobin concentration was lower in both exposure groups. Blood glucose levels and urine pH were higher in exposed rats, but the increase was not dose-related. After a 14-day recovery period, no differences were noted between 1,3-DCB exposed rats and controls.

A comparison of organ/body weight ratios between test and control rats showed no compound-related changes following the last exposure. After the 14-day recovery period, lung weights were significantly heavier in the rats exposed to 100 ppm (520 mg/m3) than in controls. The significance of this increase in lung weight was difficult to interpret since no specific microscopic lesions were observed at the end of the recovery period.

Pathological examination following the 10th exposure showed no compound-related macroscopic changes in any of the test rats and no microscopic changes in the rats exposed to 10 ppm (52 mg/m3). Rats exposed to 100 ppm (520 mg/m3) showed mild lung congestion (3/5 rats) and mild, but diffuse, degeneration of alveolar lining cells (1/5 rats). After the 14-day recovery period, no compound-related changes were noted.

Reliability : (2) valid with restrictions
Comparable to guideline study with acceptable restrictions

Flag : Critical study for SIDS endpoint

11.01.2006 (29)

Type :
Species : rat
Sex :
Strain :
Route of admin. : inhalation

Exposure period	:	15 or 30 exposures
Frequency of treatm.	:	4 hours/day
Post exposure period	:	
Doses	:	0, 0.1, 0.5 mg/L (0, 20, 100 ppm)
Control group	:	yes
Method	:	other
Year	:	
GLP	:	no
Test substance	:	other TS: 1,3-DCB, purity not reported

Method : Six white rats/group were exposed to 1,3-DCB in stationary chambers with a capacity of 760 L.

After 15 exposures, half of the animals were sacrificed and dissected. Their adrenal glands were separated and fixed in neutral formalin, in Orth's and Wiesel's fluids. After preliminary treatment, the adrenal glands were immersed in paraffin and a series of sections were cut. The preparations were stained with hematoxylin-eosin, hematoxylin green after Heidenhain, picrofuchsin after Van Gieson and Wiesel. Some of the material was processed for lipids with scarlet red staining of the nuclei with Erlich's hematoxylin. The remaining animals/group were sacrificed and had their adrenal glands removed for investigation after 30 exposures.

Result : Repeat exposure at a concentration of 0.5 mg/L caused morphological changes in the adrenal cortex. Both the glomerular and the fascicular zones showed destructive changes, mainfested as caryolysis and plasmolysis. Repeated exposure to 0.1 mg/L caused no noticeable morphological changes in the adrenal glands.

Reliability : (3) invalid
Documentation insufficient for assessment

19.12.2005 (82)

Type	:	
Species	:	rat
Sex	:	
Strain	:	
Route of admin.	:	inhalation
Exposure period	:	92 exposures
Frequency of treatm.	:	
Post exposure period	:	
Doses	:	0, 0.01, 0.1 mg/L (0, 2, 20 ppm)
Control group	:	yes
Method	:	other
Year	:	
GLP	:	no
Test substance	:	other TS: 1,3-DCB, purity not reported

Method : Twelve white rats/group were exposed to 1,3-DCB in stationary chambers with a capacity of 760 L.

After 92 exposures, half of the animals were sacrificed and dissected. Their adrenal glands were separated and fixed in neutral formalin, in Orth's and Wiesel's fluids. After preliminary treatment, the adrenal glands were immersed in paraffin and a series of sections were cut. The preparations were stained with hematoxylin-eosin, hematoxylin green after Heidenhain, picrofuchsin after Van Gieson and Wiesel. Some of the material was processed for lipids with scarlet red staining of the nuclei with Erlich's hematoxylin. The remaining animals/group were sacrificed and had their adrenal glands removed for investigation after 30 exposures.

Both kidneys were fixed in 10% formalin solution and in Ort's liquid; pieces were cast with paraffin. Sections were stained with hematoxylin-eosin, iron hematoxylin according to Heidenhain and picrofusion according to Van Gieson.

Result : Repeated exposure to 0.1 mg/L 1,3-DCB produced slight morphological changes to the adrenal tissue. Necrosis of the capillaries of the malpighian glomerulus and also the epithelium of the renal tubules was noted at 0.1 mg/L.

No noticeable changes to adrenal tissue were observed after repeated exposure to 0.01 mg/L. Granular dystrophy of the epithelium of the renal tubules, mostly of the proximal limb of the nephron, and focal hemorrhaging were noted at 0.01 mg/L.

Reliability : (3) invalid
Documentation insufficient for assessment

17.10.2005 (82) (91)

Type	:	
Species	:	rat
Sex	:	male/female
Strain	:	
Route of admin.	:	inhalation
Exposure period	:	5 weeks
Frequency of treatm.	:	4 hours/day
Post exposure period	:	
Doses	:	0, 0.28, 0.85 mg/L (0, 54, 160 ppm)
Control group	:	
Method	:	
Year	:	
GLP	:	no data
Test substance	:	other TS: 1,3-DCB, purity not specified

Method : Intoxication was carried out in 750 L chambers by the dynamic method. The rats (15/exposure group) weighed an average of 126 g at study start.

Body weights, oxygen demand, working capacity, the subthreshold impulse summation, the prothrombin time, and peripheral blood were evaluated. The quantity of hippuric acid in the urine was determined. Thymol turbidity of the blood serum was determined by the Maclaham method in the modification of Yu. A. Kechek. Cholinesterase activity was evaluated by the method of T. V. Pravdich-Neminskaya. Prothrombin time was investigated at the end of the experiments after decapitation of the rats. The prothrombin time was determined by the Quick-Leman method in the modification of V. N. Tugolukov. Microscopic examination of the livers was also conducted.

Result : At 0.28 mg/L, a significant reduction in the oxygen demand and suppression of the capacity of the central nervous system for subthreshold impulse summation were observed.

At 0.85 mg/L, mortality was observed in 3/15 rats. 1,3-DCB caused a lag in weight gain. There was also a decrease in oxygen demand, a reduction in working capacity (determined after swimming), and suppression of the capability of the central nervous system for subthreshold impulse summation. In addition, the quantity of hemoglobin in the peripheral blood was decreased by the end of the experiment and the number of leukocytes was increased. A significant reduction in the activity of blood serum cholinesterase was observed and a reduction in the quantity of hippuric acid in the urine was noted. The prothrombin time was increased and the thymol test was positive. These biochemical shifts in the blood serum

testified to significant liver damage. A microscopic examination of the liver revealed degenerative changes (protein and fatty dystrophy of the cells and hyperemia of the vessels which contained altered erythrocytes).

Reliability : (3) invalid
Documentation insufficient for assessment

19.12.2005 (4) (5)

Type	:	
Species	:	rat
Sex	:	
Strain	:	
Route of admin.	:	inhalation
Exposure period	:	2 weeks
Frequency of treatm.	:	6 hours/day, 5 days/week
Post exposure period	:	
Doses	:	1, 10, 50, 100 ppm (5.2, 52, 260, 520 mg/m3)
Control group	:	

Method : In a cell proliferation study, groups of rats were exposed 6 hours a day, 5 days a week, for 2 weeks to 1, 10, 50, or 100 ppm of 1,3-DCB. Other groups of rats were similarly exposed to 0.1, 0.3, 1.0, or 10 ppm (0.5, 1.6, 5.2, or 52 mg/m3) of 1,4-DCB so that the cell proliferation activity of these two isomers could be compared. Following the 7th exposure, a minipump containing the thymidine analog bromodeoxyuridine was implanted in the rats. Bromodeoxyuridine is taken up by DNA and can be measured in the respiratory and olfactory epithelium as an indicator of cell proliferation.

Result : A significant decrease in body weight gain was noted in the rats exposed to the high concentrations of both 1,3-DCB and 1,4-DCB. However, the cell proliferation results of 1,3-DCB were markedly different from those of 1,4-DCB. 1,4-DCB induced dose-related cell proliferation at 1 and 10 ppm (5.2 and 52 mg/m3) but not at 0.1 and 0.3 ppm (0.5 and 1.6 mg/m3). Hypertrophy of the respiratory epithelium was also seen at 1 and 10 ppm (5.2 and 52 mg/m3). For the rats exposed to 1,3-DCB, a decrease in cell proliferation of the respiratory epithelium was observed. Additionally, no significant histopathological changes were seen in the olfactory epithelium of the rats exposed to 1,3-DCB.

Reliability : (2) valid with restrictions

19.12.2005 (33)

Type	:	
Species	:	rat
Sex	:	male/female
Strain	:	Fischer 344
Route of admin.	:	inhalation
Exposure period	:	28 days
Frequency of treatm.	:	6 hours/day, 5 days/week
Post exposure period	:	
Doses	:	3.81, 10.09, 29.51 ppm (17.1, 45.4, 132.7 mg/m3)
Control group	:	yes, concurrent vehicle
LOAEL	:	3.81 ppm
Method	:	
Year	:	1978
GLP	:	no data
Test substance	:	other TS: 1,3-DCP

Method : Groups of 40 animals were divided into 4 groups of 10 animals and exposed to analyzed concentrations under dynamic conditions.

Result : All compound-treated female rats showed stained fur around the back and head after week 3 and 4. The 29.51 ppm males showed a significant

increased body weight.

At gross necropsy, a greenish cast was observed in 1 male of the 3.81 and 10.09 ppm groups, and 3 males of the 29.51 ppm group (no occurrence in control group).

In all compound-treated males, an increased incidence of pale and granular liver was observed.

Test substance : Telone II, purity not reported
Reliability : (2) valid with restrictions
Similar to guideline study with acceptable restrictions.
Flag : Critical study for SIDS endpoint
19.12.2005 (17)

Type :
Species : rat
Sex : male/female
Strain : Fischer 344
Route of admin. : inhalation
Exposure period : 90 days
Frequency of treatm. : 6 hours/day, 5 days/week
Post exposure period :
Doses : 11.98, 32.14, 93.02 ppm (53.9, 144.6, 418.6 mg/m3)
Control group : yes, concurrent vehicle
NOAEL : 11.98 ppm
LOAEL : 32.14 ppm
Method :
Year : 1979
GLP : no data
Test substance : other TS: 1,3-DCP

Method : Groups of 40 animals were divided into 4 groups of 10 animals and exposed to analyzed concentrations under dynamic conditions. Mortality, body weight, gross necropsy, and histopathology exams were conducted.
Result : No mortality or clinical signs were observed. In the 93 ppm (419 mg/m3) males and females, body weight gain was significantly decreased during the study.

At gross necropsy, all compound-treated males showed an increased incidence of discoloration of the kidney (percentage not known).

Compound-related histomorphological nasal changes were observed in all 93 ppm (419 mg/m3) males and females and in 9/10 32 ppm (145 mg/m3) female rats (decreased height of epithelial cells due to apparent loss of cytoplasm, disorganized nuclei and necrotic cells).

Test substance : Telone II, purity not reported
Reliability : (2) valid with restrictions
Similar to guideline study with acceptable restrictions.
Flag : Critical study for SIDS endpoint
19.12.2005 (18)

Type :
Species : mouse
Sex :
Strain : CD-1
Route of admin. : inhalation
Exposure period : 28 days
Frequency of treatm. : 6 hours/day, 5 days/week
Post exposure period :

Doses : 3.81, 10.09, 29.51 ppm (17.1, 45.4, 132.7 mg/m3)
Control group : yes, concurrent vehicle
LOAEL : 3.81 ppm
Method :
Year : 1978
GLP : no data
Test substance : other TS: 1,3-DCP

Method : Groups of 40 animals were divided into 4 groups of 10 animals and exposed to analyzed concentrations under dynamic conditions.
Result : In the 29.51 ppm group, stained fur and unkempt appearance were noted after 1, 2, and 3 weeks.

At gross necropsy in all compound-treated groups, an increased incidence of pale liver was observed.
Test substance : Telone II, purity not reported
Reliability : (2) valid with restrictions
Similar to guideline study with acceptable restrictions.
Flag : Critical study for SIDS endpoint
22.03.2006 (17)

Type :
Species : mouse
Sex : male/female
Strain : CD-1
Route of admin. : inhalation
Exposure period : 90 days
Frequency of treatm. : 6 hours/day, 5 days/week
Post exposure period :
Doses : 11.98, 32.14, 93.02 ppm (53.9, 144.6, 418.6 mg/m3)
Control group : yes, concurrent vehicle
NOAEL : 32.14 ppm
LOAEL : 93.02 ppm
Method :
Year : 1979
GLP : no data
Test substance : other TS: 1,3-DCP

Method : Groups of 40 animals were divided into 4 groups of 10 animals and exposed to analyzed concentrations under dynamic conditions. Mortality, body weight, gross necropsy, and histopathology examinations were conducted.
Result : No mortality was observed. Wet fur was incidently observed in the 93 ppm group. In the 93 ppm females, body weight gain was significantly reduced during the study.

In the 93 ppm females (6/10), compound-related histomorphological changes were observed in the nose (decreased height of epithelial cells due to apparent loss of cytoplasm and necrotic cells).
Test substance : Telone II, purity not reported
Reliability : (2) valid with restrictions
Similar to guideline study with acceptable restrictions.
Flag : Critical study for SIDS endpoint
22.03.2006 (18)

Type :
Species : dog
Sex :
Strain :

Route of admin.	:	inhalation
Exposure period	:	
Frequency of treatm.	:	17 exposures - two months
Post exposure period	:	
Doses	:	0.1, 0.25, 0.5 mg/L (20, 48, 100 ppm)
Control group	:	
Method	:	other
Year	:	
GLP	:	no
Test substance	:	other TS: 1,3-DCB, purity not reported
Method	:	The effect 1,3-DCB has on carbohydrate metabolism was studied in 6 dogs (2 dogs/exposure level).
Result	:	Seventeen or 34 exposures to 98 ppm produced marked effects, including an increase in blood glucose and pyruvic acid, changes in the hyperglycemic curve, disturbances in the regulation of carbohydrate metabolism by insulin and adrenalin, an initial increase in leukocytes followed by leukopenia, and appearance of pathological forms of erythrocytes. At 48.9 ppm, the same changes were produced, but were observed later. Two months' exposure to 19.65 ppm caused no marked changes in glucose or pyruvic acid levels.
Reliability	:	(3) invalid Documentation insufficient for assessment

19.12.2005 (83)

Type	:	
Species	:	dog
Sex	:	female
Strain	:	other: Mixed black-white fox-terrier
Route of admin.	:	oral feed
Exposure period	:	1 month
Frequency of treatm.	:	once/week
Post exposure period	:	
Doses	:	
Control group	:	no
Method	:	other
Year	:	
GLP	:	no
Test substance	:	other TS: 1,3-DCB, purity not reported
Method	:	The dog, weighing 10.4 k, was fed weekly 1 cc of 1,3-DCB which was mixed with flour and given to the dog in a capsule so she would swallow it whole. The dog was fed 2.5 cc 1,3-DCB in the first 20 days.
Result	:	During the first week, the dog lost weight and hair. Gastric juices were acidic suggesting inflammation of the stomach. No histopathology was performed. After cessation of the experiment, the dog regained its lost weight and its fur began to grow.
Reliability	:	(3) invalid Documentation insufficient for assessment Inadequate test substance characterization

26.10.2005 (96)

Type	:	
Species	:	other: rat, guinea pig, rabbit, dog
Sex	:	male/female
Strain	:	
Route of admin.	:	inhalation
Exposure period	:	6 months
Frequency of treatm.	:	7 hours/day, 5 days/week

Post exposure period	:	3 months
Doses	:	0.9, 2.6 ppm (4.0, 11.8 mg/m3)
Control group	:	yes
NOAEL	:	.9 ppm
Method	:	
Year	:	1977
GLP	:	no data
Test substance	:	other TS: 1,3-DCP
Method	:	Rats, guinea pigs, rabbits, and dogs were exposed to analyzed concentrations of the test substance. Appearance, body weight, hematology, organ weights, gross necropsy, and histopathology were evaluated.
Result	:	The animals which were exposed to 0.9 ppm (4.0 mg/m3) showed no effects. The only effect observed in the 2.6 ppm (11.8 mg/m3) group was a slight, apparently reversible cloudy swelling of the renal tubular epithelium of male rats. In female rats dosed at 2.6 ppm (11.8 mg/m3), relative liver weight was increased. A recovery group of rats was maintained for 3 months after the 6 month exposue of 0.9 (4.0 mg/m3) or 2.6 ppm (11.8 mg/m3). No abnormalities were observed in this group.
Test substance	:	1,3-DCP, 46% cis isomer, 53% trans-isomer
Reliability	:	(2) valid with restrictions Study conducted with accepted scientific principles.

19.12.2005 (108)

Type	:	
Species	:	other: rat, mouse
Sex	:	male/female
Strain	:	other: Fischer 344, B6C3F1
Route of admin.	:	inhalation
Exposure period	:	13 weeks
Frequency of treatm.	:	6 hours/day, 5 days/week
Post exposure period	:	
Doses	:	0, 10, 30, 90, 150 ppm (0, 45, 136, 409, 681 mg/m3)
Control group	:	yes
Method	:	
Year	:	1988
GLP	:	no data
Test substance	:	other TS: 1,3-DCP
Result	:	The primary target tissues of inhaled DCPT were identified as the nasal mucosa of both sexes of rats and mice, and the urinary bladder of female mice. In addition, depressed growth rates of all animals exposed to 90 (409 mg/m3) or 150 ppm (681 mg/m3) DCPT (up to 20% in rats and 12% in mice) resulted in a variety of alterations in hematolgoic and clinical chemistry parameters, and in changes in organ weights relative to controls. Nasal mucosal effects consisted of a dose-related slight degenerative effect of nasal olfactory epithelium or a mild hyperplasia of the respiratory epithelium or both in all animals exposed to 90 (409 mg/m3) or 150 ppm (681 mg/m3), and 2/10 male rats exposed to 30 ppm (136 mg/m3) DCPT. No treatment-related effects were observed in rats or mice exposed to 10 ppm (45 mg/m3) DCPT vapors.
Test substance	:	DCPT (technical grade 1,3-DCP)
Reliability	:	(1) valid without restriction Similar to guideline study.

Flag : Critical study for SIDS endpoint
29.04.2006 (105)

Type	:	
Species	:	other: rats and rabbits
Sex	:	
Strain	:	
Route of admin.	:	inhalation
Exposure period	:	4.5-5.5 months
Frequency of treatm.	:	6 hours/day
Post exposure period	:	
Doses	:	0, 0.01, 0.1 mg/L (0, 2, 20 ppm)
Control group	:	
NOAEL	:	2 ppm
Method	:	
Year	:	
GLP	:	no
Test substance	:	other TS: 1,3-DCB, purity not reported

Method : Intoxication was carried out in 750 L chambers by the dynamic method. There were 20 albino rats in each group and 3 rabbits.

Body weights, oxygen demand, working capacity, the subthreshold impulse summation, the prothrombin time, and peripheral blood were evaluated. The quantity of hippuric acid in the urine was determined. Thymol turbidity of the blood serum was determined by the Maclaham method in the modification of Yu. A. Kechek. Cholinesterase activity was evaluated by the method of T. V. Pravdich-Neminskaya. Prothrombin time was investigated at the end of the experiments after decapitation of the rats. The prothrombin time was determined by the Quick-Leman method in the modification of V. N. Tugolukov. Microscopic examination of the liver, lung, heart, kidney, brain, and spleen was also conducted. Internal organs were preserved by fixation in formalin and, in part, in Carnois' solution. Paraffin sections were stained with hematoxilin-eosin, picrofuchsin according to Van-Gison, Toluidine Blue, pyronine according to Brache, for elastica according to Weigert, and impregnated according to Foote. The PAS reaction was also used.

Result : At 0.1 mg/L, a lag in weight gain was observed. In addition, an increase in fatique of the animals in the case of forced swimming (working capacity), a reduction in the capacity of the central nervous system for subthreshold impulse summation, a reduction in the cholinesterase activity in the blood serum, a significant increase in the turbidity of the blood serum in the thymol test, a lengthening in the prothrombin time, a reduction in the sulfhydryl groups in the blood and in the homogenates of the internal organs, and a reduction in the quantity of hippuric acid in the urine were noted. In rabbits, a reduction in the resistance of the erythrocytes and the cholinesterase activity in the liver homogenate were also observed.

Microscopic examination of the liver revealed degenerative changes (protein and fatty dystrophy of the cells and hyperemia of the vessels which contained altered erythrocytes). 1,3-DCB caused changes in lung arterioles and capillaries, as well as in parenchymatous elements of internal organs. Plasmorrhagia in the initial stages, followed by arteriosclerosis and hyalinosis of the vessels of the lung led to ischemization of lung tissue, leading to its atrophy and development of emphysema. Necrobiosis of the parenchyma of the liver, heart, and kidney were observed with consequent substitutive growth of connecting tissue. There was also observed growth of young connecting tissue between the lobes of the liver, and in the stroma of kidneys. Focal and diffuse

cardiosclerosis was noted as well as the appearance of glial cell fields in the brain.

At 0.01 mg/L, an increase in intensity of turbidity of the blood serum was noted. However, this disturbance was only functional in nature, as indicated by the absence of morphological changes in the microscopic examination.

Reliability : (2) valid with restrictions
23.03.2005 (4) (5) (48)

Type	:	
Species	:	other: rats and rabbits
Sex	:	
Strain	:	
Route of admin.	:	inhalation
Exposure period	:	various time periods
Frequency of treatm.	:	4 hours/day, 6 days/week
Post exposure period	:	
Doses	:	0.1-0.5 mg/L (20-100 ppm)
Control group	:	
Method	:	
Year	:	
GLP	:	no data
Test substance	:	other TS: 1,3-DCB, purity not reported

Result : Animals exhibited plethora, hemorrhage, granular and fatty dystrophy of the liver cells, and depletion of the hepatic glycogen reserves. Alterations observed in biochemical indices were increased serum bilirubin and urinary urobilin levels, decreased blood glucose tolerance, cholesterol and cholesterol ester, and delayed removal of bromosulphthalein from the blood.

Reliability : (3) invalid
Documentation insufficient for assessment
19.12.2005 (81)

5.5 GENETIC TOXICITY 'IN VITRO'

Type	:	other: Salmonella typhimurium reverse mutation assay and spot test
System of testing	:	Salmonella typhimurium strains TA1535, TA1537, TA98, and TA100.
Test concentration	:	0, 10, 50, 100, 500, 1000, 2500 ug/plate (without activation) 0, 50, 100, 500, 1000, 2500 ug/plate (with activation)
Cycotoxic concentr.	:	
Metabolic activation	:	with and without
Result	:	positive
Method	:	other
Year	:	
GLP	:	no
Test substance	:	other TS: 1,3-DCB, purity 99.5% (cis and trans)

Method : No specific test guideline was available at the time of testing; however, a scientifically defensible approach was used to conduct the study. The assay was performed in the presence and absence of a rat-liver homogenate activation system similar to the method described by Ames et al. (1975). Mutat. Res., 31:347-364.

Plate Incorporation Assay - Solids and Nonvolatile Liquids:
Treatments without activation were conducted by adding 0.1 mL of the solvent or a solution of the test sample and 0.1 mL of an overnight culture

containing approximately 10E8 bacteria to top agar. These components were mixed and poured on the surface of a plate containing Davis minimal agar. Treatments with activation were conducted by adding 0.5 mL of S-9 mix to the bacteria/test sample/top agar and pouring the mixture onto a minimal agar plate.

The S-9 contained S-9, MgCl2, KCl, glucose 6-phosphate, NADP, and sodium phosphate.
Positive (2-aminoanthracene, 9-aminoacrdine, N-methyl-N'-nitro-N-nitrosoguanidine, 2-nitro-fluorene, chloroethene and negative (solvent, dimethyl sulfoxide) controls were included in all assays.

The cytotoxicity of the test sample in the presence and absence of an activation system, as measured in strain TA1535, was the basis for selecting concentrations for the mutagenesis experiments.

Spot Test in a Closed System:
A spot test in a closed system was performed to test whether the test substance would vaporize appreciable when the plate incorporation method was used. Experiments without activation were performed by adding 10E8 bacteria to top agar, mixing immediately, and pouring on a Davis minimal agar plate. Experiments with activation were performed in the same manner except that 0.5 mL of S-9 mix was also added before mixing.
A sterile disk saturated with test compound was placed in the center of 1 of 2 replicate plates. The plate with the disk was inverted and the other plate was stacked on top of it. Both plates were sealed in plastic bags and incubated for 48 hours at 37ºC. A plate incorporation assay (solids and nonvolatile liquids) was performed if the spot test was negative. If the spot test was positive, a limited plate incorporation assay (solids and nonvolatile liquids) was performed with only the strains and conditions in which mutagenic activity was suggested in the spot test. A complete assay was performed if mutagenic activity was observed in the limited assay. If the limited assay was negative, the test sample was assayed according to the plate assay protocols for testing gases and volatile liquids.

Plate Assay - Volatile Liquids
Treatments without activation were conducted by adding approximately 10E8 bacteria to top agar. Prior to exposure to the test compound, these components were mixed and poured on the surface of a plate containing Davis minimal agar. Treatments with activation were conducted by adding 0.5 mL of S-9 mix to the bacteria/top agar and pouring the mixture onto a minimal agar plate.

The minimal agar plates with the bacteria were exposed to the volatile liquid in 9-L glass chambers. The plates, without lids, were placed in chambers on stainless steel racks. Measured volumes of the liquid test sample were placed in an uncovered glass dish in each chamber. The chambers were closed and incubated at 37ºC for 48 hours. At the end of the exposure period, the chambers were flushed with 5 volumes of air, the plates removed, and the revertants were counted.

The concentrations of the test sample in the chambers were determined 2 to 3 hours after initiating treatment, and just before the end of the treatment period. Samples were analyzed via gas chromatography.

The data points (number of revertants/plate) were transformed prior to analysis. Two analyses were performed. In the first analysis, the response observed at each concentration was compared to the control by a t-test of significance. In the second analysis, the significance of the dose-response

relationship was tested. Linear, quadratic, and higher order dose-response effects were tested in an F-test of significance. In addition, an analysis was conducted to determine whether the dose-response was different in different trials.

The test sample was classified as a nonmutagen when: 1) the probability was greater than 0.05 that the numbers of revertants at each of the test sample concentrations studied were not greater than the number of revertants in the solvent control and 2) the probability was greater than 0.05 that there was not a positive correlation between the numbers of revertants and increasing concentrations of the test substance.

The test substance was classified as a mutagen when: 1) the probability was less than 0.01 that the numbers of revertants at one or more of the test sample concentrations studied was not greater than the number of revertants in the solvent control, and 2) the probability was less than 0.01 that there was not a positive correlation between the number of revertants and increasing concentrations of the test substance.

Result : In the initial cytotoxicity experiment with strain TA1535, 1,3-DCB was tested at concentrations up to 2500 ug/plate. Significant toxicity was observed at 1000 ug/plate in both the presence and absence of an activation system.

A spot test in a closed system was performed at the same time as the cytotoxicity experiment. A positive spot test was observed for strain TA1535 and TA100 without an activation system, and TA100 with an activation system.

Two trials of the plate incorporation assay were performed. Subsequently, the test substance was tested according to the protocol for testing volatile liquids in a single trial using starins TA1535 and TA100 in the presence and absence of an activation system, and in a second trial using strains TA1535, TA1537, TA98, and TA100.

The test material was mutagenic in the plate incorporation assay in strain TA100 with an activation system. The test material was also mutagenic in the volatile liquid assay in strains TA100 without an activation system and TA1535 and TA100 with an activation system. Mutagenic activity was observed in strain TA1535 without an activation system in trial 2 of the volatile liquid assay, but not in trial 1.

Positive control materials showed expected mutagenic responses.

Reliability : (1) valid without restriction
27.04.2006 (28)

Type : Salmonella typhimurium reverse mutation assay
System of testing : Salmonella typhimurium strains TA1978, TA1535, TA100, TA1537, TA98
Test concentration : Not stated
Cycotoxic concentr. :
Metabolic activation : with and without
Result : negative
Method : other
Year :
GLP : no data
Test substance : other TS: 1,3-DCB, purity not reported

Method : No specific test guideline was available at the time of testing; however, the assay was performed in the presence and absence of a rat-liver homogenate activation system similar to the method described by Ames, B.

N. in A. Hollaender (ed). (1971). Chemical Mutagens, Vol 1, pp. 267-282, Plenum Press, New York and McCann, J. et al. (1975). Detection of Carcinogens and Mutagens: Bacterial Tester Strains with R-Factor Plasmids, PRoc. Natl., Acad. Sci., 72:975-983.

Reliability : (2) valid with restrictions
Not tested as a volatile liquid.

23.03.2005 (15)

Type : other: Salmonella typhiurium reverse mutation assay and Saccharomyces cerevisiae gene mutation test
System of testing : Salmonella typhiurium starins TA1535, TA1537, TA1538 and Saccharomyces cerevisiae strain D4
Test concentration : Salmonella: 0.008, 0.016% Saccharomyces: 0.016, 0.032%
Cycotoxic concentr. :
Metabolic activation : with and without
Result :
Method : other
Year :
GLP : no
Test substance : other TS: 1,3-DCB, purity 100%

Method : Toxicity Test: 1,3-DCB was tested for surivival against strains TA1537 and D4 over a range of doses to determine the 50% survival dose.

Plate Tests: Only 3 Salmonella tester strains were used in the qualitative plate tests. In the non-activation procedure, approximately 10E9 cells of a log phase culture of the bacterial indicator strains were spread over the surface of a minimal plate, and a measured amount of the test chemical was placed in the center of the test plate. In activation tests, the test chemical was added to the cells, and an aliquot of the mixture was spread on the surface of the test plate. The reaction mixture plus tissue extract was then spotted on the surface of the plate. Positive (ethylmethane sulfonate, 2-nitrosofluorene, quinacrine or quinacrine mustard, dimethylnitrosamine, and 2-acetylaminofluorene) and solvent controls were included. All plates were incubated at 37ºC for 4 days and then scored.

Suspension Tests: Tests were conducted in plastic tissue culture flasks. Cells plus appropriate volume of test chemical were added to the flasks to give a final volume of 2 mL. Solvent replaced the test chemical in the negative controls. Treatment was at 30ºC for 4 hours for yeast tests and at 37ºC for 1 hour for bacterial tests. All flasks were shaken during treatment. Following treatment, the flasks were set in ice. Aliquots of cells were removed, diluted in saline, and plated on the appropriate complete media. Undiluted samples from flasks containing the bacteria were plated on minimal selective medium. Samples from a 10E-1 dilution of treated cells were plated on the selected media for enumeration of gene conversions with strain D4. Bacterial plates were scored after incubation for 48 hours at 37ºC. The yeast plates were incubated at 30ºC for 3-5 days before scoring. The trials with activation were prepared as described above except that the cell densities were increased approximately 5-fold for working stock suspensions. Measured amounts of the test and control chemicals plus 0.25 mL of the stock cell suspension were added to a 30 mL plastic tissue homogenate. All flasks (yeast and bacteria) were incubated at 37ºC with shaking. The treatment times as well as the dilutions, plating procedures, and scoring of the plates were the same as described for the non-activated tests.

The tissue homogenates and supernatants were prepared from liver, lung,

and testes of mouse, rat, and non-human primate.

All population plates were scored by an automatic colony counter. All minimal or other types of selective media plates were hand scored.

Retests were conducted whenever the test compound exhibited increased reversion or gene conversion frequencies in 1 or 2 tests in the total assay.

If the initial test was positive and the retest was clearly negative, the negative results are used for evaluation assessments.

If the initial test and the retest were both positive, the original results were used for evaluation assessments.

Result : At a concentration of 0.016% (v/v), 1,3-DCB was not mutagenic in TA1535, TA1537, and TA1538 in any of the plate tests.

All non-activation Salmonella suspension tests resulted in negative results.

The activation Salmonella suspension tests were negative. Three separate dose levels from TA1538 and TA1537 were retested because the initial tests suggested slightly elevated reversion frequencies. All repeat tests resulted in negative results.

The initial results of the non-activation Saccharomyces tests indicated a relatively strong response at both loci. Subsequent retests of the high and low dose levels for Try+ convertants produced negative results.
As in the non-activation tests, the activation tests for Saccharomyces appeared to indicate genetic activity. Results from retests of 2 dose levels might be interpreted as either negative or weakly positive.

Positive control substances showed expected mutagenic responses.

Conclusion : 1,3-DCB is clearly non-mutagenic in Salmonella strains TA1535, TA1537, and TA1538. The results of the tests, and retests, run with S. cerevisiae, strain D4, were equivocal.

Reliability : (2) valid with restrictions
Not tested as a volatile liquid.

22.03.2006 (27)

5.6 GENETIC TOXICITY 'IN VIVO'

Type	:	Micronucleus assay
Species	:	rat
Sex	:	male/female
Strain	:	other: Crl:CD(R) BR
Route of admin.	:	inhalation
Exposure period	:	6 hours/day, 5 days/week for 2 weeks
Doses	:	0, 10, 50, 100 ppm
Result	:	negative
Method	:	OECD Guide-line 474 "Genetic Toxicology: Micronucleus Test"
Year	:	
GLP	:	yes
Test substance	:	other TS: 1,3-DCB, purity 98% (mixture of cis and trans)

Method : The study was also conducted according to EPA guidelines published in 40 CFR 798.5395.

Five male and 5 female rats/group were treated by nose-only inhalation. Conditioned, filtered, house-line air was the negative (vehicle) control. The

positive control indicator was cyclophosphamide (CP). The rats in the positive control group received CP 24 hours prior to sacrifice.

Rats were 47 days old at study start. Rats were housed in suspended, stainless steel wire-mesh cages.

Test atmospheres were generated by metering nitrogen over or through glass impingers containing a reservoir holding 1,3-DCB. The nitrogen swept the 1,3-DCB vapors into each test chamber via Teflon tubing. The concentration in each chamber was controlled by varying the flow of nitrogen to the impinger. The impingers were kept in a 15ºC barh and were isolated from the rest of the generation system. Filtered, dried dilution air was introduced into each chamber at 40 L/min. For the control chamber, the air flow was 28 L/min.

During exposure, each rat was inidividually confined in a polycarbonate restrainer placed in a glass and stainless steel 150-L chamber. Only the nose of the animal protruded into the chamber. The positions of the animals within the chambers were randomly rotated daily. The chambers were operated in a one-pass, flow-through mode with air flow rates adequate to provide 16 air changes/hour for the air control chambers. The flow rates provided sufficient oxygen for the test animals and adequate distribution of the test material in the chambers.

At approximately 30-minute intervals, chamber samples of the test atmospheres were drawn and delivered to a gas chromatograph. During exposures, the relative humidity, temperature, and oxygen concentration of each chamber were recorded. An Omega thermocouple was used to measure chamber temperatures, a psychrometer was used to measure relative humidity, and an oxygen monitor was used to measure chamber oxygen.

Each animal was observed for clincial signs prior to and after exposure each day of treatment. Clinical signs observed during the 6-hour exposure periods were also noted. Body weights were taken throughout the study.

On the day of the last treatment, the animals were sacrificed. The marrow from both femurs of each animal was aspirated and flushed into fetal bovine serum. The marrow button was collected by centrifugation at approximately 200 x g for 5 minutes. Most of the supernatant was removed, and the cells were resuspended in the remaining 1-2 drops of serum. An automatic blood smearing instrument was used to make the bone marrow smears. At least 2 slides per animal were prepared and fixed in absolute methanol. The slides were stained with acridine orange in sodium phosphate buffer.

Representative slides from each animal were examined in a blind manner using epifluoresence microscopy at a magnification of 630X. A minimum of one thousand polychromatic erythrocytes (PCEs) were scored for the presence of micronuclei. The number of micronucleated normochromatic erythrocytes (NCEs) seen in the optic fields scored to obtain at least 1000 PCEs was also recorded. In addition, the ratio of polychromatic to normochromatic erythrocytes (NCEs) was determined.

Data for the percent micronucleated PCEs and proportion of PCEs among total erythrocytes were transformed prior to analysis using the arcsine square-root function. Weight gain data were not transformed. Data for each sex were analyzed separately by a one-way Analysis of Variance (ANOVA). The positive indicator group was not included in the analysis for effects of the test substance. All analyses were one-tailed.

Result	:	The test chamber concentrations were within normal range and delivered the approximate doses of 0, 10, 50, and 99 ppm 1,3-DCB. Chamber temperatures ranged from 22 to 26ºC. The relative humidity in the test chambers ranged from 13 to 32%. Chamber oxygen concentrations were 21% throughout the study. A significant decrease in body weight gain occurred in all groups of 1,3-DCB exposed male animals after 10 days of exposure. No weight effects were observed in the female 1,3-DCB groups, and no other significant clincial signs of toxicity were noted. There were no statistically significant increase in micronucleated PCEs (MN-PCEs) and no significant depression in the proportion of PCEs among total erythrocytes observed in any 1,3-DCB treated group. The CP-treated animals showed significant increases in MN-PCEs when compared to concurrent controls.
Reliability	:	(1) valid without restriction
Flag	:	Critical study for SIDS endpoint

12.02.2004 (32)

Type	:	Sister chromatid exchange assay
Species	:	rat
Sex	:	male
Strain	:	Wistar
Route of admin.	:	i.p.
Exposure period	:	
Doses	:	40 mg/kg
Result	:	
Method	:	
Year	:	
GLP	:	
Test substance	:	other TS: 1,3-DCB, purity not reported

Method	:	Experiments were conducted on 5 male rats weighing 120 g. 1,3-DCB was dissolved in oil and was administered to the rats intra-abdominally in doses equivalent to 1/5 of the LD50. After 24 hours, the rats received 1 mg/kg colchicine intra-abdominally. After 2 hours, the rats were killed by administration of an overdose of ether narcosis. The chromosome preparations were prepared according to the method described in Ail'fyan, V. N. et al. (1985). Genetika, 21(19):1507-1511. One hundred cells from each animal were evaluated. The results were processed statistically using the Student's criterion.
Result	:	1,3-DCB significantly increased the number of cells with cytogenetic damage. 1,3-DCB only induced chromatid breaks. The number of cells cells analyzed for sister chromatid exchanges was 500. The frequency of aberrant cells was 4.2+/-0.8%. The chromosome disruptions (as individual fragments) per 100 cells was 4.2. 1,3-DCB was considered a weak mutagen.
Reliability	:	(3) invalid Documentation insufficient for assessment

17.10.2005 (87)

5.7 CARCINOGENICITY

Species	:	rat
Sex	:	male/female
Strain	:	Fischer 344

Route of admin. : gavage
Exposure period : 2 years
Frequency of treatm. : 3 days/week
Post exposure period :
Doses : 25, 50 m/kg
Result :
Control group : yes, concurrent vehicle
Method :
Year : 1985
GLP : no data
Test substance : other TS: 1,3-DCP

Method : Groups of 104 rats (52 male/52 female) were dosed by gavage. In an ancillary study, groups of 5 male/5 female rats were dosed similarily and were sacrified after 9, 16, 21, 24 and 27 weeks.

Observations included: mortality, body weight, hematology, clinical chemistry, neoplastic/non-neoplastic lesions. Tissues/organs examined histopathologically included: gross lesions and tissue masses, blood smears, submandibular and mesenteric lymph nodes, salivary glands, femur (including marrow), thyroid gland, parathyroids, small intestine, colon, liver, prostate/testes or ovaries/uterus, lungs and bronchi, mammary gland, skin, esophagus, stomach, brain, heart, thymus, trachea, pancreas, spleen, kidneys, adrenal glands, urinary bladder, and pituitary.

Remark : The test sample contained 1.0% epichlorohydrin (as stabilizer) which might have contributed to the carcinogenic effects observed.

Result : In the 50 mg/kg males, mean body weight was slightly (5%) decreased from week 28 to the end of the study. In the 50 mg/kg females, blood glucose levels were significantly increased after 21 weeks.

In the 50 mg/kg and, less pronounced, in the 25 mg/kg males and females, erythrocyte ChE and lactic acid dehydrogenase were significantly decreased.

The primary organs that were affected were the forestomach and liver. Compound-related non-neoplastic lesions were basal cell or epithelial hyperplasia of the forestomach.
Under the conditions of this study, the NTP concluded that there was "clear" evidence of carcinogenicity for "male rats" as indicated by a compound-related increased incidence of squamous cell papillomas and carcinomas of the forestomach as well as a dose-related increased incidence of neoplastic nodules of the liver. In "female rats", there was "some" evidence of carcinogenicity as indicated by a dose-related increased incidence of squamous cell papillomas of the forestomach. An increased incidence of neoplastic nodules of the liver was found in the 50 mg/kg females only. The results of the interim kills support the findings of the main study.

	Male Rats		
	Control	25 mg/kg	50 mg/kg
FORESTOMACH			
Squamous cell papilloma:			
Overall rate	1/52(2%)	1/52(2%)	9/52(17%)
Adjusted rate	2.3%	2.4%	21.3%
Terminal rate	1/43(2%)	0/38(0%)	7/40(18%)
Life table tests	p=0.002	p=0.739	p=0.008
Incidental tumor tests	p=0.002	p=0.702N	p=0.011

Historical control incidence in NTP studies: 2/1114 (0.2%)

Squamous cell carcinoma:			
Overall rate	0/52(0%)	0/52(0%)	4/52(8%)
Adjusted rate	0.0%	0.0%	10.0%
Terminal rate	0/43(0%)	0/38(0%)	4/40(10%)
Life table tests	p=0.014	no p value	p=0.054
Incidental tumor tests	p=0.014	no p value	p=0.054
Historical control incidence not reported			
Squamous cell papilloma or carcinoma:			
Overall rate	1/52(2%)	1/52(2%)	13/52(25%)
Adjusted rate	2.3%	2.4%	30.8%
Terminal rate	1/43(2%)	0/38(0%)	11/40(28%)
Life table tests	p<0.001	p=0.739	p<0.001
Incidental tumor tests	p<0.001	p=0.702N	p<0.001
Historical control incidence in NTP studies: 6/1114 (0.5%)			
LIVER			
Neoplastic nodule			
Overall rate	1/52(2%)	6/52(12%)	7/52(13%)
Adjusted rate	2.3%	15.8%	17.5%
Terminal rate	1/43(2%)	6/38(16%)	7/40(18%)
Life table tests	p=0.023	p=0.040	p=0.025
Incidental tumor tests	p=0.023	p=0.040	p=0.025
Historical control incidence in NTP studies: 31/1141(2.7%)			
Hepatocellular carcinoma			
Overall rate	0/52	0/52	1/52
Historical control incidence in NTP studies: 9/1141(0.8%)			
Neoplastic nodule or carcinoma			
Overall rate	1/52(2%)	6/52(12%)	8/52(15%)
Adjusted rate	2.3%	15.8%	20.0%
Terminal rate	1/43(2%)	6/38(16%)	8/40(20%)
Life table tests	p=0.011	p=0.040	p=0.013
Incidental tumor tests	p=0.011	p=0.040	p=0.013
Historical control incidence in NTP studies: 40/1141(3.5%)			

		Female Rats	
	Control	25 mg/kg	50 mg/kg
FORESTOMACH			
Squamous cell papilloma:			
Overall rate	0/52(0%)	2/52(4%)	3/52(6%)
Adjusted rate	0.0%	4.9%	7.4%
Terminal rate	0/34(0%)	1/36(3%)	2/38(5%)
Life table tests	p=0.097	p=0.241	p=0.138
Incidental tumor tests	p=0.093	p=0.350	p=0.116

Historical control incidence of squamous cell papilloma or carcinoma in NTP studies: 5/1125 (0.4%)
Historical control incidence of squamous cell papilloma (forestomach) in NTP studies: 1/1125 (0.09%)

LIVER			
Neoplastic nodule			
Overall rate	6/52	6/52	10/52
No historical control incidence was reported			
Hepatocellular carcinoma			

Overall rate(a)	0/52	0/52	0/52	

No historical control incidence was reported

Test substance : Telone II (technical grade 1.3-dichloroprorene containing 1.0% epichlorohydrin as a stabilizer)

Reliability : (1) valid without restriction
Study conducted by national standards.

Flag : Critical study for SIDS endpoint

30.04.2006 (90)

Species : mouse
Sex : male/female
Strain : B6C3F1
Route of admin. : gavage
Exposure period : 2 years
Frequency of treatm. : 3 days/week
Post exposure period :
Doses : 50, 100 mg/kg
Result :
Control group : yes, concurrent vehicle
Method :
Year : 1985
GLP : no data
Test substance : other TS: 1,3-DCP

Method : Groups of 100 mice (50 male/50 female) were dosed by gavage.

Observations included: mortality, body weight, neoplastic/non-neoplastic lesions. Tissues/organs examined histopathologically included: gross lesions and tissue masses, blood smears, submandibular and mesenteric lymph nodes, salivary glands, femur (including marrow), thyroid gland, parathyroids, small intestine, colon, liver, prostate/testes or ovaries/uterus, lungs and bronchi, mammary gland, skin, esophagus, stomach, brain, heart, thymus, trachea, pancreas, spleen, kidneys, adrenal glands, urinary bladder, pituitary, and gallbladder.

Remark : The test sample contained 1.0% epichlorohydrin, (as stabilizer) which might have contributed to the carcinogenic effects observed.

Result : For male and female mice, initial body weight in the dose and control groups were not similar (the weight of the dose-groups was 6-22% below that the control group). Weight differences decreased to 5-9% by the end of the study.

In the control group, extreme mortality occured: 25 males died during week 48-51 from myocarditis. At the end of study, survival rates were 8/50, 28/50 and 31-50 for the control, mid- and high-dose males repectively. Survival rates of female were significantly decreased in the 100 mg/kg group (36/50 animals survived, comparing to 46/50 in the control group).

The primary organs that were affected were the forestomach, urinary bladder and the lungs. Compound-related non-neoplastic lesions were basal cell or epithelial hyperplasia of the forestomach, epithelial hyperplasia of the urinary bladder and kidney hydronephrosis.

The NTP considered the study "inadequate" for determination of carcinogenicity in "male mice", because of reduced survival in the vehicle control group. The product was "probably" associated with the increased incidence of transitional cell carcinomas of the urinary bladder, with the squamous cell papillomas of the forestomach and with alveolar/bronchial adenomas and carcinomas of the lungs in male mice.

The NTP concluded that there was "clear" evidence of carcinogenicity in "female mice", as indicated by a dose-related increase in transitional cell carcinomas of the urinary bladder, of alveolar/bronchiolar adenomas and carcinomas of the lung and of squamous cell papillomas or carcinomas of the forestomach in female mice.

		Male Mice	
	Control	50 mg/kg	100 mg/kg
FORESTOMACH			
Squamous cell papilloma			
Overall rate	0/50(0%)	2/50(4%)	3/50(6%)
Adjusted rate	0.0%	6.7%	7.4%
Terminal rate	0/8(0%)	1/28(4%)	1/31(3%)
Life table tests	p=0.234	p=0.510	p=0.280
Incidental tumor tests	p=0.051	p=0.403	p=0.037
Historical control incidence for squamous cell papilloma (forestomach) was not reported			
Squamous cell carcinoma	0/50	0/50	0/50
Historical control incidence for squamous cell carcinoma (forestomach): 1/1055(0.09%)			
LUNG			
Alveolar/bronchiolar adenoma			
Overall rate	1/50(2%)	11/50(22%)	9/50(18%)
Adjusted rate	11.1%	33.4%	27.0%
Terminal rate	0/8(0%)	7/28(25%)	7/31(23%)
Life table tests	p=0.419	p=0.147	p=0.312
Incidental table tests	p=0.185	p=0.026	p=0.162
Historical control incidence in NTP studies: 99/1082 (9.1%)			
Alveolar/bronchiolar carcinoma			
Overall rate	0/50	2/50	3/50
Historical control incidence in NTP studies: 58/1082 (5.4%)			
Alveolar/bronchiolar adenoma or carcinoma			
Overall rate	1/50(2%)	13/50(26%)	12/50(24%)
Adjusted rate	11.1%	39.8%	33.5%
Terminal rate	0/8(0%)	9/28(32%)	8/31(26%)
Life table tests	p=0.264	p=0.097	p=0.166
Incidental table tests	p=0.072	p=0.015	p=0.040
Historical control incidence in NTP studies: 155/1082(14%)			
URINARY BLADDER			
Epithelial hyperplasia	0/50(0%)	9/50(18%)	18/50(36%)
No historical control incidence reported			
Transitional cell carcinoma	0/50(0%)	0/50(0%)	2/50(4%)
Historical control incidence in NTP studies: 0/1033			
KIDNEY			
Hydrohephrosis	1/50	0/50	0/50
No historical control incidence reported			
		Female Mice	
FORESTOMACH			
Squamous cell papilloma	0/50(0%)	1/50(4%)	2/50(4%)
Historical control incidence for squamous cell papilloma (forestomach):			

1/1077(0.09%)

Squamous cell carcinoma	0/50(0%)	0/50(0%)	2/50(4%)
No historical control incidence reported			
Squamous cell papilloma and carcinoma			
Overall rate	0/50(0%)	1/50(2%)	4/50(8%)
Adjusted rate	0.0%	2.2%	10.6%
Terminal rate	0/46(0%)	1/45(2%)	3/36(8%)
Life table tests	p=0.014	p=0.496	p=0.040
Incidental tumor tests	p=0.021	p=0.496	p=0.059
Historical control incidence in NTP studies: 4/1077(0.4%)			
LUNG			
Alveolar/bronchiolar adenoma			
Overall rate	0/50(0%)	3/50(6%)	8/50(16%)
Adjusted rate	0.0%	6.7%	21.3%
Terminal rate	0/46(0%)	3/45(7%)	7/36(19%)
Life table tests	p<0.001	p=0.118	p=0.312
Incidental tumor tests	p=0.001	p=0.118	p=0.003
Historical control incidence in NTP studies: 36/1103 (3.3%)			
Alveolar/bronchiolar carcinoma			
Overall rate	2/50	1/50	0/50
Historical control incidence in NTP studies: 16/1103 (1.5%)			
Alveolar/bronchiolar adenoma or carcinoma			
Overall rate	2/50(4%)	4/50(8%)	8/50(16%)
Adjusted rate	4.3%	8.9%	21.3%
Terminal rate	2/46(4%)	4/45(9%)	7/36(19%)
Life table tests	p=0.011	p=0.327	p=0.020
Incidental tumor tests	p=0.019	p=0.327	p=0.032
Historical control incidence in NTP studies: 52/1103(4.7%)			
URINARY BLADDER			
Transitional cell carcinoma			
Overall rate	0/50(0%)	8/50(16%)	21/48(44%)
Adjusted rate	0.0%	17.4%	56.5%
Terminal rate	0/46(0%)	7/45(16%)	19/35(54%)
Life table tests	p<0.001	p=0.005	p<0.001
Incidental tumor tests	p<0.001	p=0.006	p<0.001
Historical control incidence in NTP studies: 0/1025			

Test substance : Telone II (technical grade 1.3-dichloroprorene containing 1.0% epichlorohydrin as a stabilizer) diluted in corn oil

Reliability : (1) valid without restriction
Study conducted by national standards.

Flag : Critical study for SIDS endpoint

30.04.2006 (90)

Species : rat
Sex : male/female
Strain : Fischer 344
Route of admin. : inhalation
Exposure period : 2 years
Frequency of treatm. : 6 hours/day, 5 days/week
Post exposure period :
Doses : 0, 5, 20, 60 ppm (0, 22.7, 90.8, 272.4 mg/m3)
Result :

Control group : yes, concurrent vehicle
Method :
Year : 1987
GLP : no data
Test substance : other TS: 1,3-DCP

Method : Groups of 70 male/70 female rats were exposed.

Observations included: mortality, behavior, body weight, hematology, clinical chemistry, urinalysis, gross necropsy, organ weights, histopathology, tumor incidence. Lung weights (abs./rel.) were not determined. Tissues/organs examined histopathologically included: adrenals, aorta, bone, bone marrow, brain, cecum, cervix, coagulating glands, colon, duodenum, dpididymides, esophagus, eyes, gross lesions, heart, jejunum, ileum, kidneys, lacrimal glands, larynx, liver, lungs, mammary gland, mediastinal lymph node, mediastinal tissues, mesenteric lymph nodes, mesenteric tissues, nasal tissues, oral tissues, ovaries, oviducts, pancreas, parathyroid glands, peripheral nerve, pituitary, prostate, rectum, salivary glands, seminal vesicles, skeletal muscle, skin, spinal cord, spleen, stomach, testes, thymus, thyroid gland, tongue, trachea, urinary bladder, uterus, and vagina.

Result : NOEL: 0.091 mg/L
LOEL: 0.272 mg/L

In the 60 ppm (male and female), body weights were significantly decreased during the first 425 days (male) or 327 days (female) of study, and back to normal afterwards.
In the 20 ppm (males), body weights were significantly decreased during days 117-327 of study.

In the 60 ppm (females), mean total protein and albumin values were significantly decreased.

In the 60 ppm group, at histopathology, significantly increased incidences of unilaterally/bilaterally decreased thickness of the olfactory epithelium (40% male/31% female affected), unilateral/bilateral erosions of the olfactory epithelium (30% male/12% female affected) and unilateral/bilateral submucosal fibrosis of the underlying olfactory mucosa (12% male/4% female affected) were observed.

In the 60 ppm (male), a slightly increased incidence of primary benign subcutaneous fibromas was observed (10% incidence versus 6% in the control group). Historical control data from 2-year studies showed a mean incidence of 5.7% for benign subcutaneous fibromas in the control (m) rats.

In the 60 ppm (female), a slightly increased incidence of these fibromas was observed (6% incidence versus 2% in the control group). Historical control data showed a mean incidence of 1.8%.

Incidence of Neoplasms:

Male Rats:	0 ppm	5 ppm	20 ppm	60 ppm
Adrenal:pheochromocoytoma:	8	4	8	2
Auditory sebaceous gland: carcinoma	0	2	3	0
Body cavity: mesothelioma	5	1	2	0
Hematopoietic system:				
leukemia, mononuclear cell	16	16	16	15
Liver: hepatocellular adenoma	3	3	3	0
Lungs: adenoma (bronchioalveolar)	2	1	0	0

Mammary gland: fibroadenoma	3	4	4	2
Mammary gland: adenoma	1	0	0	0
Mammary gland: adenocarcinoma/carcinoma	0	0	1	0
Oral tissue: hard palate squamous papilloma	2	1	3	0
Ovaries: granulose-thecal cell tumor	-	-	-	-
Pancreatic islets: adenoma	8	9	4	2
Pituitary (pars distalis) adenoma	14	18	17	19
Pituitary (pars distalis) carcinoma	2	0	0	0
Preputial/clitoral gland adenoma	3	1	1	1
Skin: squamous cell papilloma	0	2	3	1
Subcutis: fibroma	3	3	3	5
Testes: interstitial cell tumor	45	46	44	39
Thyroid: C-Cell adenoma	6	6	7	5
Thyroid: C-Cell carcinoma	0	0	0	0
Uterus: endometrial stromal polyp	-	-	-	-
Total rats with primary tumors:	49	48	50	48
Total rats with malignant tumors:	29	26	27	24

N = 50 per exposure level

Female Rats:	0 ppm	5 ppm	20 ppm	60 ppm
Adrenal:pheochromocoytoma:	0	1	4	0
Auditory sebaceous gland: carcinoma	0	1	0	0
Body cavity: mesothelioma	0	0	0	0
Hematopoietic system: leukemia, mononuclear cell	7	14	12	8
Liver: hepatocellular adenoma	1	0	1	1
Lungs: adenoma (bronchioalveolar)	0	0	0	0
Mammary gland: fibroadenoma	12	12	11	13
Mammary gland: adenoma	1	0	1	2
Mammary gland: adenocarcinoma/carcinoma	4	2	0	2
Oral tissue: hard palate squamous papilloma	1	1	2	0
Ovaries: granulose-thecal cell tumor	0	1	2	0
Pancreatic islets: adenoma	1	1	2	0
Pituitary (pars distalis) adenoma	26	22	17	23
Pituitary (pars distalis) carcinoma	1	0	0	0
Preputial/clitoral gland adenoma	0	0	1	0
Skin: squamous cell papilloma	2	1	1	1
Subcutis: fibroma	1	0	2	3
Testes: interstitial cell tumor	-	-	-	-
Thyroid: C-Cell adenoma	3	4	1	5
Thyroid: C-Cell carcinoma	0	2	0	0
Uterus: endometrial stromal polyp	17	16	12	13
Total rats with primary tumors:	45	46	43	41
Total rats with malignant tumors:	16	24	18	14

N = 50 per exposure level
No statistically significant differences reported
All diagnosed tumors were within the historical control range of previous chronic studies conducted in this laboratory using Fischer 344 rats. Historical control incidence data was not reported.

On the basis of these data the compound is not considered as a carcinogen.

Test substance : Telone II (d)
Reliability : (1) valid without restriction

Guideline study.

Flag : Critical study for SIDS endpoint
30.04.2006 (24) (68)

Species	:	mouse
Sex	:	male/female
Strain	:	B6C3F1
Route of admin.	:	inhalation
Exposure period	:	2 years
Frequency of treatm.	:	6 hours/day, 5 days/week
Post exposure period	:	
Doses	:	0, 5, 20, 60 ppm (0, 22.7, 90.8, 272.4 mg/m3)
Result	:	
Control group	:	yes, concurrent vehicle
Method	:	
Year	:	1987
GLP	:	no data
Test substance	:	other TS: 1,3-DCP

Method : Groups of 70 m/70 f mice were exposed.

Observations included: mortality, behavior, body weight, hematology, clinical chemistry, urinalysis, gross necropsy, organ weights, histopathology, tumor incidence. Lung weights (abs./rel.) were not determined. Tissues/organs examined histopathologically included: adrenals, aorta, bone, bone marrow, brain, cecum, cervix, coagulating glands, colon, duodenum, dpididymides, esophagus, eyes, gross lesions, gallbladder, heart, jejunum, ileum, kidneys, lacrimal glands, larynx, liver, lungs, mammary gland, mediastinal lymph node, mediastinal tissues, mesenteric lymph nodes, mesenteric tissues, nasal tissues, oral tissues, ovaries, oviducts, pancreas, parathyroid glands, peripheral nerve, pituitary, prostate, rectum, salivary glands, seminal vesicles, skeletal muscle, skin, spinal cord, spleen, stomach, testes, thymus, thyroid gland, tongue, trachea, urinary bladder, uterus, and vagina.

Result : NOEL = 0.023 mg/L
LOEL = 0.091 mg/L

In the 60 ppm (male and female), body weights were significantly decreased during the whole study (male) and during months 1-5 of study (female).

In the 60 ppm (male), RBC and Ht levels were significantly decreased, and serum BUN and AP activity increased, and serum globulin decreased; mean relative brain weight was significantly increased, and mean relative heart and kidney weights decreased.

At gross necropsy, in the 60 ppm (male), a significantly increased incidence of one or more lung masses is observed; in the 60 ppm (female), a significantly increased incidence of uterine mass/nodules was observed; in the 20 and 60 ppm (female), a dose-related signicantly increased incidence of roughened, irregular and opaque surface of the urinary bladder was observed.

In the 20 and 60 ppm (male and female), the most prominent non-neoplastic lesions were hyperplasia in the transitional epithelium of the urinary bladder and degeneration of the olfactory epithelium. In the 20 ppm (female) and the 60 ppm (male and female), hyperplasia of the respiratory epithelium was observed.

In the 60 ppm (male), a significantly increased incidence of hyperplasia of the non glandular stomach was observed; in the 60 ppm (female), a significantly increased incidence of decreased vacuolation of the liver and of dilatation/hypercellularity of the larynx and of chronic inflammation of the urinary bladder were observed.

In the 60 ppm (male), an increased incidence (22/50) of benign lung tumors (bronchioloalveolar adenomas) was observed comparing to the control group (9/50). In the females, no increased incidences were observed for this lesion.

Incidence of Neoplasms in Mice:

Male Mice:	0 ppm	5 ppm	20 ppm	60 ppm
Adrenal:pheochromocoytoma:	0	0	0	1
Bone: osteogenic sarcoma	0	0	0	0
Lacrimal gland: cystadenoma	1	6	9	4
Liver: hepatocellular adenoma	15	17	13	11
Liver: hepatocellular carcinoma	11	7	4	4
Liver:combined adenoma & carcinoma	25	22	16	14*
Lungs: adenoma (bronchioalveolar)	9	6	13	22*
Mammary gland: adenocarcinoma/carcinoma	-	-	-	-
Mesenteric lymph node: lymphosarcoma	2	3	2	0
Ovaries: hemangioma	-	-	-	-
Pituitary(pars distalis) adenocarcinoma	0	0	0	0
Pituitary(pars distalis) adenoma	0	0	0	1
Preputial gland: squamous cell carcinoma	0	2	0	0
Skeletal muscle: hemangiosarcoma	0	0	0	0
Spleen: hemangioma	0	0	1	0
Spleen: histiocytic sarcoma	1	3	0	0
Stomach: squamous papilloma	0	3	2	0
Urinary bladder: carcinoma	0	0	0	0
Urinary bladder: adenoma	0	0	0	0
Uterus: endometrial stromal polyp	-	-	-	-
Uterus: hemangioma	-	-	-	-
Uterus: leiomyoma	-	-	-	-
Uterus: leiomyosarcoma	-	-	-	-
Combined lymphoreticular tumors	6	8	3	0*
Total mice with primary tumors:	32	34	35	36
Total mice with malignant tumors:	18	17	11	7

N = 50 per exposure level

Female Mice:	0 ppm	5 ppm	20 ppm	60 ppm
Adrenal:pheochromocoytoma:	0	2	1	0
Bone: osteogenic sarcoma	2	0	0	0
Lacrimal gland: cystadenoma	6	3	3	3
Liver: hepatocellular adenoma	9	6	8	9
Liver: hepatocellular carcinoma	1	1	1	1
Liver:combined adenoma & carcinoma	10	7	9	10
Lungs: adenoma (bronchioalveolar)	4	3	5	3
Mammary gland: adenocarcinoma/carcinoma	2	0	0	1
Mesenteric lymph node: lymphosarcoma	3	11	5	6
Ovaries: hemangioma	3	1	2	0

Pituitary(pars distalis) adenocarcinoma	1	1	3	0
Pituitary (pars distalis) adenoma	9	16	11	7
Preputial gland:				
squamous cell carcinoma	-	-	-	-
Skeletal muscle: hemangiosarcoma	0	0	2	0
Spleen: hemangioma	0	0	2	2
Spleen: histiocytic sarcoma	6	0*	1	0*
Stomach: squamous papilloma	3	2	0	3
Urinary bladder: carcinoma	0	0	2	0
Urinary bladder: adenoma	0	0	1	0
Uterus: endometrial stromal polyp	3	4	1	4
Uterus: hemangioma	0	0	0	2
Uterus: leiomyoma	0	2	1	0
Uterus: leiomyosarcoma	0	0	1	2
Combined lymphoreticular tumors	10	14	9	8
Total mice with primary tumors: 39	40	36	36	
Total mice with malignant tumors:	19	17	20	13

N = 50 per exposure level

* = statistically significant difference from control by Yate's X2 pairwise test

On the basis of these data the compound is not considered as a carcinogen.

Test substance : Telone II (d)
Reliability : (1) valid without restriction
Guideline study.
Flag : Critical study for SIDS endpoint
30.04.2006 (23) (68)

5.8.1 TOXICITY TO FERTILITY

Type : other: sub-acute
Species : rat
Sex : male
Strain : other: Crl:CD(R)
Route of admin. : inhalation
Exposure period : 2 weeks
Frequency of treatm. : 6 hours/day, 5 days/week
Premating exposure period
Male :
Female :
Duration of test :
No. of generation studies :
Doses : 0, 10, 100 ppm
Control group : yes
Method : other
Year :
GLP : no
Test substance : other TS: 1,3-DCB, purity 99.5% (cis and trans mixture)

Method : General study details regarding standard repeated-dose toxicity endpoints are summarized in the repeated dose section of this document. Specific study details in regards to reproductive toxicity are below.

After the 10th exposure, 5 rats from each group were selected at random and sacrificed for gross and histopathological examination. Remaining rats

were sacrificed on the 14th day of recovery for identical examinations. Microscopic pathological evaluations were conducted on the testes and epididymides.

Result : No compound-related effects were observed in the testes and epididymides.

Reliability : (2) valid with restrictions
Study was valid with restrictions as a repeated-dose study. It was comparable to a guideline study with acceptable restrictions.

17.10.2005 (29)

Type : Two generation study
Species : rat
Sex : male/female
Strain : Fischer 344
Route of admin. : inhalation
Exposure period : > 10 weeks
Frequency of treatm. : every day
Premating exposure period
Male : 10 weeks
Female : 10 weeks
Duration of test :
No. of generation studies :
Doses : 10, 30, 90 ppm (45.4, 136.2, 408.6 mg/m3)
Control group : yes, concurrent vehicle
NOAEL parental : 30 ppm
NOAEL F1 offspring : 30 ppm
Method :
Year : 1987
GLP : no data
Test substance : other TS: 1,3-DCP

Method : Groups of 30 male/30 female rats were exposed to the product in air. After 10 weeks of exposure, the F0 generation was mated twice to produce F1a/F1b generations. Following 12 weeks of exposure, F1b adults were mated twice to produce F2a/F2b litters (during day 1-7 of study, exposure levels were 5, 20 and 60 ppm).
Exposure for 6 hours/day and 5 days/week prior to breeding, and 6 hours/day and 7 days/week during breeding, gestation and lactation.

Maternal animals were not exposed to the product from gestation day 21 through day 4 post-partum, or an equal no. of days for non-pregnant females.

Observations included:
Parental: mortality, behavior, body weight, gross necropsy, histopathology.
Litter: litter size, parturition date, no. live and dead fetuses, pup sex, litter weight, individual pup weight, gross necropsy.

Result : Mean body weights of F0 and F1 90 ppm (males) were decreased throughout most of the treatment-periods, and of F0 and F1 90 ppm (females) were slightly decreased during the pre-mating period (significantly in weeks 5 for F0 and in weeks 2 and 7 for F1). During gestation, body weight was slightly decreased in the F1 90 ppm (females) and during lactation, in the F0 and F1 90 ppm (females).

At histopathology, in the F0 and F1 90 ppm (male and female), an increased incidence of stomach lesions was observed (active and/or healing ulcers). Also a markedly increased incidence of changes in the nasal mucosa was observed in the F0 ans F1 90 ppm (male and female)

(25/60 F0 rats, 57/60 F1 rats). Changes consisted of slight subacute inflammation of the respiratory mucosa (F0-gen. only) and slight focal hyperplasia of the nasal respiratory mucosal epithelium. Additionally, in 3/60 F0 90 ppm and 15/60 F1 ppm rats, very slight focal degeneration of the nasal olfactory epithelium was observed.

No effects were observed on reproductive performance.

Test substance : Telone II (a)
Reliability : (1) valid without restriction
Guideline study.
Flag : Critical study for SIDS endpoint
19.12.2005 (20)

5.8.2 DEVELOPMENTAL TOXICITY/TERATOGENICITY

Species : rat
Sex : female
Strain : Fischer 344
Route of admin. : inhalation
Exposure period : gestation days 6-15
Frequency of treatm. : 6 hours/day
Duration of test :
Doses : 20, 60, 120 ppm (90.8, 272.4, 554.8 mg/m3)
Control group :
NOAEL maternal tox. : < 20 ppm
NOAEL teratogen. : > 120 ppm
Method :
Year : 1987
GLP : no data
Test substance : other TS: 1,3-DCP

Method : Groups of 30 (female) inseminated rats were exposed. Sacrifices took place on day 21 of gestation.

Observations included: mortality, clinical signs, body weight, food/water consumption, liver/kidney weights, no. of live/dead foetuses, no. resorption sites, corpora lutea, foetal sex/length/body weight, gross external foetal alterations, visceral/skeletal abnormalities.

Result : Dose-related decreased food consumption and body weight (gain) were observed in all compound-treated groups.

In the 120 ppm group, relative kidney weights were increased. In the 120 ppm group, a slightly but significantly increased no. of fetuses showed delayed ossification of vertebral centra; in the 60 ppm group, a slight increase was also observed (6% in the 120 ppm group, 5% in the 60 ppm group, 3% in the 30 ppm group and in control group).

No teratogenic effects were observed.

Test substance : Telone II (a)
Reliability : (1) valid without restriction
Guideline study.
Flag : Critical study for SIDS endpoint
19.12.2005 (50)

Species : rabbit
Sex : female
Strain : New Zealand white
Route of admin. : inhalation

Exposure period	:	gestation days 6-18
Frequency of treatm.	:	6 days/week
Duration of test	:	
Doses	:	20, 60, 120 ppm (90.8, 272.4, 554.8 mg/m3)
Control group	:	
NOAEL maternal tox.	:	20 ppm
NOAEL teratogen.	:	> 120 ppm
Method	:	
Year	:	1987
GLP	:	no data
Test substance	:	other TS: 1,3-DCP
Method	:	Groups of 25-31 (female) inseminated rabbits were exposed. Sacrifices took place on day 29 of gestation. Observations included: mortality, clinical signs, body weight, food/water consumption, liver/kidney weights, no. of live/dead fetuses, no. resorption sites, corpora lutea, fetal sex/length/body weight, gross external fetal alterations, visceral/skeletal abnormalities.
Result	:	During day 1-3 of exposure, weight loss was observed in the 60 and 120 ppm groups. No embryotoxic or teratogenic effects were observed.
Test substance	:	Telone II (a)
Reliability	:	(1) valid without restriction Guideline study.
Flag	:	Critical study for SIDS endpoint

19.12.2005 (50)

5.8.3 TOXICITY TO REPRODUCTION, OTHER STUDIES

5.9 SPECIFIC INVESTIGATIONS

5.10 EXPOSURE EXPERIENCE

Type of experience	:	Human
Remark	:	Exposure of workers to vapors of 1,3-DCB can cause dizziness and nausea.

20.02.2003 (31)

Type of experience	:	Human
Remark	:	To determine the irritating effect of 1,3-DCB on man, a test was performed on 12 volunteers. The threshold concentration causing only the perception of an odor was equal to 0.01 mg/L (1.9 ppm). The concentration producing an irritating effect on the mucous membranes of the eyes and upper respiratory tract was 0.02 mg/L (3.8 ppm).

19.12.2005 (4) (94)

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