FOREWORD INTRODUCTION

3,4-DICHLOROBUT-1-ENE

CAS N°: 760-23-6

SIDS INITIAL ASSESSMENT PROFILE

CAS No.	760-23-6
Chemical Name	3,4-Dichlorobut-1-ene
Structural Formula	CH_2=CH-CHCl-CH_2Cl

RECOMMENDATIONS

The chemical is a candidate for further work.

SUMMARY CONCLUSIONS OF THE SIAR

Human Health

Oral LD_{50} and inhalation LC_{50} of 3,4-dichlorobut-1-ene (3,4-DCB) are about 940 mg/kg and 2100 ppm, respectively. Inhalation repeated dose study in rats conducted for 14 days, 6 hours/day, 5 days/week at doses of 104 mg/m^3 (20 ppm) and 1037 mg/m^3 (200 ppm) of 3,4-DCB. Relative liver weight increased and change in liver cell morphology was observed at 1037 mg/m^3 dose. This chemical is slightly irritating to skin and eyes. Acute skin irritation in rabbits according to OECD TG 404 causes erythema but does not cause systemic intolerance reaction. Acute eye irritation study by instillation into the conjunctival sac of rabbits according to OECD TG 405 causes corneal opacity and conjunctival redness but does not cause systemic intolerance reaction.

In an oral study in rats by OECD combined repeated dose and reproductive/developmental toxicity screening test [OECD TG 422] at doses of 0, 0.4, 2, 10 and 50 mg/kg/day for at least 44 days, organ weight and histopathological changes were induced. In males, absolute kidney weights were slightly increased with 10 mg/kg and absolute and relative weights of the liver and kidneys were increased with 50 mg/kg. Blood chemical examination revealed an increase in total protein. The histopathological examination revealed increased hyaline droplets in the renal tubular epithelium with doses of 10 and 50 mg/kg and hepatocellular hypertrophy with dose of 50 mg/kg. In females, an increase in relative kidney weights was observed at the dose of 50 mg/kg. However, no histopathological changes related to the change of the kidney weight were detected. Hepatocellular hypertrophy was observed at the dose of 50 mg/kg. The NOAELs in this repeat dose study are 2 mg/kg/day for males and 10 mg/kg/day for females, but the renal toxicity in males is considered to be male rat specific, probably due to $alpha_{2U}$-globulin involvement. Therefore, the NOAEL for repeated dose toxicity is considered to be 10 mg/kg/day.

In a reproductive/developmental toxicity, there were no statistically significant adverse effects noted at any doses. Therefore a NOAEL for reproductive/developmental toxicity was considered to be 50 mg/kg/day. Evidence of malformations was not observed at any dose.

Three *in vitro* genotoxicity tests, bacterial reverse mutation, HPRT assay in CHO cells and chromosomal aberration in CHL/IU, indicate positive results. It also induced chromosomal aberration in rat bone marrow *in vivo* by inhalation. The carcinogenicity study of 3,4-DCB has not

been reported, but 1,4-dichlorobut-2-ene, an isomer of 3,4-DCB, was reported to induce nasal tumors in rats following long term inhalation exposure. Based on weight of evidence, this chemical could be considered as a potential carcinogen.

Environment

3,4-DCB is classified as not readily biodegradable [OECD TG 301C: 1-28% (av. 11%, based on BOD), 44-45% (av. 45 %, based on GC) after 28-days, OECD TG 301D: 0 % (based on BOD) after 28-days], but bioaccumulation potential is low (OECD TG 305C: <0.28 to 13.34). According to the fugacity calculation, this chemical mainly exists in the compartment where it is released. Considering the actual production and use, the chemical is released mainly in water. This chemical has been tested in a certain number of aquatic species. For the alga *Selenastrum*, 72 h EbC50 was 49 mg/L, and 72 h NOEC (biomass) was 14 mg/L. For *Daphnia*, the acute toxicity value of 10 mg/L (48 h EC50 for immobilization) and the chronic value of 0.83 mg/L (21 d NOEC for reproduction) were obtained. For fish acute toxicities, values of 27 mg/L (96 h LC50 for *Oryzias latipes*) and 7.17 mg/L (96 h LC50 for *Pimephales promelas*) were considered to be reliable. Assessment factor of 100 was chosen and applied to the lowest chronic value (NOEC for *Daphnia*; 0.83 mg/L) to determine PNEC, which is 8.3 micro-g/L.

Exposure

3,4-DCB is manufactured in closed system as the intermediate of chloroprene in Europe, US, and Japan. The production volume in Japan and Germany was approximately 50,000 and 50,000 - 100,000 tonnes/year in 1998, respectively. The worldwide production volume of this compound amounts to 300,000 - 400,000 tonnes/year by estimation.

All of the 3,4-DCB produced is also used in a closed system as an intermediate for the production of chloroprene. The use is limited to chloroprene manufacturing at the same facilities. Therefore, it does not have widespread use. Possible occupational exposure occurs through dermal contact and inhalation of vapour. The process is constructed by closed system and workers wear protective mask, gloves and goggles during the operation, so significant exposure is not expected. Marketed product, polychloroprene, does not contain 3,4-DCB as impurity. Therefore, there is no possibility of release of this compound to the environment from the consumer use.

NATURE OF FURTHER WORK RECOMMENDED

An exposure assessment is recommended in situations where there is the potential for exposure during the manufacture and/or use of the chemical (because of genotoxicity concerns).

FULL SIDS SUMMARY

CAS NO: 760-23-6		SPECIES	PROTOCOL	RESULTS
PHYSICAL-CHEMICAL				
2.1	Melting Point			- 61°C
2.2	Boiling Point			118.6 °C (at 1.013 hPa)
2.3	Density			1.153 at 25°C
2.4	Vapour Pressure			29.1 hPa at 25 °C
2.5	Partition Coefficient (Log Pow)		OECD TG 107	2.37
	BCF	*Cyprinus carpio*	OECD TG 305 C	< 0.28 – 13.34
2.6 A.	Water Solubility			1600 mg/l at 20 °C 1100 mg/l at 25 °C
B.	pH			
	pKa			
2.10	Explosiv Properties			UEL: 13.3%, LE : 22.4%
ENVIRONMENTAL FATE AND PATHWAY				
3.1.1	Photodegradation		Calculated (acc. to Atkinson)	In air (reaction with OH radicals)$T_{1/2}$: 14 hr (5×10^5 OH/cm^3) In air (reaction with ozone)$T_{1/2}$: 23 hr ($7x10^{11}$ ozone /cm3)
3.1.2	Stability in Water		OECD TG 111	$T_{1/2}$: 20.9 day at pH4 at 25 °C
				$T_{1/2}$: 33.3 day at pH7 at 25 °C
				$T_{1/2}$: 35.0 day at pH9 at 25 °C
3.2	Monitoring Data			
3.3	Transport and Distribution		Henry's law constant (Bond Contribution method)	$1.61*10^{+03}$ (Pa*m^3/mol)
			Calculated (Fugacity Level III)	If released to the air: in Air 98.3 % in Water 1.5 % in Sediment 0 % in Soil 0.2 %
3.5	Biodegradation		OECD TG 301 C	1-28 % (av. 11%) based on BOD
				44-45%(av. 45%) based on GC
				Not readily biodegradable
			OECD TG 301 D	0 %, based on BOD
ECOTOXICOLOGY				
4.1	Acute/Prolonged Toxicity to Fish	*Oryzias latipes*	OECD-TG 203	LC_{50} (96 hr) : 27 mg/l
			OECD-TG 204	LC_{50} (14 day) >21 mg/l
				NOEC (14 day) : 3.9 mg/l
		Pimephales promelas	OECD-TG 203	LC_{50} (96 hr) : 7.17 mg/l

CAS NO: 760-23-6		SPECIES	PROTOCOL	RESULTS
4.2	Acute Toxicity to Aquatic Invertebrates	*Daphnia magna*	OECD TG202	EC_{50} (24 hr) : 13 mg/l EC_{50} (48 hr) : 10 mg/l NOEC (48 hr): 4.6 mg/l
		Mysidopsis bahia	Other	LC50 (96 hr) : 7.4 mg/l
4.3	Toxicity to Aquatic Plants e.g. Alga	*Selenastrum capricornutum*	OECD TG 201	EC_{50} (72 h) : 49 mg/l (biomass) NOEC(72 h) : 14 mg/l (biomass)
4.5.2	Chronic Toxicity to Aquatic Invertebrates (*Daphnia*)	*Daphnia magna*	OECD TG 202	EC_{50}(21 day) : 4.0 mg/l (Reproduction)
				NOEC(21 day) : 0.83 mg/l (Reproduction)
4.6.1	Toxicity to Soil Dwelling Organisms			None
4.6.2	Toxicity to Terrestrial Plants			None
(4.6.3)	Toxicity to Other Non-Mammalian Terrestrial Species (Including Birds)			None
TOXICOLOGY				
5.1.1	Acute Oral Toxicity	Rat	OECD TG 401	LD_{50} : male: 943 mg/kg
				LD_{50} : female: 946 mg/kg
5.1.2	Acute Inhalation Toxicity	Rat		LC_{50} : 2100 ppm
5.1.3	Acute Dermal Toxicity	Rabbit	OECD TG 402	LD_{50} > 2000 mg/kg
5.2.1	Skin Irritation	Rabbit	OECD TG 404	Erythema was observed
5.2.2	Eye Irritation	Rabbit	OECD TG 405	Corneal opacity and irritation of the iris were observed.
5.2.3	Sensitisation			No available information.
5.4	Repeated Dose Toxicity			
	Oral	Rat	OECD TG 422	NOAEL: 10 mg/kg
5.5	Genetic Toxicity In Vitro			
A.	Bacterial Test (Gene mutation)	*S. typhimurium* (Ames test)	OECD TG 471, 472 and Japanese guide line	+ (with metabol. act.) + (without metabol. act.)
	Non-Bacterial In Vitro Test (Gene mutation)	CHO cells (HGPRT test)	According to OECD TG 476	- (with metabol. act.) + (without metabol. act.)
B.	Non-Bacterial In Vitro Test (Chromosomal aberrations)	CHL cells	OECD TG473 and Japanese guideline	+ (with metabol. act.) + (without metabol. act.)
5.6	Genetic Toxicity In Vivo	Rat (Cytogenetic assay)		+ (after inhalation exposure)
5.8	Toxicity to Reproduction	Rat	OECD TG 422	NOAEL: 50 mg/kg (Repro. Tox. parental) NOAEL: 50 mg/kg (Repro. Tox. F1 gen.)
5.9	Developmental Toxicity/ Teratogenicity			
5.11	Experience with Human Exposure			slightly irritating to skin

SIDS INITIAL ASSESSMENT REPORT (SIAR)

3,4-Dichlorobut-1-ene

1. IDENTITY

IUPAC Name: 3,4-Dichlorobut-1-ene
CAS Number: 760-23-6
Molecular formula: $C_4H_6Cl_2$

Structural formula:

CH_2=CH-CHCl-CH_2Cl

Synonym: 1-Butene, 3,4-dichloro-
3,4-Dichlorobutene-1
1,2-Dichloro-3-butene
1,2-Dichlorobut-3-ene

Purity: 98.5 %
3,4-Dichlorobut-1-ene (3,4-DCB) is produced as an intermediate for the production of chloroprene. 3,4-DCB is produced by the chlorination of butadiene in a mixture with cis- and trans-1,4-dichlorobut-2-ene. Those are isomerized to 3,4-dichlorobut-1-ene.
Impurities are as follows:
2,3-dichlorobutane
cis- and trans-1,4-dichlorobut-2-ene
1-chloro-1,3-butadiene
The ratio of the impurities of 3,4-DCB is considered to depend on the production processes.

Physical and chemical properties:

Melting Point	-61 °C
Boiling Point	118.6 °C
Vapour Pressure	29.1 hPa at 25 °C
Partition Coefficient (Log P_{ow})	2.37
Water Solubility:	1.6 g/l at 20 °C

2. GENERAL INFORMATION ON EXPOSURE

The production volume of 3,4-DCB in Japan and Germany was approximately 50,000 and 50,000 - 100,000 tonnes/year in 1998, respectively. The worldwide production volume of this compound amounts to 300,000 - 400,000 tonnes/year by estimation. In the above countries, all of the 3,4-DCB is produced and used in closed system as an intermediate for the production of chloroprene, which is polymerized to polychloroprene following process in the same facility. Therefore, there is no source of potential release to the environment except for sampling and maintenance of the production facilities.

Marketed product, polychloroprene, does not contain 3,4-DCB as impurity. Therefore, there is no possibility of release of this compound to the environment from the consumer use.

2.1 Environmental Fate

If released to the atmosphere, 3,4-DCB will react with photochemically produced hydroxyl radicals or ozone. Based upon an atmospheric concentration of 5 x 10^5 OH/ cm^3 and 7 x 10^{11} O_3/cm^3, the atmospheric half-life of this chemical has been estimated to be 14 and 23 hrs at 25 °C, respectively [Meylan W. M. et al. (1993)].

If released to water, abiotic degradation may occur through hydrolysis. The most likely degradation product of 3,4-DCB is 1,4-dihydroxybut-2-ene.

The hydrolysis half-life of 3,4-DCB has been experimentally determined to be 20.9, 33.3 and 35.0 days at pH 4, 7 and 9, respectively at 25 °C [MITI, Japan (1992)].

Based upon the biodegradation measurement (OECD TG 301C: 1-28% (av. 11%, based on BOD), 44-45% (av. 45%, based on GC) and 301D: 0% (based on BOD) after 28 days, respectively), 3,4-DCB is classified as not readily biodegradable[MITI, Japan(1992), Bayer(1999)]. Bioconcentration Factors ranging from <0.28 to 13.34 show that this chemical has low bioaccumulation potential [MITI, Japan (1992)].

2.2 Human Exposure

2.2.1 Occupational exposure

In Japan, 3,4-DCB is produced and used in closed system. Therefore, occupational exposure is limited in the case of sampling and maintenance at the production facilities. Moreover, the exposure time is very short. The major route of occupational exposure to 3,4-DCB is inhalation and dermal.

The atmospheric concentration was measured at two production sites in Japan. The monitoring data are shown in Annex. The maximum exposure level is estimated according to working schedules as follows. If the worker (Body weight; 70 kg, respiratory volume; 1.25 m^3/hour) is assigned to implement this operation without protection, the highest daily intake (EHE) is calculated as 0.048 mg/kg/day as the worst case.

Table 1: Available workplace monitoring data for 3,4-DCB

	Frequency Times/day	Duration hr	Working hr/day	Average Concentration ppm	Maximum EHE mg/kg/day	Combined EHE mg/kg/day
Cleaning of the strainer	<1	0.33	<0.33	0.46	0.014	
Sampling	1	0.017	0.017	0.12	1.86 x 10^{-4}	
Analysis	1	1.5	1.5	0.25	0.034	0.048

EHE: Estimated Human Exposure
Source: Japan Industrial Safety and Health Association Report

In Germany/Europe no workplace limit concentration is laid down. At Bayer AG the measurements show that exposure is well below the value of 0.02 ppm (= 0.1 mg/m3) for production and processing of 3,4-DCB in 1998 and 1999.

During sampling gas filter masks, goggles, and rubber gloves are worn. Depending on the work to be done during maintenance, gas filter masks or a respirator with independent air supply is used as well as full protective clothing.

There are no exposure limitation regulations enacted in the Sponsor countries.

2.2.2 Consumer exposure

There is no occupational exposure to this substace except at the chloroprene facility. The marketed product, polychloroprene, contains no 3,4-DCB as impurity, so it is not expected that downstream users or consumers of polychloroprene may expose to this compound.

2.2.3 Public human exposure

In Japan and Germany, there is no public human exposure.

In Germany, daily monitoring data (1998 and 1999) at the release of the industrial sewage treatment plant into the river Rhein showed no emission of 3,4-DCB from production and processing on the basis of the determination limit of 2 micro-g/l.

The exhaust from production and processing of 3,4-DCB at the Bayer AG site is connected to a thermal exhaust purification plant. Thus during normal operation of the thermal exhaust purification plant no 3,4-DCB is emitted. In 1998 and 1999 less than 25 kg/a (German threshold limit for the official emission declaration) 3,4-DCB were emitted into the atmosphere.

According to the monitoring data, 3,4-DCB was not detected in the general environment in Japan.

3. HUMAN HEALTH HAZARDS

3.1 Effects on Human Health

a) Toxicokinetics and metabolism and mechanism of action

There is no available information on toxico kinetics and metabolism and mechanisms of action of 3,4-DCB.

b) Acute toxicity

Acute toxicity data are reported for rats, mice, and rabbits. The data is shown in Table 2. The LD_{50} value of ca. 940 mg/kg bw and the LC_{50} value of 2100 ppm were reported for rats. 3,4-DCB is of moderate oral and inhalation toxicity.

The dermal LD_{50} in rabbits was > 2000 mg/kg bw (no fatalities) in a guideline study and under GLP. The acute toxicity of 3,4-DCB is low in dermal application.

Table 2. Summary of effects of 3,4-DCB on animals (Acute Toxicity)

Route	Animals	Values	Type	References
Oral	Rat	943 mg/kg for males 946 mg/kg for females	LD_{50}	Ministry of Health & Welfare, Japan, 1996
	Rat	879 mg/kg	LD_{50}	Gizhlaryan, M. S, 1981
	Rat	577 - 1153 mg/kg	LD_{50}	Bayer AG, 1959
Inhalation	Rat	2100 ppm	LC_{50}	Du Pont, Haskell Lab., 1967
Dermal	Rabbit	>2000 mg/kg bw	LD_{50}	Du Pont, Haskell Lab., 1993

Among the above, an oral rat study (MHW, Japan) was identified as the key study because it was well conducted and described in detail. Details of the study are as follows.

Male and female Crj:CD(SD) rats were administered orally at doses of 670, 804, 965, 1158, 1389 and 1667 mg/kg and observed for two weeks. Clinical signs of decreased locomotor activity, deep respiration, ptosis, salivation, flaccidity, adoption of a prone position, plioerection and perinasal soiling with nasal discharge were observed in the treated groups. At autopsy, lung enlargement, urine retention and crystalline materials in the urinary bladder, and hemorrhagic black spots in the glandular stomach mucosa were observed in animals. Fatalities were found for both sexes at doses of more than 804 mg/kg.

Conclusions:

The LD_{50} values were 943 mg/kg for males and 946 mg/kg for females. Based on these informations, acute toxicity of this chemical is likely moderate.

c) Repeated dose toxicity

Inhalation study in rats conducted for 14 days, 6 hours/day, 5 days/week at doses of 104 mg/m^3 (20 ppm) and 1037 mg/m^3 (200 ppm) of 3,4-DCB (purity 98.74%). An increased liver to body weight ratio and changes in liver cell morphology were observed at dose of 200 ppm. The NOAEL for repeated inhalation dosing (14 days) was considered to be 104 mg/m^3 (20 ppm), but the details are unknown [DuPont, Haskell Laboratory, USA (1987)].

In an oral study (via gavage) in rats by OECD combined repeated dose and reproductive / development toxicity screening test [OECD TG422], organ weight and histopathological changes were induced [MHW, Japan (1996)]. This MHW study was identified as the key study because it was well conducted and used a current protocol. Details of the study are as follows.

The study was conducted at doses of 0, 0.4, 2, 10 and 50 mg/kg/day for at least 44 days. In males, absolute kidney weights were slightly increased with 10 mg/kg/day dose. Absolute and relative weights of the liver and kidneys were increased with 50 mg/kg/day dose. Blood chemical examination revealed an increase in total protein. The histopathological examination revealed increased hyaline droplets in the renal tubular epithelium with doses of 10 and 50 mg/kg/day and hepatocellular hypertrophy with dose of 50 mg/kg/day.

In females, one female was sacrificed in a moribund condition on day 2 of lactation. An increase in relative kidney weights were observed at the dose of 50 mg/kg/day. However, no histopathological changes considered to be related to the change of the kidney weight were detected. Hepatocellular hypertrophy was observed at the dose of 50 mg/kg/day.

NOAELs in this repeat dose study are 2 mg/kg/day for males and 10 mg/kg/day for females, but the renal toxicity in males is considered to be male rat specific, probably due to α_{2U}-globulin involvement. Therefore, the NOAEL for repeated dose toxicity is considered to be 10 mg/kg/day.

There is no available information on human toxicity.

Conclusions:

Inhalation repeated dose study in rats conducted for 14 days, 6 hours/day, 5 days/week at doses of 104 mg/m^3 (20 ppm) and 1037 mg/m^3 (200 ppm) of 3,4-DCB. Relative liver weight increased and change in liver cell morphology was observed at 1037 mg/m^3 dose.

The NOAEL for repeat dose toxicity by oral administration is considered to be 10 mg/kg/day. The major toxicity is hepatocellular hypertrophy.

d) Reproduction/developmental toxicity

The OECD repeat dose and reproductive toxicity study was reported [MHW, Japan (1996)]. This study was identified to be well conducted and reported.

There were no significant differences in the number of offspring, sex ratio, live birth index, viability index and body weight. Number of pups alive on day 4 of lactation tended to be slight decreased with the 50 mg/kg/day dose, caused by litter loss from loss of nursing activity in one dam that was sacrificed in extremes on day 2 of lactation. No external or visceral anomalies related to the test substance administration were detected in any of the offspring. The NOAEL for the reproductive and offspring development is considered to be 50 mg/kg/day.

Conclusions:

The NOAEL for both reproductive performance and offspring development are considered to be 50 mg/kg/day (highest dose tested) in rats. No external or visceral anomalies related to the gavage administration of 3,4-DCB were detected in any of the offspring.

e) Genotoxicity (*in vitro*)

3,4-DCB has been tested for bacterial reverse mutation in Salmonella typhimurium and Escherichia coli with and without an exogenous metabolic activation by OECD TG 471 test. This chemical shows mutagenicity only in TA1535 at 1000 μg/plate, but not in other Salmonella typhimurium strains or Escherichia coli strain. In the case of TA1535, the number of induced colonies/plate, 20-30/mg-dose, indicates that this chemical is weakly mutagenic [MHW, Japan (1996)]. This study was identified to be a key stdudy because it was well conducted and reported.

The *in vitro* mammalian cell gene mutation test (HPRT assay) was conducted using Chinese Hamster Ovary cells with and without metabolic activation (OECD TG 476). The positive result was observed only without metabolic activation. [Du Pont, Haskell Laboratory, USA (1980)].

In the chlomosomal aberration test (OECD TG 473), this chemical induced structural chromosome aberrations and polyploidy in Chinese hamster lung cells (CHL/IU) with and without metabolic activation at the 50% growth inhibition - concentrations of 0.01 and 0.2 mg/ml, respectively [MHW, Japan (1996)].

Among these studies MHW study was identified to be a key study because it was well conducted and reported.

Conclusions:

3,4-DCB is mutagenic in bacterial and mammalian cells and induced chromosomal aberrations in mammalian cells *in vitro* assays.

f) Genotoxicity (in vivo)

3,4-DCB induced chromosomal aberrations in rat bone marrow cells after inhalation exposure for 30 and 120 days (4 hours/day, 5 days/week). The concentration of 13.7 and 81.3 mg/m^3 caused chromosome damages, mainly of the chromatid type. [Nalbandyan, T. I. et al. (1985)]

Another positive cytogenetic study is reported at the concentration of 13.9 and 107.8 mg/m^3 in the bone marrow. [Gizhalaryan, M. S. et al. (1984)]

Conclusions:

3,4-DCB is clastogenic in rat bone marrow *in vivo* assays.

g) Other human health related information

Irritation and Sensitisation

Animal data

This chemical is slightly irritating to skin and eyes.

According to the LTP study by acute skin irritation test (OECD TG 404), all three rabbits exposed for 4 hours of undiluted 3,4-DCB showed an erythema (grade 1 or 2) for up to 72 hours after patch removal. But systemic intolerance reaction does not occured. [Laboratory of Pharmacology and Toxicology KG, Germany, Report No. 9300/382/95(1999)]. This study was identified as the key study because it was well conducted by GLP Lab.

In the eye irritation study, LPT study was also identified as the key study because it was well conducted by GLP Lab. According to the acute eye irritation study (OECD TG 405) by instillation into the conjunctival sac of three rabbits, corneal opacity (grade 1) and irritation of the iris (grade 1) were observed in a rabbit 1 to 48 hours after instillation and conjunctival redness (grade 1) was observed in all three rabbits 1 hour after instillation. But there was no systemic intolerance reaction. 3,4-DCB is slightly irritating to the eyes [Laboratory of Pharmacology and Toxicology KG, Germany Report No. 9301/382/95 (1999)].

There are no available data for sensitisation.

Human data

It is reported that protracted contact with skin causes dermatitis and blistering. High concentrations in vapour apparently have delayed toxic effect on eyes, causing onset of irritation and lacrimation several hours after the exposure [Grant, W. M. (1986)].

It is also reported that after application of a 3,4-DCB-soaked cotton swab for 0.5 to 1 hour, only slight irritation effects were seen on the skin of 5 test persons [Bayer AG (1959)].

Conclusion

This chemical is slightly irritating to skin and eyes. Acute skin irritation in rabbits according to OECD TG 404 causes erythema but does not cause systemic intolerance reaction. Acute eye

irritation study by instillation into the conjunctival sac of rabbits according to OECD TG 405 causes corneal opacity and conjunctival redness but does not cause systemic intolerance reaction.

There are no available data for sensitisation.

Structure related information

The chlorination of butadiene gives a mixture of 3,4-DCB and cis-1,4-dichlorobut-2-ene and trans-1,4-dichlorobut-2-ene. The toxicity of 1,4-dichlorobut-2-ene is reported to be LD_{50}: 89 mg/kg in rat [AMA Archives of Industrial Hygiene and Occupational Medicine], LC_{50}(4 hr): 86 ppm in rat [Kennedy GL Jr et al (1982)]. On the other hand, in the case of 3 weeks repeated dose inhalation study with the mixture (37.3 % of 3,4-DCB, 17 % of *cis*-1,4-dichlorobut-2-ene, and 45.7 % of *trans*-1,4-dichlorobut-2-ene), the 18-ppm dose rat-group appeared to have progressive weight loss, lungs hemorrhagic, thymus atrophied, lungs emphysematous with areas of hemorrhage and edema (histol.). The 6-ppm dose appeared to have initial weight loss, thymus slight atrophy; 2-3 ppm appeared to have no toxic signs, organs normal (autopsy) [Gage, J. C. (1970)].

It is also reported that the mutagenic activity of 1,4-dichlorobut-2-ene is higher than that of 3,4-DCB because of the chlor-methyl carbon of the aryl substituent. In the case of 3,4-DCB, it is in the middle of carbon chain, not at the end of the chain. [Nalbandyan, T. I. et al. (1985)]

1,4-Dichlorobut-2-ene is classified in the EU as a carcinogen in Category 2. It was reported to induce malignant nose tumors in Chr:CD rats by inhalation exposure of 5 ppm of 1,4-dichlorobut-2-enes for 30 weeks followed by exposure for 2.5 ppm for 23 weeks.

Conclusion

One of the isomers of 3,4-DCB is 1, 4-dichlorobut-2-ene and its toxicity is higher than that of 3,4-DCB. The difference of the toxicity is considered to be the position of the chlorine atom in aryl substance.

3.2 Initial Assessment for Human Health

Oral LD_{50} and inhalation LC_{50} of 3,4-DCB are about 940 mg/kg and 2100 ppm, respectively. This chemical is moderately irritating to skin and irritating to eyes.

In an oral study in rats by OECD combined repeated dose and reproductive/developmental toxicity screening test, organ weight and histopathological changes were induced.

The NOAEL for repeat dose toxicity is considered to be 10 mg/kg/day.

In a reproductive/developmental toxicity, there were no statistically significant adverse effects noted at any doses. Therefore a NOAEL for reproductive / developmental toxicity was considered to be 50 mg/kg/day. Evidence of malformations was not observed at any dose.

Three *in vitro* genotoxicity tests, bacterial reverse mutation, HPRT assay in CHO cells and chromosomal aberration in CHL/IU, indicate positive results. It also induced chromosomal aberration in rat bone marrow *in vivo* by inhalation. The carcinogenicity study of 3,4-DCB has not been reported, but 1,4-dichlorobut-2-ene, an isomer of 3,4-DCB, was reported to induce nasal tumors in rats following long term inhalation exposure. Based on weight of evidence, this chemical could be considered as a potential carcinogen.

4. EFFECTS ON THE ENVIRONMENT

4.1 Aquatic Effects

Effects of 3,4-DCB on aquatic organisms are summarized in Table 3. The acute toxicity data (96 h LC_{50}) for fish ranged from 7.17 to 27 mg/l. We chose 27 mg/l for *Oryzias latipes* as a reliable value, because purity of the chemical used in the experiment was high enough to neglect toxicity of impurities. The crude product of 3,4-DCB contains cis-, and trans-1,4-dichlorobut-2-ene, those toxicities are more toxic than that of 3,4-DCB. Their aquatic toxicity to fish, 96 hour TLm, was reported to be as follows: 85 ppm (3,4-DCB) and 0.37 ppm (mixture of 3,4-DCB: 14 % and 1,4-dichlorobut-2-ene: 86 %) [ANSP, 1971].

The lower values of LC50 are reported by Geiger. Though the purity used in those tests are unknown, the tests are based on measured concentration. Therefore, the lowest value, 7.17 mg/l should not be considered unreliable.

In conclusion, the LC50 of 3,4-DCB for fish is concidered to be 7 – 27 mg/l.

Based on weight of evidence, this chemical indicats the modelate toxicity for aquatic biota.

Table 3: Summary of effects of 3,4-DCB on aquatic organisms

Organism	Test duration	Result (mg/l)	Reference
Micro organisms			
Pseudomonas putida	3 day	EC_{50} : 2,950	Bayer AG, 1999
Invertebrates			
Water flea (*Daphnia magna*)	24 hr (cl, s)	EC_{50} (Imm) : 13 (m)	Environment Agency of Japan, 1997
Water flea (*Daphnia magna*)	48 hr (cl, s)	EC_{50} (Imm): 10 (m) NOEC(Imm):4.6(m)	Environment Agency of Japan, 1997
Water flea (*Daphnia magna*)	48 hr (cl, s)	EC_{50} (Imm): 13.4 (nc*)	Bayer AG, 1999
Water flea (*Daphnia magna*)	21 day (cl, ss)	EC_{50}(Rep): 4.0(m) NOEC (Rep): 0.83 (m)	Environment Agency of Japan, 1997
Misid (*Mysidopsis bahia*)	96 hr (op, f)	LC_{50} : 7.4	Du Pont, Haskell Laboratory, 1994
Fish			
Medaka(*Oryzias latipes*)	48 hr (op, ss)	LC_{50} : 22.6 (nc*)	MITI, Japan, 1992
Medaka (*Oryzias latipes*)	96 hr (op, f)	LC_{50} : 27 (nc*)	Environment Agency of Japan, 1997
Medaka (*Oryzias latipes*)	14 day (op, f)	LC_{50}: >21 (nc*) NOEC: 3.9 (nc*)	Environment Agency of Japan, 1997
Fathead Minnows (*Pimephales promelas*)	96 hr (op, f)	LC_{50} : 7.17	Geiger, D. L., 1988
Fathead Minnows (*Pimephales promelas*)	96 hr (op, f)	LC_{50} : 9.33	Geiger, D. L., 1985
Algae			
Green alga (*Selenastrum capricornutum*)	72 hr (cl) 72 hr (cl)	EC_{50} (Bms): 49 (m) NOEC(Bms): 14 (m)	Environment Agency of Japan, 1997
Diatom (*Navicula seminulum*)	7 day (cl)	EC_{50} (Gr): 275 vol ppm	ANSP, 1971

Test method:

cl = closed system m = measured concentration f = flow through op = open system
s = static ss = semi-static nc = nominal concentration
nc* = calculated based on nominal concentrations, because measured concentrations were >80% of nominal concentrations
Bms = biomass Imm = immobilization Rep = reproduction Gr = Growth rate

4.2 Terrestrial effects

There is no available information.

4.3 Other

There is no available information.

4.4 Initial Assessment for the Environment

3,4-DCB is classified as not readily biodegradable [OECD TG 301C: 1-28% (av. 11%, based on BOD), 44-45 % (av. 45%, based on GC) after 28-days, OECD TG 301D: 0 % (based on BOD) after 28-days] , but bioaccumulation potential is low (OECD TG 305C : <0.28 to 13.34).

According to the fugacity calculation, this chemical mainly exists in the compartment where it is released. Considering the actual production and use, the chemical is released mainly in water.

As the acute and chronic toxicity data, 7 - 27 mg/l (96 h LC_{50}) of Fathead Minnows (*Pimephales promelas*) and Misid (*Mysidopsis bahia*)and 0.83 mg/l (21 d NOEC) of *Daphnia magna* were adopted, respectively. Assessment factor of 100 was chosen and applied to the lowest chronic toxicity value (0.83 mg/l) to determine PNEC, which is 8.3 μg/l.

5. CONCLUSIONS AND RECOMMENDATIONS

5.1 Conclusion

Physical/chemical property, production, use and distribution

3,4-DCB is classified as not readily biodegradable (OECD TG 301C: 1-28 % (av. 11%, based on BOD), 44-45% (av. 45%, based on GC) and TG 301D: 0 % (based on BOD) after 28-days), but bioaccumulation potential is low (OECD TG 305C : <0.28 to 13.34).

This chemical is manufactured in closed system as the intermediate of chlroprene in Europe, US and Japan. The production volume in Japan and Germany was approximately 50,000-tonnes/year and 50,000 - 100,000 tonnes/year in 1998, respectively. The word wide production volume of this compound amount to 300,000 - 400,000 tonnes/year by estimation.. The use is limited to chloroprene manufacturing at the same facilities. Therefore it has not widespread use. A generic fugacity model (Mackey level III) shows this chemical would be distributed mainly to released compartment of the environment. In actual production and use, this compound is released mainly in water, through waste stream generated at the production site, while apparatus and equipment are washed.

Occupational exposure may occur through dermal contact and inhalation of vapour. The process is constructed by closed system and workers wear protective gloves and gouges during the operation, so significant exposure is not expected. The occupational exposure route may be an inhalation in limited workers. Based on the inhalation toxicity studies, NOAEL of this compound is considered to be 104 mg/m^3. The occupational daily intake is calculated as 0.048 mg/kg/day as the worst case.

Human health

Acute toxicity of 3,4-DCB is moderate; LD_{50}: ca. 940 mg/kg.

This chemical is slightly irritating to the skin and eyes. In an oral study in rats, organ weight and histopathological changes were induced. The NOAEL for repeat dose toxicity of oral dose is considered to be 10 mg/kg/day.

The NOAEL for both reproductive performance and offspring development are considered to be 50 mg/kg/day (highest dose tested) in rats. No external or visceral anomalies related to the gavage administration of this chemical were detected in any of the offspring.

Three *in vitro* genotoxicity tests, bacterial reverse mutation, HPRT assay in CHO cells and chromosomal aberration in CHL/IU, indicate positive results. It also induced chromosomal aberration in rat bone marrow *in vivo* by inhalation. The carcinogenicity study of 3,4-DCB has not been reported, but 1,4-dichlorobut-2-ene, an isomer of 3,4-DCB, was reported to induce nasal tumors in rats following long term inhalation exposure. Based on weight of evidence, this chemical could be considered as a potential carcinogen.

Environment

3,4-DCB is classified as not readily biodegradable [OECD TG 301C: 1-28% (av. 11%, based on BOD), 44-45 % (av. 45%, based on GC) after 28-days, OECD TG 301D: 0 % (based on BOD) after 28-days], but bioaccumulation potential is low (OECD TG 305C: <0.28 to 13.34).

According to the fugacity calculation, this chemical mainly exists in the compartment where it is released. Considering to the actual production and use, the chemical is released mainly in water.

This chemical has been tested in a certain number of aquatic species. For the alga *Selenastrum*, 72 h EbC_{50} was 49 mg/l, and 72 h NOEC (biomass) was 14 mg/l. For *Daphnia*, the acute toxicity value of 10 mg/l (48 h EC_{50} for immobilization) and the chronic value of 0.83 mg/l (21 d NOEC for reproduction) were obtained. For fish acute toxicities, values of 7 - 27 mg/l (96 h LC_{50} for Fathead Minnows (*Pimephales promelas*) and Misid (*Mysidopsis bahia*)) were considered to be reliable. Assessment factor of 100 was chosen and applied to the lowest chronic value (NOEC for *Daphnia*; 0.83 mg/l) to determine PNEC, which is 8.3 μg/l.

5.2 Recommendations

An exposure assessment is recommended in situations where there is the potential for exposure during the manufacture and/or use of the chemical (because of genotoxicity concerns).

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Annex to SIAR

Table 1. Available workplace monitoring data for 3,4-DCB at 2 facilities in Japan

Activity	Monitoring data / ppm			Comment
	Max.	Min.	Mean	
Sampling	<0.25	<0.05	0.12	N=8
Analysis	1.65	<0.05	0.26	N=8
Maintenance	2.53	<0.05	0.46	N=6
Overall	2.53	<0.05	0.26	N=22

Comment: Air sample was taken at the breathing zone of the worker.
LDL: 0.05ppm
Source: Japan Industrial Safety and Health Association Report 2000

SIDS DOSSIER
ON THE HPV CHEMICAL

3,4-dichlorobut-1-ene

CAS No. 760-23-6

Sponsor Country: Japan / Germany

DATE: May 25, 2001

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Note: *; Data elements in the SIDS
†; Data elements specially required for inorganic chemicals

1. GENERAL INFORMATION

1.01 SUBSTANCE INFORMATION

***A.**	**CAS-Number**	760-23-6
B.	**Name** *(IUPAC name)*	3,4-Dichloro-1-butene
***C.**	**Name** *(OECD name)*	3,4-dichlorobut-1-ene
†D.	**CAS Descriptor**	Not applicable in this case
E.	**EINECS-Number**	212-079-0
F.	**Molecular Formula**	$C_4H_6Cl_2$
***G.**	**Structural Formula**	CH_2=CHCHClCH_2Cl
H.	**Substance Group**	Not applicable
I.	**Substance Remark**	
J.	**Molecular Weight**	125.00

1.02 OECD INFORMATION

A. Sponsor Country: Japan and Germany

B. Lead Organisation:

Name of Lead Organisation:
TOSOH CORPORATION
Akira YAMAGUCHI
Shiba-Koen First Bldg.
3-8-2, Shiba, Minato-ku, Tokyo 105-8623, Japan
Tel: 81-3-5427-5127 Fax: 81-3-5427-5203
E-mail: a_yamagu@tosoh.co.jp

Contact person of Japan:
Mr. Koji Tomita
Ministry of Foreign Affairs
Economic Affairs Bureau
Second International Organisations Div.

Address:
2-2-1 Kasumigaseki, Chiyoda-ku
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Japan
Tel: 81-3-3581-0018 Fax: 81-3-3581-9470
Em: seiichi.urauchi@mofa.go.jp

Contact person of Germany:
Mr. Ernst Goedecke
Bundesanstalt fur Arbeitsschutz und Arbeitsmedizin (BAuA)
Anmeldestelle Chemikaliengesetz

Address:
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D-44149 Dortmund, Germany
Tel: 49-231- 9071-548
Fax: 49-231-9071-679
Em: amst@baua.do.shuttle.de

C. Name of responder

Name: Same as contact persons
Address:

Tel: .....
Fax: .....

1.1 GENERAL SUBSTANCE INFORMATION

A. Type of Substance

element [ ]; inorganic [ ]; natural substance [ ]; organic [**X**]; organometallic [ ]; petroleum product [ ]

B. Physical State *(at 20°C and 1,013 hPa)*

gaseous [ ]; liquid [**X**]; solid [ ]

C. Purity 98.6% weight/weight

1.2 SYNONYMS 1-Butene, 3,4-dichloro-,3,4-Dichloro-1-butene
3,4-Dichlorobutene-1, 1,2-Dichloro-3-butene
1,2-Dichlorobut-3-ene

1.3 IMPURITIES 1-Chloro-1, 3-butadiene, 1,4-Dichlorobut-2-ene
2,3-Dichlorobutane

1.4 ADDITIVES None

***1.5 QUANTITY**

Remarks: The production volume in Japan and Germany was approximately 50,000 and 50,000 - 100,000 tones/year in 1998, respectively. The worldwide production volume of this compound amounts to 300,000 - 400,000 tones/year by estimation.
Reference: TOSOH (2000)

1.6 LABELLING AND CLASSIFICATION

***1.7 USE PATTERN**

A. General

	Type of Use:	**Category:**
(a)	main industrial use	Non dispersive use Chemical Industry: use as an intermediate in the production of chloroprene
(b)	main industrial use	Non wide dispersive use Non personal and domestic use

Remarks: (a) 100 % was used in a factory in Japan in 1997
Reference: TOSOH (1999)

B. Uses in Consumer Products

None

1.8 OCCUPATIONAL EXPOSURE LIMIT VALUE

None

*1.9 SOURCES OF EXPOSURE

3,4-DCB is manufactured in closed system as the intermediate of chloroprene in Europe, US, and Japan.

(a)

Source:	Media of release: Air and water Quantities per media: No data TOSOH's Nanyo Manufacturing complex is one of a production site in Japan.
Remarks:	**TOSOH** produced 35,000 t/y of 3,4-dichlorobut-1-ene (3,4-DCB) as an intermediate in the production of chloroprene in 1998. The processes are constructed by the closed system. Small amount of 3,4-DCB is released into the environment in the case of sampling and maintenance.
Reference:	TOSOH (1999)

(b)

Source:	Media of release: Air Quantities per media: less than 25 kg/y
Remarks:	Daily monitoring data (1998 and 1999) at the release of the industrial sewage treatment plant into the receiving river Rhein showed no emission of 3,4-DCB from production and processing on the basis of the determination limit of 2 ug/l. The exhaust from production and processing of 3,4-DCB at Bayer AG site is connected to a thermal exhaust purification plant. Thus during normal operation of the thermal exhaust purification plant no 3,4-DCB is emitted. In 1998 and 1999 less than 25 kg/y (German threshold limit for the official emission declaration) 3,4-DCB were emitted into the atmosphere.
Reference:	Bayer AG (2000)

2. PHYSICAL-CHEMICAL DATA

*2.1 MELTING POINT

Value:	- 61 °C
Decomposition:	Yes **[ ]** No **[X]** Ambiguous **[ ]**
Sublimation:	Yes **[ ]** No **[X]** Ambiguous **[ ]**
Method:	unknown
GLP:	Yes **[ ]** No **[ ]** ? **[X]**
Remarks:	
Reference:	Aldrich Chemical Co., Inc. (1999)

*2.2 BOILING POINT

(a) **Preferred result**

Value:	118.6°C
Pressure:	1,013hPa (approx. atmospheric)
Decomposition:	Yes **[ ]** No **[X]** Ambiguous **[ ]**
Method:	unknown
GLP:	Yes **[ ]** No **[ ]** ? **[X]**

Remarks:
Reference: Gerhartz, W. (1985)

(b)
Value: 115.5°C
Pressure: at 1,013 hPa (approx. atmospheric)
Decomposition: Yes **[ ]** No **[X]** Ambiguous **[ ]**
Method: unknown
GLP: Yes **[ ]** No **[ ]** ? **[X]**
Remarks:
Reference: Votko, et al (1972)

(c)
Value: 123°C
Pressure: 1,013 hPa (approx. atmospheric)
Decomposition: Yes **[ ]** No **[X]** Ambiguous **[ ]**
Method: unknown
GLP: Yes **[ ]** No **[ ]** ? **[X]**
Remarks:
Reference: Aldrich Chemical Co., Inc. (1999)

†2.3 DENSITY (Relative density)

(a) **Preferred result**
Type: Bulk density **[ ]**; Density **[ ]**; Relative Density **[X]**
Value: 1.153
Temperature: 25°C
Method: unknown
GLP: Yes **[ ]** No **[ ]** ? **[X]**
Remarks:
Reference: Gerhartz, W (1985)

(b)
Type: Bulk density **[ ]**; Density **[ ]**; Relative Density **[X]**
Value: 1.1491
Temperature: 20°C
Method: unknown
GLP: Yes **[ ]** No **[ ]** ? **[X]**
Remarks:
Reference: Ogloblin, K. A. (1961)

*2.4 VAPOUR PRESSURE

(a) **Preferred result**
Value: 29.1 hPa (21.85mmHg)
Temperature: 25 °C
Method: calculated **[ ]**; measured **[X]**
GLP: Yes **[ ]** No **[ ]** ? **[X]**
Remarks:
Reference: Daubert, T.E.et al (1989)

(b)
Value: 22.7 hPa (17mmHg)
Temperature: 25 °C
Method: calculated **[ ]**; measured **[X]**

GLP: Yes **[ ]** No **[ ]** ? **[X]**
Remarks:
Reference: Aldrich Chemical Co., Inc. (1999)

(c)
Value: 26 hPa
Temperature: 25 °C
Method: calculated **[X]**; measured **[ ]**
GLP: Yes **[ ]** No **[ ]** ? **[X]**
Remarks: value taken from vapour pressure curve
Reference: Bayer AG (1980)

(d)
Value: 34.7 hPa (26.0mmHg)
Temperature: 25 °C
Method: calculated **[ ]**; measured **[X]**
Remarks:
Reference: Jaber (1983)

***2.5 PARTITION COEFFICIENT $log_{10}P_{ow}$**

(a) **Preferred result**
Log Pow: 2.37
Temperature: 25ºC
Method: calculated **[ ]**; measured **[X]**
OECD TG107
GLP: Yes **[X]** No **[ ]** ? **[ ]**
Remarks:
Reference: Chemicals Inspection and Testing Institute of Japan (1992)

(b)
Log Pow: 2.34
Temperature: no data
Method: calculated **[ ]**; measured **[ ]**
GLP: Yes **[ ]** No **[ ]** ? **[ ]**
Remarks:
Reference: Jaber (1983)

(c)
Log Pow: 2.00
Temperature: no data
Method: calculated **[X]**; measured **[ ]**
Leo, A.: CLOGP-3.54 MedChem Software 1989. Daylight, Chemical Information System, Claremont. CA 91711, USA
GLP: Yes **[ ]** No **[ ]** ? **[ ]**
Remarks:
Reference: Bayer AG (1991)

***2.6 WATER SOLUBILITY**

A. Solubility

(a) **Preferred result**
Value: 1.6g/l
Temperature: 20 °C

Method: unknown
GLP: Yes **[ ]** No **[ ]** ? **[X]**
Remarks:
Reference: Bayer AG data (1980)

(b)
Value: 1.1g/l
Temperature: 25 °C
Method: unknown
GLP: Yes **[ ]** No **[ ]** ? **[X]**
Remarks:
Reference: DuPont, Haskell Laboratory

(c)
Value: 420 mg/l
Temperature: no data
Description: Miscible**[ ]**; Of very high solubility **[ ]**;
Of high solubility **[ ]**; Soluble **[ ]**; Slightly soluble **[ ]**;
Of low solubility **[X]**; Of very low solubility **[ ]**; Not soluble **[ ]**
Method: unknown
GLP: Yes **[ ]** No **[ ]** ? **[X]**
Remarks:
Reference: ITC/USEPA (1980)

B. pH Value, pKa Value

No data available.

2.7 FLASH POINT

(a) **Preferred result**
Value: 30°C
Pressure: unknown
Method: DIN 51755
GLP: Yes **[ ]** No **[X]** ? **[ ]**
Remarks: Type: closed cup
Reference: Bayer AG (1986)

(b)
Value: 28 °C
Pressure: unknown
Method: unknown
GLP: Yes **[ ]** No **[ ]** ? **[X]**
Remarks:
Reference: Aldrich Chem Co, (1994)

2.8 AUTO FLAMMABILITY

No data available.

2.9 FLAMMABILITY

Results: Extremely flammable **[ ]**; Extremely flammable - liquefied gas **[ ]**;
Highly Flammable **[ ]**; Flammable **[X]**; Non flammable **[ ]**;

Spontaneously flammable in air **[ ]**; Contact with water liberates highly flammable gases **[ ]**; Other **[ ]**
Method: unknown
GLP: Yes **[ ]** No **[ ]** ? **[X]**
Remarks:
Reference: Aldrich Chemical Co., Inc. (1999)

2.10 EXPLOSIVE PROPERTIES

Results: UEL: 13.3 %
LEL: 2.4 %
Method: ASTM E-681
Reference: Du Pont (2000)

2.11 OXIDIZING PROPERTIES

Results: Maximum burning rate equal or higher than reference mixture **[ ]**;
Vigorous reaction in preliminary test **[X]**;
No oxidising properties **[ ]**; Other **[ ]**
Method: unknown
GLP: Yes **[ ]** No **[ ]** ? **[X]**
Remarks: Strong oxidising agents
Reference: Aldrich Chemical Co., Inc. (1999)

†2.12 OXIDATION: REDUCTION POTENTIAL

No data available.

3. ENVIRONMENTAL FATE AND PATHWAYS

3.1 STABILITY

*3.1.1 PHOTODEGRADATION

Type: Air **[X]**; Water **[ ]**; Soil **[ ]**; Other **[ ]**
Light source: Sun light **[ ]**; Xenon lamp **[ ]**; Other **[ ]**
Light spectrum:
Relative intensity:
Spectrum of substance:
Concentration of Substance: unknown
Temperature: 25 °C
Direct photolysis: no data
Half life:
Degradation:
Quantum yield:
Indirect Photolysis:
Type of sensitises: OH radical, ozone
Concentration of sensitise: OH radical: 5 x 10^{5} mol/cm3
Ozone: 7 x 10^{11} mol/cm3
Rate constant (radical): with OH radical: 2.69 x 10^{-11} cm^{3}/molecule*sec
With ozone: 1.2 x 10^{-17} cm^{3}/molecule*sec
Degradation: 50% after 14 hours (OH radical), 23 hours (ozone)
Method: calculated **[X];** measured **[ ]**

The rate constant for the vapor-phase reaction of 3,4-DCB with photochemically produced hydroxyl radicals or ozone was calculated by the method of a computer program, which is developed by Atkinson and co-workers.

GLP: Yes **[ ]** No **[ ]** ? **[X]**
Test substance: -
Remarks:
Reference: Meylan WM et al (1993)

*3.1.2 STABILITY IN WATER

(a)
Type: Abiotic (hydrolysis) **[X]**; biotic (sediment)**[ ]**
Half life: 20.9days at pH4 at 25 °C
33.3days at pH7 at 25 °C
35.0days at pH9 at 25 °C
Method: OECD TG 111
GLP: Yes **[X]** No **[ ]** ? **[ ]**
Test substance: Tokyo Kasei Kogyo, purity: 99.6 %
Remarks:
Reference: Chemicals Inspection and Testing Institute, Japan (1992)

(b)
Type: Abiotic (hydrolysis) **[X]**; biotic (sediment)**[ ]**
Half life: 3.2 days at 25 °C
Method: Estimation from the isomers
GLP: Yes **[ ]** No **[ ]** ? **[ ]**
Test substance: -
Remarks: The hydrolysis half-life is estimated by the data of other dichlorobutenes (cis and trans-1,4-dichlorobut-2-ene).
Reference: Ellington J. J (1989)

3.1.3 STABILITY IN SOIL

Type: Field trial **[ ]**; Laboratory **[ ]**; Other **[ ]**
Radiolabel: Yes **[ ]** No **[ ]** ? **[ ]**
Concentration: mg/kg
Soil temperature: °C
Soil humidity: % of field capacity
Soil classification: DIN19863 **[ ]**; NF X31-107 **[ ]**; USDA **[ ]**; Other **[ ]**
Content of clay etc.:
Organic Carbon:
Soil pH:
Cation exchange capacity: m mol/kg
Microbial biomass:
Dissipation time: DT 50: 3.2 days
Dissipation: 10 % after 1 day, 37% after 2 days, 60% after 4 days
Method: OECD TG 304A (1981)
GLP: Yes **[ ]** No **[ ]** ? **[X]**
Test substance: purity: = unknown
Remarks: Hydrolysis may be an important degradation process for 3,4-DCB in moist soil. The hydrolysis half-life of other dichlorobutenes has been experimentally determined to be 3.2 days at 25˚C; 3,4-DCB may have a similar hydrolysis rate.
Reference: Ellington J. J (1989)

*3.2 MONITORING DATA (ENVIRONMENT)

(a)
Type of Measurement: Background **[ ]**; At contaminated site **[X]**; Other **[ ]**
Media: Air
Results: ND - 2.53 ppm (Detection limits 0.05 ppm)
Remarks: The working place of TOSOH's facility
Reference: The Ministry of Labor of Japan (2000)

(b)
Type of Measurement: Background **[ ]**; At contaminated site **[X]**; Other **[ ]**
Media: Air
Results: 0.12 - 0.46 ppm (Detection limits 0.05 ppm)
Remarks: Average of the working place of 2 facilities in Japan
Reference: The Ministry of Labor of Japan (2000)

(c)
Type of Measurement: Background **[X]**; At contaminated site **[ ]**; Other **[ ]**
Media: Air
Results: ND (ND = Not detected, Detection limits: 60 ng/m^3,) in 11 areas, 80 ng/m3 in 1 area in Japan in 1998
Remarks:
Reference: Environment Agency of Japan (1999)

(d)
Type of Measurement: Background **[X]**; At contaminated site **[ ]**; Other **[ ]**
Media: Surface water
Results: ND (ND = Not detected, Detection limits: 0.011 ng/l) in 12 areas in Japan in 1997,
Remarks:
Reference: Environment Agency of Japan (1998)

3.3 TRANSPORT AND DISTRIBUTION BETWEEN ENVIRONMENTAL COMPARTMENTS INCLUDING ESTIMATED ENVIRONMENTAL CONCENTRATIONS AND DISTRIBUTION PATHWAYS

*3.3.1 TRANSPORT

(a)
Type: Adsorption **[X]**: Desorption **[ ]**; Volatility **[ ]**: Other **[ ]**
Media: Water-Soil
Method:
Results: Based upon a water solubility of 420 mg/l, the Koc for 3,4-DCB can be estimated to be 160 from a regression-derived equation. Using a structure estimation method based on molecular connectivity indexes, the Koc for 3,4-DCB can be estimated to be approximately 130. According to a suggested classification scheme, these estimated Koc values suggest that 3,4-DCB has medium to high mobility in soil.
Remarks:
Reference: Lyman W. J. (1990)

(b)
Type: Adsorption **[ ]**: Desorption **[ ]**; Volatility **[X]**: Other **[ ]**
Media: Volatilization from Water/Soil

Method: Calculation by means of a computer soft of Chem PHESA21 developed by Japan Chemical Industry Association
Results: Based upon a measured vapour pressure of 29.1 hPa at 25 deg. C., a water solubility of 1600 mg/l, and a partition coefficient of 2.37 for 3,4-DCB, the Volatilization from environmental water is negligible.
Reference: TOSOH (1999)

***3.3.2 THEORETICAL DISTRIBUTION (FUGACITY CALCULATION)**

Media: Air-biota **[ ]**; Air-biota-sediment-soil-water **[X]**; Soil-biota **[ ]**; Water-air **[ ]**; Water-biota **[ ]**; Water-soil **[ ]**; Other **[ ]**
Method: Fugacity level I **[ ]**; Fugacity level II **[ ]**; Fugacity level III **[X]**; Fugacity level IV **[ ]**; Other (calculation) **[ ]**; Other (measurement)**[ ]**
Generic Model of OECD (FUGMOD, 1992)
Results: If 100% released to the atmosphere: Air 98.3%, water 1.5%, soil 0.2%, Sediment: 0.0%
If 100% released to water: Air 7.0%, water 92.4%, soil 0.2%, and sediment
If 100% released to soil: Air 3.1%, water 0.8%, soil 96.1%, sediment 0.0%
Remarks: The Global Reference model of OECD Existing Chemicals Programme was used for calculation. Default values for the environmental parameters were not changed. Water solubility 1600 mg/l, vapour pressure 29.1 hPa and log Pow 2.37 were used for the calculation.
Reference: TOSOH (1999)

3.3.3 Henry-constant

Method: Bond Contribution method
Results: 1.61×10^3
Remarks:
Reference: Bayer (1999)

3.4 IDENTIFICATION OF MAIN MODE OF DEGRADABILITY IN ACTUAL USE

Results: 3,4-DCB is produced as intermediate of chloroprene. This compound is released to the environment, mainly in water, through waste stream generated at production sites.
Small amount of 3,4-DCB is contaminated in chloroprene monomer but is not detected from chloroprene polymer. If released to the atmosphere, it will degrade readily in the vapour phase by reaction with OH radicals or ozone photochemically.
If released to moist soil or water, degradation may occur through hydrolysis.
Remarks
Reference: Stewart CA Jr (1993)
TOSOH (1999)

***3.5 BIODEGRADATION**

(a)
Type: aerobic **[X]**; anaerobic **[ ]**
Inoculum: adapted **[ ]**; non-adapted **[X]**;
Concentration of the chemical: 100 mg/l related to COD **[ ]**; DOC **[ ]**; Test substance **[X]**;
Medium: water **[X];** water-sediment **[ ];** soil **[ ];** sewage treatment **[ ]**
Degradation:
1 % after 28 days (based on BOD)
28 % after 28 days (based on BOD)

	3 % after 28 days (based on BOD) av. 11% 45% after 28 days (based on GC) 45% after 28 days (based on GC) 44% after 28 days (based on GC) av. 45%
Results:	*(see OECD Guidelines)* Readily biodeg. **[ ];** Inherently biodeg. **[ ]**; under test condition no biodegradation observed **[ ]**, Other **[X]**
Method:	OECD TG 301C (1992)
GLP:	Yes **[X]** No **[ ]** ? **[ ]**
Test substance:	Purity: 99.6 %
Remarks:	The results indicate that this chemical is classified as not readily biodegradable. The chemical was analysed by GC. The biodegraded product was analysed to be 1,4-dihydroxybut-2-ene.
Reference:	Chemicals Inspection and Testing Institute, Japan (1992)

(b)

Type:	aerobic **[X]**; anaerobic **[ ]**
Inoculum:	predominantly domestic sewage
Concentration of the chemical:	
Medium:	water **[ ];** water-sediment **[ ];** soil **[ ];** sewage treatment **[ ]**
Degradation:	0 % after 28 days (based on BOD)
Results:	Readily biodeg. **[ ];** Inherently biodeg. **[ ]**; under test condition no biodegradation observed **[X]**, Other **[ ]**
Kinetic (e.g. Zahn-Wellens-Test)	. . . . . % in . . . . . (time)
Method:	OECD TG 301D
GLP:	Yes **[X]** No **[ ]** ? **[ ]**
Test substance:	Purity: 99.6%
Remarks:	The results indicate that the chemical is not readily biodegradable.
Reference:	Bayer AG

3.7 BIOACCUMULATION

Species:	*Cyprinus carpio* (Carp)
Exposure period:	6 weeks
Temperature:	25 °C
Concentration:	0.26 mg/l and 0.026 mg/l
BCF:	0.26 mg/l, Steady state 0.74, 0.84 (after 2 weeks) 1.40, 0.59 (after 3 weeks) 1.19, 0.99 (after 4weeks) 0.94, 2.11 (after 6 weeks) 0.026mg/l, Steady state <0.28, <0.28 (after 2 weeks) 2.71, <0.28 (after 3 weeks) <0.28, <0.28 (after 4 weeks) <0.28, 13.34 (after 6 weeks)
Elimination:	Yes **[ ]** No **[X]** ? **[ ]**
Method:	OECD TG 305C (1992)
Type of test:	**[ ]** calculated; **[X]** measured static **[ ]**; semi-static **[ ]**; flow-through **[X]**; other *(e.g. field test)* **[ ]**
GLP:	Yes **[X]** No **[ ]** ? **[ ]**
Test substance:	Purity: 99%,
Remarks:	Dispersant HCO-20, n=2
Reference:	Chemicals Inspection and Testing Institute, Japan (1992)

4. ECOTOXICOLOGICAL DATA

*4.1 ACUTE/PROLONGED TOXICITY TO FISH

(a)

Type of test:	static **[ ]**; semi-static **[ ]**; flow-through **[X]**; other *(e.g. field test)* **[ ]** open-system **[X]**; closed-system **[ ]**
Species:	Medaka (Oryzias latipes)
Exposure period:	96 hr
Results:	$LC_{50\ (96h)}$: 27 mg/l LC_0 : 15 mg/l LC_{100}: 60 mg/l
Analytical monitoring:	Yes **[X]** No **[ ]** ? **[ ]**
Method:	OECD TG 203 (1992)
GLP:	Yes **[X]** No **[ ]** ? **[ ]**
Test substance:	Purity: 99.6 %
Remarks:	Groups of ten Medaka were exposed to the nominal concentrations of 3.8, 7.5, 15, 30, and 60mg/l, a solubilizer control (100mg/l of DMF:HCO-40=2:1 mixed solution) and laboratory water control. Measured concentration was with in ± 20% of nominal concentration. Temp. 24 ± 1ºC. OECD category Acute II
Reference:	Environment Agency of JAPAN (1997)

(b)

Type of test:	static **[ ]**; semi-static **[ ]**; flow-through **[X]**; other *(e.g. field test)* **[ ]** open-system **[X]**; closed-system **[ ]**
Species:	Medaka (Oryzias latipes)
Exposure period:	14 days
Results:	LC_{50} : >21 mg/l NOEC: 3.9 mg/l LC_0: 9.5mg/l
Analytical monitoring:	Yes **[X]** No **[ ]** ? **[ ]**
Method:	OECD TG 204 (1984)
GLP:	Yes **[X]** No **[ ]** ? **[ ]**
Test substance:	Purity: 99.6 %
Remarks:	Groups of ten Medaka were exposed to the nominal concentrations of 1.0. 2.2, 4.6, 10 and 22mg/l. Measured concentrations were 75-110% of nominal concentrations throughout the test period. Temp. 24±1ºC.
Reference:	Environment Agency of JAPAN (1997).

(c)

Type of test:	static **[ ]**; semi-static **[ ]**; flow-through **[X]**; other *(e.g. field test)* **[ ]** open-system **[X]**; closed-system **[ ]**
Species:	Bluegill (*Lepomis macrochirus*)
Exposure period:	96 hour
Results:	TLm(96h) =85 ppm by vol of 3,4-DCB TLm(96h)= 0.37 ppm by vol of a mixture (3,4-DCB 14%, 1,4- dichlorobut-2-ene 86%)
Analytical monitoring:	Yes **[X]** No **[ ]** ? **[ ]**
Method:	Not described
GLP:	Yes **[ ]** No **[ ]** ? **[X]**
Test substance:	purity: ? %
Remarks:	Constant Temperature: 18 °C Dissolved Oxygen: 5 to 9 ppm Dilution Water: Soft Water

Fish: 4 to 10 cm long
Reference: Academy of Natural Sciences of Philadelphia (1971)

(d)
Type of test: static **[ ]**; semi-static **[ ]**; flow-through **[X]**; other *(e.g. field test)* **[ ]** open-system **[X]**; closed-system **[ ]**
Species: Fathead minnow(*Pimephales promelas*)
Exposure period: 96 hour
Results: LC_{50} (96h) : 7.17 mg/l
Analytical monitoring: Yes **[X]** No **[ ]** ? **[ ]**
Method: OECD TG 203 (1992)
GLP: Yes **[ ]** No **[X]** ? **[ ]**
Test substance: purity: ? %
Remarks: Analytical monitoring: gas-liquid chromatography
Reference: Geiger, D.L. et al. (1988)

(e)
Type of test: static **[ ]**; semi-static **[ ]**; flow-through **[X]**; other *(e.g. field test)* **[ ]** open-system **[X]**; closed-system **[ ]**
Species: Fathead minnow(*Pimephales promelas*)
Exposure period: 96 hour
Results: LC_{50} (96h) : 9.33 mg/l
Analytical monitoring: Yes **[X]** No **[ ]** ? **[ ]**
Method:
GLP: Yes **[ ]** No **[X]** ? **[ ]**
Test substance: purity: unknown
Remarks: Analytical monitoring: gas-liquid chromatography
Reference: Geiger, D.L. et al. (1985)

(f)
Type of test: static **[ ]**; semi-static **[X]**; flow-through **[ ]**; other *(e.g. field test)* **[ ]** open-system **[ ]**; closed-system **[ ]**
Species: Medaka(*Oryzias latipes*)
Exposure period: 48 hour
Results: LC_{50} (48h) 22.6 mg/l
Analytical monitoring: Yes **[X]** No **[ ]** ? **[ ]**
Method: other: Japanese Industrial Standard (JIS K 0102-1986-71) 'Testing methods for industrial waste water'.
GLP: Yes **[X]** No **[ ]** ? **[ ]**
Test substance: purity: unknown
Remarks: Exposure method: Renewal of test water at 24 hrs.
Reference: MITI (1992)

4.2 ACUTE TOXICITY TO AQUATIC INVERTEBRATES

*A. Daphnia

(a)
Type of test: static **[X]**; semi-static **[ ]**; flow-through **[ ]**; other *(e.g. field test)* **[ ]**; open-system **[ ]**; closed-system **[X]**
Species: *Daphnia magna*
Exposure period: 48-hr
Results: EiC_{50}(24hr): 13 mg/l
EiC_{50} (48hr) : 10mg/l
NOEiC : 4.6 mg/l

Analytical monitoring:	Yes **[X]** No **[ ]** ? **[ ]**
Method:	OECD TG 202 (1984)
GLP:	Yes **[X]** No **[ ]** ? **[ ]**
Test substance:	Purity: 99.6%
Remarks:	20 daphnids (4 replicates by 5 organisms) were exposed to the nominal concentrations of 1.8, 3.2, 5.6, 10, and 18 mg/l in a closed system, solubilizer control (maximum 100 mg/l of DMF:HCO-40=2:1 mixed solution) and laboratory water control. Measured concentrations were 78 to 89% of the nominal concentrations throughout the 48 hrs test period. The EC50 value was calculated based on measured concentrations value.
Reference:	Environment Agency of JAPAN (1997)

(b)

Type of test:	static **[X]**; semi-static **[ ]**; flow-through **[ ]**; other *(e.g. field test)* **[ ]**; open-system **[ ]**; closed-system **[X]**
Species:	Daphnia magna
Exposure period:	48 hr
Results:	EiC_0(48hr) : 5.9 mg/l EiC_{50}(48hr): 13.4 mg/l EiC_{100} (48h) : 30.3mg/l NOEiC : 4.6 mg/l
Analytical monitoring:	Yes **[ ]** No **[ ]** ? **[ ]**
Method:	Other: Directive 92/69/EEC C.2 (1992)
GLP:	Yes **[X]** No **[ ]** ? **[ ]**
Test substance:	
Remarks:	Because of the high volatility the substance was tested in a closed system ("Karlsryher Fraschen")
Reference:	Bayer AG (1999)

B. Other aquatic organisms

Type of test:	static **[ ]**; semi-static **[ ]**; flow-through **[X]**; other *(e.g. field test)* **[ ]** open-system **[ ]**; closed-system **[ ]**
Species:	Mysid (*Mysidopsis bahia*)
Exposure period:	96 hours
Results:	LC_{50} (96h) : 7.4 mg/l
Analytical monitoring:	Yes **[X]** No **[ ]** ? **[ ]**
Method:	EPA guide line
GLP:	Yes **[X]** No **[ ]** ? **[ ]**
Test substance:	purity: 99% (assay of 1/13/94) Submitted by E. I. DuPont de Nemours and Company
Remarks:	Mysids were exposed to the nominal concentrations of 0.0 (control), 1.5, 2.4, 3.9, 5.8, and 9.7 mg/l.
Reference:	Du Pont, Haskell Laboratory (1994)

***4.3 TOXICITY TO AQUATIC PLANTS e.g. Algae**

(a)

Species:	*Selenastrum capricornutum* Printz
End-point:	Biomass **[X]**; Growth rate **[ ]**; Other **[ ]**
Exposure period:	72 hours
Results:	EbC_{50} (72h): 49mg/l NOEC(72h): 14mg/l
Analytical monitoring:	Yes **[X]** No **[ ]** ? **[ ]**
Method:	OECD TG 201 (1984)

	open-system **[ ]**; closed-system **[X]**
GLP:	Yes **[X]** No **[ ]** ? **[ ]**
Test substance:	Purity: 99.6 %
Remarks:	Static test. The ErC_{50} value for biomass was calculated based on 5 measured concentrations (10, 18, 32, 56, 100mg/l). DMF:HCO-40=2:1 mixed solution was used as a solubilizer.
Reference:	Environment Agency of JAPAN (1997)

(b)

Species:	other algae: Diatoms (*Navicula seminulum*)
End-point:	Biomass **[ ]**; Growth rate **[X]**; Other **[ ]**
Exposure period:	7 day
Results:	EC_{50} (7day) : 275 ppm
Analytical monitoring:	Yes **[ ]** No **[ ]** ? **[X]**
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 of gases in the air. Temperature: 18 ± 1°C Light: 250 – 350 foot candles and for stock cultures above. open-system **[ ]**; closed-system **[X]**
GLP:	Yes **[X]** No **[ ]** ? **[ ]**
Test substance:	purity: unknown
Remarks:	7 day 50% reduction in growth diatom is 0.024% by vol. In the same condition, the EC_{50} (7day) of the mixture of 3,4-DCB (14 %) and 1,4-dichlorobut-2-ene (86%) was 0.85 ppm
Reference:	Academy of Natural Sciences of Philadelphia (1971)

4.4 TOXICITY TO BACTERIA

(a)

Species:	Pseudomonas putida (Bacteria)
End-point:	Biomass **[ ]**; Growth rate **[ ]**; Other **[ ]**
Exposure period:	3 day
Results:	EC_{50} (3day): 2950 mg/l
Analytical monitoring:	Yes **[ ]** No **[ ]** ? **[ ]**
Method:	other: Amtsblatt der EG L 133 Teil C open-system **[ ]**; closed-system **[ ]**
GLP:	Yes **[X]** No **[ ]** ? **[ ]**
Test substance:	purity: unknown
Remarks:	
Reference:	Bayer AG (1999)

(b)

Species:	Pseudomonas fluorescens (Bacteria)
End-point:	Biomass **[ ]**; Growth rate **[ ]**; Other **[ ]**
Exposure period:	7 day
Results:	EC_0 (7day) : 1000mg/l
Analytical monitoring:	Yes **[ ]** No **[X]** ? **[ ]**
Method:	other: Bestimimmung der biologischen Schadwirkung toxischer Abwaesser gegen Bakterien. DEV, L8 (1968) modifizert open-system **[ ]**; closed-system **[ ]**
GLP:	Yes **[ ]** No **[X]** ? **[ ]**
Test substance:	purity: unknown

Remarks:
Reference: Bayer AG (1999)

4.5 CHRONIC TOXICITY TO AQUATIC ORGANISMS

4.5.1. CHRONIC TOXICITY TO FISH

No data

(*)4.5.2. CHRONIC TOXICITY TO AQUATIC INVERTEBRATES

Type of test:	static **[ ]**; semi-static **[X]**; flow-through **[ ]**; other *(e.g. field test)* **[ ]**; open-system **[ ]**; closed-system **[X]**
Species:	Daphnia magna
Exposure period:	21 days
Results:	LC_{50} (21days) : 4.5 mg/l ErC_{50} (21days) : 4.0 mg/l NOECr : 0.83 mg/l LOECr : 2.8 mg/l
Analytical monitoring:	Yes **[X]** No **[ ]** ? **[ ]**
Method:	OECD TG 202 (1984)
GLP:	Yes **[X]** No **[ ]** ? **[ ]**
Test substance:	Purity: 99.6%
Remarks:	40 daphnids (4 replicates by 10 organisms) were exposed to the nominal concentrations of 0.10, 0.32, 1.0, 3.2, and 10 mg/l, solvent control (10 mg/l of DMF:HCO-40=2:1 solution) and laboratory water control (dechlorinated tap water, pH: 7.7 to 7.9; DO: 7.5 to 8.0 mg/l). Measured concentrations were within 83 to 88 % of the nominal concentrations throughout the 21-d test period.
Reference:	Environment Agency of JAPAN (1997)

4.6 TOXICITY TO TERRESTRIAL ORGANISMS

4.6.1 TOXICITY TO SOIL DWELLING ORGANISMS

No data

4.6.2 TOXICITY TO TERRESTRIAL PLANTS

No data

4.6.3 TOXICITY TO OTHER NON MAMMALIAN TERRESTRIAL SPECIES (INCLUDING AVIAN)

No data

4.7 BIOLOGICAL EFFECTS MONITORING (INCLUDING BIOMAGNIFICATION)

No data

4.8 BIOTRANSFORMATION AND KINETICS

No data

4.9 ADDITIONAL REMARKS

No data

5. TOXICITY

*5.1 ACUTE TOXICITY

5.1.1 ACUTE ORAL TOXICITY

(a) **Preferred Result**

Type:	LD_0 **[ ]**; LD_{100} **[ ]**; LD_{50} **[X]**; LDL_0 **[ ]**; Other **[ ]**
Species/strain:	Rat (Crj:CD(SD))
Sex:	male/female
Number of animals:	5
Value:	943 mg/kg males 946 mg/kg females Discriminating dose: N/A
Method:	OECD TG 401 (1981)
GLP:	Yes **[X]** No **[ ]** ? **[ ]**
Test substance:	Purity: 99.7%
Remarks:	Administered at 0, 670, 804, 965, 1158, 1389, and 1667 mg/kg in sesame oil by oral gavage. Fatalities were found both sexes at doses of more than 804 mg/kg. Clinical signs of decreased locomotor activity, deep respiration, ptosis, salivation, flaccidity, adoption of a prone position, piloerection and perinasal soiling with nasal discharge were observed in the treated groups, Body weights in the treatment groups were lower than those of the control group on the day after dosing. At autopsy, lung enlargement, urine retention and crystalline materials in the urinary bladder, and hemorrhagic black spots in the glandular stomach mucosa were observed in animals. LD50 values were 943 mg/kg for males and 946 mg/kg for females.
Reference:	Ministry of Health & Welfare, Japan, 1996

(b)

Type:	LD_0 **[ ]**; LD_{100} **[ ]**; LD_{50} **[X]**; LDL_0 **[ ]**; Other **[ ]**
Species/strain:	Rat
Value:	879 mg/kg Discriminating dose: N/A
Method:	unknown
GLP:	Yes **[ ]** No **[ ]** ? **[X]**
Test substance:	Substance grade and purity not stated
Remarks:	dose: 7.04 mM/kg bw
Reference:	Gizhlaryan, M. S (1981)

(c)

Type:	LD_0 **[ ]**; LD_{100} **[ ]**; LD_{50} **[X]**; LDL_0 **[ ]**; Other **[ ]**
Species/strain:	Rat
Sex:	male
Vehicle:	other: oil
Value:	577 – 1153 mg/kg bw
Method:	other: see remark
GLP:	Yes **[ ]** No **[X]** ? **[ ]**
Test substance:	Substance grade and purity not stated
Remarks:	3 or 5 animals per dose used. Treatment by gavage (no further information)
Doses:	0.1, 0.25, 0.5, 1.0 or 2.5 ccm/kg (converted into mg/kg bw by a density of 1.153 g/cm3 at 25-c)

Result:	mortality:	0/3 animals after 115 mg/kg bw. 0/3 animals after 288 mg/kg bw. 0/5 animals after 577 mg/kg bw. 4/5 animals after 1153 mg/kg bw. 3/3 animals after 2883 mg/kg bw.
	Clinical signs:	anorexia, weakness, narcotic symptoms.
Reference:	Bayer AG. (1959)	

5.1.2 ACUTE INHALATION TOXICITY

(a)

Type:	LC_0 **[ ]**; LC_{100} **[ ]**; LC_{50} **[X]**; LCL_0 **[ ]**; Other **[ ]**
Species/strain:	Rat (ChR-CD)
Sex:	male
Number of animals:	6
Exposure time:	4 hours
Value:	2100ppm
Method:	The test material was metered by a syringe drive into a stainless steel T-tube where it was vaporised at 120-150 centigrade. The resulting vapours were carried by a stream of air into a 16-liter exposure chamber containing six ChR-CD male rats of 246-295 grams body weight per exposure. Each exposure lasted for four hours. The chamber atmosphere was analysed at least once every hour by a gas chromatographic method.
GLP:	Yes **[ ]** No **[X]** ? **[ ]**
Test substance:	purity: 98% Measured by gas chromatography.
Remarks:	dose: 1000, 2250, 3000ppm This material classified as slightly toxic by inhalation based on 4 hrs exposure.
Result:	Clinical signs of irregular breathing, incoordination, unresponsiveness and lacrimation (only at the beginning of the exposure) were observed. Deaths occurred 2-6 days post-exposure.
Reference:	Du Pont, Haskell Laboratory, 1967, Report No. 96-67

(b)

Type:	LC_0 **[ ]**; LC_{100} **[ ]**; LC_{50} **[ ]**; LCL_0 **[ ]**; Other **[X]** Histopathologic study
Species/strain:	Rat
Exposure time:	4 hours
Method:	Each of eight male rat was given a single 4 hrs exposure to the test substance at a concentration of about 500 ppm. Tissues were collected on the first, second, seventh or fourteenth day after exposure.
GLP:	Yes **[X]** No **[ ]** ? **[ ]**
Test substance:	purity: 98%, measured by gas chromatography.
Remarks:	dose: 500 ppm
Result:	An increased number of mitotic figures was observed in the hepatic cells of rats exposed to a single four hour inhalation of 500 ppm of the test material when the livers of the animals were fixed on the first day after exposure. Other morphologic effects were not observed in the tissues of rats which were exposed to a single four hour inhalation dose of 500 ppm of the test material as judged by histologic examination of the tissues listed below; kidney, trachea, lung, brain, testes, bone marrow, spleen, thymus, and gastro-intestinal tract.
Reference:	Du Pont, Haskell Laboratory, 1967, Report No. H4724

(c)

Type:	LC_0 **[ ]**; LC_{100} **[ ]**; LC_{50} **[ ]**; LCL_0 **[ ]**; Other **[X]** Histopathologic study
Species/strain:	Rat
Exposure time:	4 hours
Method:	Inhalation at both the high and low dosage levels was followed by degenerative lesions of the livers and /or kidneys of rats which died or were killed within two days of exposure. Exposure: 1000, 2000, 3000 ppm
GLP:	Yes **[X]** No **[ ]** ? **[ ]**
Test substance:	purity: ? %
Remarks:	dose: 1000, 2250, and 3000 ppm
Result:	Observable lesions were not present in the tissues examined from rats killed at seven days following low level exposure or fourteen days following medium level exposure. The liver lesions varied with age and consisted of centrilobular hepatocellular degeneration. In both rats which received the high dosage level and died during the first day, the lesion was characterized by centrilobular reduction of hepatocellular glycogen and fatty change. In both rats killed one day following the low level exposure, the lesions had advanced to centrilobular necrosis. The livers of rats killed at two and seven days following low level exposure and fourteen days following the medium level exposure were not remarkable.
Reference:	Du Pnt, Haskell Laboratory, 1967 , Report No. H4988

(d)

Type:	LC_0 **[ ]**; LC_{100} **[ ]**; LC_{50} **[ ]**; LCL_0 **[ ]**; Other **[X]**
Species/strain:	Rat
Exposure time:	? hours
Results:	Inhalation at a concentration from 2000 to 12000 mg/cu m caused hypervolemia and stasis in brain cortex, cerebellum, lungs, liver, spleen, stomach mucosa, adrenal cortex, and kidneys.
GLP:	Yes **[ ]** No **[ ]** ? **[X]**
Test substance:	purity: ? %
Reference:	Petrosyan FR, 1982

5.1.3 ACUTE DERMAL TOXICITY

Type:	LD_0 **[ ]**; LD_{100} **[ ]**; LD_{50} **[X]**; LDL_0 **[ ]**; Other **[ ]**
Species:	Rabbit
Sex:	male/female
Number of animals:	10
Value:	>2000 mg/kg bw
Method:	OECD TG 402
GLP:	Yes **[X]** No **[ ]** ? **[ ]**
Test substance:	purity: Sample 1: 99.67 wt % Sample 2: 98.26 wt %
Remarks:	Single doses of 3,4-DCB were administered to the shaved, intact skin of groups of 5 male and 5 female rabbits each at dosages of 700 or 2000 mg/kg. Additionally, 1 female rabbit was treated at 1000 mg/kg, and an additional group of 5 male and 5 female rabbits was treated at a dosage of 2000 mg/kg to document the onset and duration of clinical for 24hours. All rabbits, except the additional group dosed at 2000 mg/kg, were observed for 14 days following application of the substance and then necropsied. The additional

group dose at 2000 mg/kg was sacrificed 2 days after application of the test substance and the animals were not necropsied.

Result: Slight to severe erythema and no to mild edema were observed the day after dosing in the treated rabbits. Dermal erythema persisted in most rabbits throughout the observation period. Most rabbits exhibited epidermal scaling and sloughing from day 5 to 6 throughout the remainder of the observation period. Some rabbits dosed at 2000 mg/kg also exhibited superficial necrosis, raw areas, epidermal thickening, fissuring, fissuring with bleeding, or eschar formation.
Under the conditions of this study, the skin absorption LD50 for 3,4-DCB was greater than 2000 mg/kg of body weight. No deaths occurred during the study.
Most rabbits from all dose groups were hypo-responsive to auditory (finger snap and hand clap) and tactile (face touching) stimuli up to approx. 4 hours after dosing. No adverse clinical signs of toxicity were observed throughout the remainder of the study.

Reference: Du Pont, Haskell Laboratory (1993)

5.1.4 ACUTE TOXICITY, OTHER ROUTES OF ADMINISTRATION

No data available

5.2 CORROSIVENESS/IRRITATION

5.2.1 SKIN IRRITATION/CORROSION

(a) Preferred result

Species: Rabbit
Result: slightly irritating
Method: OECD TG 404
GLP: Yes **[X]** No **[ ]** ? **[ ]**
Test substance: purity: approx. 99%
Remarks: Dose: 0.5 ml of the undiluted test substance were applied to the test site (area: approx. 6 cm^2, semi-occlusive).
Exposure time: 4 hrs
All three rabbits showed an erythema (grade 1 or 2) for up to 72 hours after patch removal.
Reference: Laboratory of Pharmacology and Toxicology KG, Germany, LPT Report No. 9300/382/95 (1999).

(b)
Species: Rabbit
Result: moderately irritating
Method: other: 0.5 ml/animal were applied to intact or abraded skin (no further information)
GLP: Yes **[ ]** No **[X]** ? **[ ]**
Test substance: Commercial, purity: unknown
Remarks: effect: strong to moderate erythema and moderate to mild edema which disappeared within seven days.
Reference: Du Pont, Haskell Laboratory

(c)
Species: Rabbit
Result: effect: erythema, edema, necrosis

Method: other: The test material (on gauze) was applied into the ear by a plaster bandage for 1.5 h
GLP: Yes **[ ]** No **[X]** ? **[ ]**
Test substance: Commercial, purity: unknown
Remarks:
Reference: Bayer AG (1959)

5.2.2 EYE IRRITATION/CORROSION

(a)
Species/strain: Rabbit
Results: slightly irritating
Classification: Irritating **[ ]**; Not irritating **[X]**; Risk of serious damage to eyes **[ ]**
Method: OECD TG 405
GLP: Yes **[X]** No **[ ]** ? **[ ]**
Test substance: purity: approx. 99%
Remarks: Concentration: undiluted
Dose: 0.1 ml
Exposure time: 72 hrs
Effect: Corneal opacity (grade 1) and irritation of the iris (grade 1) were observed in animal no. three 1 to 48 hours after instillation. Conjunctival redness (grade 1) was seen in all three animals 1 hour after instillation.
Reference: Laboratory of Pharmacology and Toxicology KG, Germany, LTP Report No. 9301/382/95 (1999).

(b)
Species/strain: Rabbit
Results: Highly corrosive **[ ]**; Corrosive **[ ]**; Highly irritating **[ ]**;
Irritating **[X]**; Moderate irritating **[ ]**; Slightly irritating **[ ]**; Not irritating **[ ]**
Classification: Irritating **[X]**; Not irritating **[ ]**; Risk of serious damage to eyes **[ ]**
Method: Drop application
GLP: Yes **[ ]** No **[ ]** ? **[X]**
Test substance: Commercial, purity: ?%
Remarks: Test by drop application to rabbit eyes caused only moderate injury, graded 5 on scale of 10 after 24 hrs.
Reference: Grant, W.M. (1986)

5.3 SKIN SENSITISATION

Type: no data
Species: Guinea pig
Result: not sensitizing
Concentration: no data
Vehicle: no data
Method: no data
GLP: Yes **[ ]** No **[X]** ? **[ ]**
Test substance: no data
Reference: Gizhlaryan, M.S .et al. (1984)

*5.4 REPEATED DOSE TOXICITY

(a)
Species/strain: Rat / Crj. CD (SD)
Sex: Female **[ ]**; Male **[ ]**; Male/Female **[X]**; No data **[ ]**
Route of Administration: oral (gavage)

Exposure period: Males: 44 days; Females: 41-46 days, from 14 days before mating to day 3 of lactation
Frequency of treatment: 7 days/week, once daily.
Post exposure observation period: none
Dose: 0, 0.4, 2, 10, 50 mg/kg bw (10 males, 10 females)
Control group: Yes **[X]**; No **[ ]**; No data **[ ]**;
Concurrent no treatment **[ ]**; Concurrent vehicle **[*X*]**; Historical **[ ]**
NOAEL: 10 mg/kg bw
Results: In males, absolute kidney weights were slightly increased with 10 mg/kg/day dose. Absolute and relative weights of the liver and kidneys were increased with 50 mg/kg/day dose. Blood chemical examination revealed an increase in total protein. The histopathological examination revealed increased hyaline droplets in the renal tubular epithelium with doses of 10 and 50 mg/kg/day and hepatocellular hypertrophy with dose of 50 mg/kg/day.
In females, one female was sacrificed in a moribund condition on day 2 of lactation. An increase in relative kidney weights were observed at the dose of 50 mg/kg/day. However, no histopathological changes considered to be related to the change of the kidney weight were detected. Hepatocellular hypertrophy was observed at the dose of 50 mg/kg/day.
NOAELs in this r repeat dose study are 2 mg/kg/day for males and 10 mg/kg/day for females, but the renal toxicity in males is considered to be male rat specific, probably due to α_{2U}-globulin involvement. Therefore, the NOAEL for repeated dose toxicity is considered to be 10 mg/kg/day.
Method: OECD TG 422 (1981)
Vehicle: Sesame oil
GLP: Yes **[X]** No **[ ]** ? **[ ]**
Test substance: Commercial, purity: 99.7 %
Reference: Ministry of Health & Welfare, Japan (1996)

(b)
Species/strain: Rat / ChR-CD and Long-Evans
Sex: Female **[ ]**; Male **[X]**; Male/Female **[ ]**; No data **[ ]**
Route of Administration: Inhalation
Exposure period: 2 weeks
Frequency of treatment: 6 hours/day, 5 days/week
Post exposure observation period: 14 days
Dose: 104 or 1037 mg/m^3 (20 or 200 ppm)
Control group: Yes **[X]**; No **[ ]**; No data **[ ]**;
Concurrent no treatment **[X]**; Concurrent vehicle **[ ]**; Historical **[ ]**
NOAEL: 104 mg/m^3 (20 ppm)
Results: 1037 mg/m^3 (200 ppm) appeared to have a slight effect on both ChR.CD and Long-Evans rats. This was evidenced by an increased liver to body weight ratio and changes in liver cell morphology. These effects were not present in the ChR-CD rats after a 14-day recovery period, but the increased liver-to-body weight did persist in 2/3 Long-Evans rats 14 days post-exposure.
Method: half of the animals in recovery group
GLP: Yes **[ ]** No **[X]** ? **[ ]**
Test substance: Commercial, purity: 98.74 %
Reference: Du Pont, Haskell Laboratory (1987)

(c)
Species/strain: Rat
Sex: Female **[ ]**; Male **[ ]**; Male/Female **[X]**; No data **[ ]**
Route of Administration: Inhalation

Exposure period: up to 3 weeks
Frequency of treatment: 15 x 6 hrs (low and mid conc.) or 8 x 6 hrs (high conc.)
Post exposure observation period: no data
Dose: 2-3, 6, and 18 ppm (10-16, 31, and 93 mg/m3)
Control group: Yes [ ]; No [ ]; No data [**X**];
Concurrent no treatment **[ ]**; Concurrent vehicle **[ ]**; Historical **[ ]**
Remark The test substance is a mixture. So this data is not adopted.
Results: 18 ppm: progressive weight loss, lungs haemorrhagic, thymus atrophied, lungs emphysematous with areas of haemorrhage and edema (histol.); 6 ppm: initial weight loss, thymus slight atrophy; 2-3 ppm: no toxic signs, organs normal (autopsy).
Method: The animals have been exposed to dynamic atmospheres. The vapor concentrations were generated by injecting the liquid test material in pet. ether at a known rate into a metered stream of air by means of a controlled fluid-feed atomizer (no further information).
GLP: Yes [ ] No [**X**] ? [ ]
Test substance: Commercial, purity: other TS: mixed isomers administrated (37.3% 3,4-dichloro-1-butene, 17% cis-1,4-dichloro-2-butene, 45.7% trans-1,4-dichloro-2-butene)
Reference: Gage, J. C. (1970)

(d)
Species/strain: Rat
Sex: Female **[ ]**; Male **[ ]**; Male/Female **[X]**; No data **[ ]**
Route of Administration: inhalation
Exposure period: 1 to 4 months
Frequency of treatment: 4h/day 5days/week
Post exposure observation period: 1 month
Dose: 14.4, 126 or 203 mg/m3
Control group: Yes **[ ]**; No **[ ]**; No data **[X]**;
Concurrent no treatment **[ ]**; Concurrent vehicle **[ ]**; Historical **[ ]**
Remark incomplete and inexact data on study design and study results
Results: effects on liver, kidney, lung, testes and functional state of the nervous system; 14.4 mg/m3: no effects
Method: unknown
GLP: Yes **[ ]** No **[ ]** ? **[X]**
Test substance: Commercial, purity: no data
Reference: Gizhlaryan, M. S., et al. (1984)

(e)
Species/strain: Rat
Sex: Female **[ ]**; Male **[ ]**; Male/Female **[ ]**; No data **[X]**
Route of Administration: oral unspecified
Exposure period: 6 months
Frequency of treatment: no data
Post exposure observation period: no data
Dose: 1.0, 0.1, or 0.01 mg/kg
Control group: Yes **[ ]**; No **[ ]**; No data **[X]**;
Concurrent no treatment **[ ]**; Concurrent vehicle **[ ]**; Historical **[ ]**
Remark incomplete and inexact data on study design and study results
Results: All dose groups: body weight gain unchanged; 1.0 mg/kg: degenerative changes in liver, kidneys, heart, stomach, small intestine and testes; 0.1 mg/kg: deg. changes in liver; 0.01 mg/kg: apparently tolerated without lesions.
Method: unknown

GLP: Yes [ ] No [ ] ? [**X**]
Test substance: Commercial, purity: no data
Reference: Gizhlaryan, M. S. et al. (1986)

(f)
Species/strain: Syrian hamster
Sex: Female **[ ]**; Male **[X]**; Male/Female **[ ]**; No data **[ ]**
Route of Administration: inhalation
Exposure period: 2 weeks
Frequency of treatment: 6 h/day, 5 days/week
Post exposure observation period: 14days
Dose: 104 or 1037 mg/m3
Control group: Yes **[X]**; No **[ ]**; No data **[ ]**;
Concurrent no treatment **[ ]**; Concurrent vehicle **[ ]**; Historical **[ ]**
Remark dose: 20 or 200 ppm; half of the animals in recovery group
Results: no compound-related effects
Method: unknown
GLP: Yes **[ ]** No **[X]** ? **[ ]**
Test substance: Commercial, purity: 98.74 %
Reference: Du Pont, Haskell Laboratory (1987)

*5.5 GENETIC TOXICITY IN VITRO

A. BACTERIAL TEST

(a)
Type: Bacterial reverse mutation assay
System of testing: S. typhimurium TA 98, TA 100, TA 1535, TA 1537, Escherichia coli WP2 uvrA
Concentration: -S9mix: 0, 250-2500 µg/plate(TA100, TA1535), 0, 39-2500 µg/plate(WP2), 0, 78-2500 µg/plate(TA98), 39-2500 µg/plate(TA1537)
+S9mix: 0, 1000-3000 µg/plate(TA100), 0,500-2500 µg/plate(TA1535), 0,39-2500 µg/plate(TA1537, WP2), 0, 39-5000 µg/plate(TA98)
Metabolic activation: With **[ ]**; Without **[ ]**; With and Without **[X]**; No data **[ ]**
Results:
Cytotoxicity conc: With metabolic activation: 1250 µg/plate(WP2, TA98, TA1537), 2000 µg/plate(TA1535), 2200 µg/plate(TA100)
Without metabolic activation: 625 µg/plate(TA98, TA1537), 850 µg/plate (TA100), 1000 µg/plate(TA1535), 1250 µg/plate(WP2)
Precipitation conc:
Genotoxic effects:

	TA98	TA100	TA1535	TA1537	WP2
With metabolic activation:	-	-	+	-	-
Without metabolic activation:	-	-	+	-	-

Method: Guidline for Screening Mutagenicity Testing of Chemicals(Japan) and OECD TG 471 and 472
GLP: Yes **[X]** No **[ ]** ? **[ ]**
Test substance: Commercial, purity: 99%
Remarks: Procedure: Plate incubation method
Plates/test: 3
No. replicates: 2
Solvent: Acetone
This chemical shows mutagenisity only in TA1353 at 1000 µg/plate, but not in other Salmonella typhimurium strains or Escherichia coil strain. The number of induction colonies, 20-30/mg-dose, indicates that this chemical

is weak mutagenic Toxicity was observed at 625 µg/plate(TA98, TA1537), 850 µg/plate(TA100), 1000 µg/plate(TA1535), 1250 µg/plate(WP2) with the –S9 mix, and at 1250 µg/plate(WP2, TA98, TA1537), 1500 µg/plate (TA1535), 2200 µg/plate(TA100) with +S9 mix.

Reference: Ministry of Health & Welfare, Japan (1996)

(b)

Type: Bacterial reverse mutation assay (Ames test)
System of testing: S. typhimurium TA 100
Concentration: 0, 0.1, 0.5, 1 % (v/v) in air (gas phase)
Metabolic activation: With **[ ]**; Without **[ ]**; With and Without **[X]**; No data **[ ]**
Results: positive
Method: other: Tests were performed by exposing inverted Petri dishes. DMSO and the test compound were omitted, to various conc. of the test compound in air in 10 l desicators for 2 hours at 37 degree centigrade in the dark. For 3,4-DCB, the weight calculated to give the desired volume of vapour was cooled and placed in the desiccator. The plates were covered with lids, inverted and placed in an incubator; they were scored for his+ revertants after 48 hours of total incubation time at 37 degree centigrade.
GLP: Yes **[ ]** No **[X]** ? **[ ]**
Test substance: Commercial, purity: 99.6 %
Remarks: Exposure of *S. typhimurium* TA 100 to up to 1% 3,4-dichloro-1-butene vapour in air, in the absence of an NADPH-generating system, caused a concentration-dependent increase in mutagenicity; this was enhanced up to two-fold in the presence of a fortified liver S-9 fraction from PB-treated mice.
Reference: Barbin, A. G. et al (1978)
Bartsch, H. et al. (1979)

B. NON-BACTERIAL IN VITRO TEST

(a)

Type: Cytogenetic assay
System of testing: Chinese hamster lung (CHL/IU) cells
Concentration: -S9 mix (continuous treatment): 0, 0.025, 0.05 and 0.1 mg/ml;
-S9 mix (short-term treatment): 0, 0.05, 0.1 and 0.2 mg/ml
+S9 mix (short-term treatment): 0, 0.0025, 0.005 and 0.01 mg/ml
Metabolic activation: With **[ ]**; Without **[ ]**; With and Without **[X]**; No data **[ ]**
Results:

Cytotoxicity conc:	With metabolic activation: (short-term treatment)	0.01mg/ml(clastogenicity, polyploidy)					
	Without metabolic activation:						
	(continuous treatment)	0.05 mg/ml(clastogenicity)					
		0.1 mg/ml(polyploidy)					
	(short-term treatment)	0.2 mg/ml(clastogenicity)					
Precipitation conc:	not stated						
Genotoxic effects:		clastogenicity			polyploidy		
		+	?	-	+	?	-
	With metabolic activation:	**[X]**	**[ ]**	**[ ]**	**[X]**	**[ ]**	**[ ]**
	Without metabolic activation:	**[X]**	**[ ]**	**[ ]**	**[X]**	**[ ]**	**[ ]**

Method: Guidelines for Screening Mutagenicity Testing of Chemicals(Japan) and OECD TG 473.
GLP: Yes **[X]** No **[ ]** ? **[ ]**
Test substance: Commercial, purity 99 %
Remarks: Solvent: Acetone

Plates/test:2
This chemical induced structural chromosome aberrations and polyploidy in chinese hamster lung cells (CHL/IU) with and without metabolic activation at the respective LC_{50} concentration, namely 0.01 and 0.2 mg/ml.
Reference: Ministry of Health & Welfare, Japan (1996)

(b)
Type: HGPRT assay
System of testing: Chinese Hamster Ovary (CHO) cells
Concentration: 0, 0.2, 1.2, 2.0, 2.2, 2.4, 2.6 mM
Metabolic activation: With **[ ]**; Without **[ ]**; With and Without **[X]**; No data **[ ]**
Results: This chemical was found to be mutagenic without activation.
Method: Other: in accordance with OECD Guideline 476
GLP: Yes **[ ]** No **[X]** ? **[ ]**
Test substance: purity 96.2% dissolved in physiological medium
Remarks:
Reference: Du Pont, Haskell Laboratory, 1980

(c)
Type: Sister chromatid exchange assay
System of testing: human lymphocytes
Concentration:
Metabolic activation: With **[ ]**; Without **[ ]**; With and Without **[ ]**; No data **[X]**
Results: positive
Method:
GLP: Yes **[ ]** No **[X]** ? **[ ]**
Teat substance: Commercial, purity: no data
Remarks:
Reference: Gu. Z. W. (1981)

5.6 GENETIC TOXICITY IN VIVO

(a)
Type: Cytogenetic assay
System of testing: Species/strain: Rat
Route of administration: Inhalation
Exposure period: once 24 hours or 30 and 120 days (4 hours/day, 5 days/week)
Doses: 13.7 or 81.3 mg/m3
Remarks: Rats were sacrificed after 24 hours, 30days, 120days of exposure time and 45 days recovery period after the end of exposure.
50 well-spread and complete metaphase cells per animal were analysed. Aberations were classified as general method.
Results: The concentration of 13.7 mg/m3 caused chromosome damages in the bone marrow, mainly of the chromatid type. Other structural aberrationa and numerical aberrations including polyploidy were not observed.
They were reversible after a recovery period of 45 days. 81.3 mg/m3 caused these changes already after a single inhalation of 24 hours. After the 45-day recovery period they were smaller, but still significantly existing.
GLP: Yes **[ ]** No **[X]** ? **[ ]**
Method: Not described
Test substance: Commercial, purity: 99.2 %
References: Nalbandyan, T. I. et al. (1985)

(b)
Type: Cytogenetic assay

System of testing: Species/strain: Rat
Sex : male
Route of administration: Inhalation
Exposure period: once 24 hours or 30 and 120 days (4 hours/day, 5 days/week)
Doses: 13.9 or 107.8 mg/m3
Remarks: Rats were sacrificed after 24 hours, 30days, 120days of exposure time and 45 days recovery period after the end of exposure.
Results: Both concentrations caused chromosome damages in the bone marrow, mainly of the chromatid type. In the low conc. they were reversible after a recovery period of 45 days. Referring chromosome aberrations 13.9 mg/m3 proved to be the threshold concentration.
GLP: Yes **[ ]** No **[X]** ? **[ ]**
Method: Not described
Test substance: Commercial, purity: no data
References: Gizhlaryan, M. S. et al. (1984)

5.7 CARCINOGENICITY

No data available

*5.8 TOXICITY TO REPRODUCTION

Type: other: Reproductive/Developmental Toxicity
Species/strain:` Rat / Crj: CD(SD)
Sex: Female **[ ]**; Male **[ ]**; Male/Female **[X]**; No data **[ ]**
Route of Administration: gavage
Exposure period: Males for 44 days; females for 41- 46 days, from 14 days before mating to day 3 of lactation.
Frequency of treatment: daily
Postexposure observation period: no data
Premating exposure period: male and female: 14 days
Duration of the test: males: 45 days; females: to day 4 of lactation
Doses: 0, 0.4, 2, 10, 50 mg/kg bw (10 /animals /sex)
Control group: Yes **[X]**; No **[ ]**; No data **[ ]**;
Concurrent no treatment **[ ]**; Concurrent vehicle **[X]**; Historical **[ ]**
NOAEL Parental: 50 mg/kg/day
NOAEL F1 Offspring: 50 mg/kg/day
Results: The parental animals exhibited no effects on reproductive parameters including the copulation index, fertility index, gestation length, number of corpora lutea or implantation index, gestation index, delivery index, and behaviour at delivery and lactation. There were no significant differences in the number of offspring, sex ratio, live birth index, viability index and body weight. Number of pups alive on day 4 of lactation tended to be slight decreased with the 50 mg/kg dose, caused by litter loss in one dam sacrificed in extremes on day 2 of lactation. No external or visceral anomalies related to the test substance administration were detected in any of the offspring.
The NOELs for both reproductive performance and offspring development are considered to be 50 mg/kg bw. For maternal toxicity see chapter 5.4.
Method: OECD Combined Repeated Dose and Reproductive/Development Toxicity Screening Test
GLP: Yes **[X]** No **[ ]** ? **[ ]**
Test substance: purity 99.7%
Remarks: Vehicle: Sesame oil
Reference: Ministry of Health & Welfare, Japan (1996)

*5.9 DEVELOPMENTAL TOXICITY/TERATOGENICITY

Species/strain: Rat / Crj:CD(SD)
Sex: Female **[ ]**; Male **[ ]**; Male/Female **[X]**; No data **[ ]**
Route of Administration: gavage
Duration of the test: See Section5.8
Exposure period:
Frequency of treatment:
Doses:
Control group: Yes **[ ]**; No **[ ]**; No data **[ ]**;
Concurrent no treatment **[ ]**; Concurrent vehicle **[ ]**; Historical **[ ]**
NOEL Maternal Toxicity:10 mg/kg
NOEL teratogenicity:
Results: There were no significant differences in the number of offspring, sex ratio, live birth index, viability index and body weight. Number of pups alive on day 4 of lactation tended to be slight decreased with the 50 mg/kg dose, caused by litter loss from loss of nursing activity in one dam that was sacrificed in extremes on day 2 of lactation. No external or visceral anomalies related to the test substance administration were detected in any of the offspring.
The NOELs for the offspring development are considered to be 50 mg/kg bw.
Method: See Section 5.8
GLP: Yes **[X]** No **[ ]** ? **[ ]**
Test substance: See Section 5.8
Remarks:
Reference: Ministry of Health & Welfare, Japan (1996)

5.10 OTHER RELEVANT INFORMATION

A. Specific toxicities

No data available

B. Toxicodynamics, toxicokinetics

No data available

*5.11 EXPERIENCE WITH HUMAN EXPOSURE

(a)
Results: Protracted contact with skin causes dermatitis and blistering. High concentration of vapour apparently have delayed toxic effect on eyes, causing onset of irritation and lacrimation several hr after the exposure, seeming similar to dimethyl sulfate and other alkylating agents in mode of action.
Remarks:
Reference: Grant, W. M. (1986)

(b)
Results: 3,4-DCB markedly induced sister chromatid exchanges in testes (in vitro) with lymphocytes of blood from workers chronically exposed to chloroprene.
Remarks:
Reference: Gu Z (1981)

(c)

Results: Sold with the warning that both liquid and vapour are highly dangerous to skin, eyes, lungs, and internal organs.
Remarks:
Reference: Grant, W. M. (1986)

(d)
Results: After application of a 3,4-DCB-soaked cotton swab for 0.5 to 1 hour, only slight irritation effects were seen on the skin of 5 test persons.
Remarks:
Reference: Bayer AG (1959)

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PROPOSED ROBUST SUMMARY

for

3,4-Dichlorobut-1-ene

CAS No. 760-23-6

Sponsor Country: Japan & Germany

DATE: May 25, 2001

PHYSICAL/CHEMICAL ELEMENTS

MELTING POINT

TEST SUBSTANCE

- 3,4-Dichlorobut-1-ene (CAS No 760-23-6)
- Remarks: Source: Unavailable.

METHOD

- **Method/guideline:** Not specified.
- **GLP:** Not stated.
- **Year:** Not stated.
- **Remarks:** Not stated.

RESULTS

- **Melting point value:** -61°C
- **Decomposition:** No
- **Sublimation:** No
- **Remarks:** Not stated.

CONCLUSIONS

Melting point is -61°C.

DATA QUALITY

- **Reliabilities:** Key study
- **Remarks:** Not stated.

REFERENCES (Free Text)

Aldrich Chemical Co., Inc. (1999), unpublished data.

OTHER

- **Last changed:**
- **Order number for sorting**
- **Remarks:**

BOILING POINT

TEST SUBSTANCE

- 3,4-Dichlorobut-1-ene (CAS No 760-23-6)
- Remarks: Source: Unavailable.

METHOD

- **Method:** Not specified.
- **GLP:** Not stated.
- **Year:** Not stated.
- **Remarks:** Not stated.

RESULTS

- **Boiling point value:** 118.6 °C
- **Pressure:** 1,013
- **Pressure unit:** hPa
- **Decomposition:** No
- **Remarks:** Not stated.

CONCLUSIONS

Boiling point is 118.6 °C at 1,013 hPa.

DATA QUALITY

- **Reliabilities:** Key study.
- **Remarks:** Not stated.

REFERENCES (Free Text)

Gerhartz, W. (exec ed.). Ullmann's Encyclopaedia of Industrial Chemistry. 5th ed. Vol. A1

OTHER

- **Last changed:**
- **Order number for sorting**
- **Remarks:**

VAPOR PRESSURE

TEST SUBSTANCE

- 3,4-Dichlorobut-1-ene (CAS No 760-23-6)
- Remarks: Source: Unavailable.

METHOD

- **Method:** Not specified.
- **GLP:** Not stated.
- **Year:** Not stated.
- **Remarks:** Not stated.

RESULTS

- **Vapour Pressure value:** 29.1 hPa
- **Temperature:** 25 °C
- **Decomposition:** Not stated.
- **Remarks:** Not stated.

CONCLUSIONS

Vapour Pressure is 29.1 hPa at 25 °C.

DATA QUALITY

- **Reliabilities:** Key study
- **Remarks:** Not stated.

REFERENCES (Free Text)

Daubert, T. E., Physical and Thermodynamic Properties of Pure Chemicals Data Compilation (1989).

OTHER

- **Last changed:**
- **Order number for sorting**
- **Remarks:**

PARTITION COEFFICIENT

TEST SUBSTANCE

- 3,4-Dichlorobut-1-ene (CAS No 760-23-6)
- Remarks: Source: Tokyo Kasei Kogyo – purity: 99.6%

METHOD

- **Method/guideline:** OECD TG107
- **GLP:** Yes
- **Year:** 1992
- **Remarks field for Test Conditions (Detail and discuss any signification protocol deviations.)**

RESULTS

- **Log P_{ow} :** 2.37
- **Temperature:** 25°C
- **Remarks:**

CONCLUSIONS

Log P_{ow} is 2.37.

DATA QUALITY

- **Reliabilities:** Key study
- **Remarks:** Well conducted study, carried out by Chemicals Inspection & Testing Institute, Japan

REFERENCES (Free Text)

Chemicals Inspection & Testing Institute, Japan, unpublished data (1992).

OTHER

- **Last changed:**
- **Order number for sorting:**
- **Remarks:**

WATER SOLUBILITY

TEST SUBSTANCE

- 3,4-Dichlorobut-1-ene (CAS No 760-23-6)
- Remarks: Source: Not specified.

METHOD

- **Method:** Not stated.
- **GLP:** Not stated.
- **Year:** Not stated.
- **Remarks:** Not stated.

RESULTS

- **Value (mg/L):** 1.6 g/L at 20 °C
- **Description of solubility:** low solubility.
- **pH value:**
- **pKa value:** There is no pertinent function group.
- **Remarks:**

CONCLUSIONS

This chemical is slightly soluble in water.

DATA QUALITY

- **Reliabilities:** Key study
- **Remarks:** Not stated.

REFERENCES (Free Text)

Bayer AG, unpublished data (1980).

OTHER

- **Last changed:**
- **Order number for sorting:**
- **Remarks:**

ENVIRONMENTAL FATE AND PATHWAYS ELEMENTS

STABILITY IN WATER

TEST SUBSTANCE

- 3,4-Dichlorobut-1-ene (CAS No 760-23-6)
- Remarks: Source: Tokyo Kasei Kogyo– purity: 99.6%.

METHOD

- **Method/guideline:** OECD TG111
- **Type (test type):** Hydrolysis as a function of pH
- **GLP:** Yes
- **Year:** 1997
- **Remarks:** Hydrolysis rates at pH 9 were determined at 60, 70 and 80 °C, and they were extrapolated to 25 °C using Arrhenius relationship. Half life at 25 °C was calculated from the rate constant.

RESULTS

- **Nominal:** 200 mg/L
- **Measured value:** Not stated.
- **Degradation:**
- **Half-life ($t_{(1/2)}$):** 20.9, 33.3 and 35.0 days at pH 4, 7, and 9, respectively.
- **Breakdown products:** 1,4-dihydroxybut-2-ene
- **Remarks:**

CONCLUSIONS

This chemical is hydrolized at pH 4, 7 and 9 at 25 °C with half-life of 20-35 days.

DATA QUALITY

- **Reliabilities:** key study
- **Remarks:** Well conducted study, carried out by Chemicals Inspection & Testing Institute, Japan

REFERENCES (Free Text)

Chemicals Inspection & Testing Institute, Japan, unpublished data.

OTHER

- **Last changed:**
- **Order number for sorting:**
- **Remarks:**

TRANSPORT BETWEEN ENVIRONMENTAL COMPARTMENTS (FUGACITY)

TEST SUBSTANCE

- 3,4-Dichlorobut-1-ene (CAS No 760-23-6)
- Remarks: Source: Not applicable.

METHOD

- **Test (test type):** Calculation
- **Method:** Fugacity level III
- **Year:** 2000
- **Remarks:** The parameters used are shown in Appendix.

RESULTS

- **Media**
- **Estimated Distribution under three emission scenarios**

Compartment	Release100% to air	Release100% to water	Release100% to soil
Air	98.3 %	7.0 %	3.1 %
Water	1.5 %	92.4 %	0.8 %
Soil	0.2 %	0.0 %	96.1 %
Sediment	0.0 %	0.6 %	0.0 %

- **Remarks:**

CONCLUSIONS

If this chemical is released into air, it is likely to be distributed into air (98%), but it is released into water, it is likely to be distributed into water (92%) and air (7%). If it is released into soil, it is likely to be distributed in soil (96%), air (3%) and water (1%).

DATA QUALITY

- **Reliabilities:** Key study.
- **Remarks:** Not stated.

REFERENCES (Free Text)

TOSOH CORPORATION, unpublished report (2000).

OTHER

- **Last changed:**
- **Order number for sorting:**
- **Remarks:**

Appendix: Parameters used in calculation of distribution by Mackay level III fugacity model

Physicochemical parameter

molecular weight		125.00	Measured
melting point [˚C]		- 61	Measured
vapour pressure [Pa]		29.1E+02	Measured
water solubility [g/m^3]		1600	Measured
log Kow		2.37	Measured
half life [h]	in air	14	Estimated
	in water	792	Estimated
	in soil	77	Estimated
	in sediment	792	Estimated

Temp. [˚C]	25

Environmental parameter

		volume	depth	area	organic	lipid content	density	residence
		[m^3]	[m]	[m^2]	carbon [-]	[-]	[kg/m^3]	time [h]
bulk air	air	1.0E+13					1.2	100
	particles	2.0E+03						
	total	1.0E+13	1000	1E+10				
bulk water	water	2.0E+10					1000	1000
	particles	1.0E+06			0.04		1500	
	fish	2.0E+05				0.05	1000	
	total	2.0E+10	10	2E+09				
bulk soil	air	3.2E+08					1.2	
	water	4.8E+08					1000	
	solid	8.0E+08			0.04		2400	
	total	1.6E+09	0.2	8E+09				
bulk sediment	water	8.0E+07					1000	
	solid	2.0E+07			0.06		2400	50000
	total	1.0E+08	0.05	2E+09				

Intermedia Transport Parameters [m/h]

air side air-water MTC	5	soil air boundary layer MTC	5
water side air water MTC	0.05	sediment-water MTC	1E-04
rain rate	1E-04	sediment deposition	5E-07
aerosol deposition	6E-10	sediment resuspension	2E-07
soil air phase diffusion MTC	0.02	soil water runoff	5E-05
soil water phase diffusion MTC	1E-05	soil solid runoff	1E-08

BIODEGRADATION

TEST SUBSTANCE

- 3,4-Dichlorobut-1-ene (CAS No 760-23-6)
- Remarks: Source: Tokyo Kasei Kogyo, Purity: 99.6 %,

METHOD

- **Method/guideline:** OECD TG301C
- **Test Type:** aerobic
- **GLP:** Yes
- **Year:** 1992
- **Contact time:** 28 days
- **Inoculum:** activated sludge for OECD TG301C
- **Remarks:** Not stated.

RESULTS

- **Degradation:** 1-28 % after 28 days (av. 11%, based on BOD)
  44-45 % after 28 days (av. 45%, based on GC)
- **Results:** not ready biodegradable
- **Kinetic:**
- **Breakdown products:** 1,4-dihydroxybut-2-ene
- **Remarks:**

CONCLUSIONS

This chemical is not ready biodegradable.

DATA QUALITY

- **Reliabilities:** Key study
- **Remarks:** Well conducted study, carried out by Chemicals Inspection & Testing Institute, Japan

REFERENCES (Free Text)

Chemicals Inspection & Testing Institute, Japan, unpublished data.

OTHER

- **Last changed:**
- **Order number for sorting:**
- **Remarks:**

ECOTOXICITY ELEMENTS

ACUTE TOXICITY TO FISH (1)

TEST SUBSTANCE

- **Identity:** 3,4-Dichlorobut-1-ene (CAS No 760-23-6)

=>Remarks: Source: Kanto Chemical Industries - purity = 99.6 %

METHOD

- **Method/guideline followed (experimental/calculated):** OECD TG203
- **Type (test type):** 96 h mortality
- **GLP (Y/N):** Yes
- **Year (study performed):** 1997
- **Species/Strain/Supplier:** Medaka (*Oryzias latipes*)
- **Analytical monitoring:** Yes
- **Exposure period (h):** 96 hrs
- **Statistical methods:** LC_{50} was calculated by means of Probit method for LC_{50} (48 h) and Binomial method for LC_{50} (72 and 96 h).

=> Remarks field for Test Conditions. Detail and discuss any significant protocol deviations, and detail differences from the guideline followed including the following as appropriate:

– Test fish (Age/length/weight, loading, pretreatment): Acclimated for above12 days before testing; any groups showing >5% mortality during 7 days before dosing were not used for testing; fish with 20-24 mm in length were selected at random. Average body weight of fish was 0.18 g (n=10).

– Test conditions, e.g.

· Details of test (static, semi-static, flow-through): flow-through (water changed 10 times/day).

· Dilution water source: Tap water after dechlorinatted and passed through active carbon.

· Dilution water chemistry (hardness, alkalinity, pH, DOC, TSS, salinity): Hardness: 63.1 mg/l as CaCO3; pH: 8.1

· Stock and test solution and how they are prepared: Stock solution was prepared to mix the appropriate amount of the chemical and vehicle and diluted with the dilution water to the 10 times concentration for testing. The stock solution and dilution water were poured into the test vessel by the each floe-through rate.

· Concentrations dosing rate, flow-through rate, in what medium: Concentrations of 0, 3.8, 7.5, 15, 30, and 60 mg/l were tested

· Vehicle/solvent and concentrations: DMF : Castor oil (HCO-40) = 2:1 (w/w)

· Stability of the test chemical solutions: The test chemical was identified by IR spectrum before and after testing. The stability of the test chemical solution was analysed by GC-MS at 0 and 96 hours after testing.

· Exposure vessel type (e.g., size, headspace, sealed, aeration, lighting, # per treatment): 10 fish per 5-L glass vessel (semi-closed).

· Number of replicates, fish per replicate: One replication was done.

· Water chemistry in test (O2, pH) in the control and one concentration where effects were observed: Dissolved oxygen readings and pH values were taken daily during 96 h exposure period.
Dissolved oxygen concentration: 7.3-8.0 mg/l.
PH values: 7.8-8.1

– Test temperature range: Containers used for testing were placed in a room at 23.1-24.5 °C.
– Method of calculating mean measured concentrations (i.e. arithmetic mean, geometric mean, etc.): Geometric mean

RESULTS

- **Nominal concentrations (as mg/L):** 0, 3.8, 7.5, 15, 30, 60
- **Measured concentrations (as mg/L):** 0, 3.6, 6.9, 15, 29, 54
- **Unit (results expressed in what unit):** % survival after 24, 48, 72, 96 h
- **Element value:** LC_{50} at 96 hours=27 mg/l based on nominal concentrations
- **Statistical results, as appropriate:** LC_{50}(96 hr): Binominal method

=> Remarks field for Results. Discuss if the effect concentration is greater than materials solubility. Describe additional information that may be needed to adequately assess data for reliability and use, including the following, if available:

Only % survival was shown in a table; At 15 mg/l 100% of fish survived until 96 h; at 30 mg/l 40% of fish survived until 96 h; at 60 mg/l survival decreased, 60% (24 h), 10% (48 h), 0% (72 h), 0% (96 h)

– Biological observations: 7.5 mg/l: abnormal respiration; 15 mg/l: abnormal swimming; 30 mg/l: abnormal respiration and impossible swimming.
– Table showing cumulative mortality:

Percent mortarity of Oryzias latipes exposed to the test chemical

Nominal concentration	Cumulative number of dead fish (% mortality)			
mg/l	24 hours	48 hours	72 hours	96 hours
Control	0 (0)	0 (0)	0 (0)	0 (0)
Solvent Control	0 (0)	0 (0)	0 (0)	0 (0)
3.8	0 (0)	0 (0)	0 (0)	0 (0)
7.5	0 (0)	0 (0)	0 (0)	0 (0)
15	0 (0)	0 (0)	0 (0)	0 (0)
30	0 (0)	2 (20)	4 (40)	6 (60)
60	3 (30)	9 (90)	10 (100)	10 (100)

– Lowest test substance concentration causing 100% mortality: <60mg/l (the highest concentration tested)
– Mortality of controls: 0 %
– Abnormal responses: Abnomal respiration (7.5 mg/l, 48-96hours), abnormal swimming (30mg/l, 24-48 hours), inverted (30 mg/l, 72-96 hours, 60 mg/l, 24-48 hours)
– Reference substances (if used) – results: Not described
– Any observations, such as precipitation that might cause a difference between measured and nominal values.

CONCLUSIONS

The 96 hours LC_{50} for *Medaka(Oryzias latipes)* exposed to 3,4-DCB is 27 mg/l from the concentration-response curve, with 95% confidence limits of 15 and 60 mg/l. The estimated 96 hours no observed effect concentration was 15 mg/l, and 100% death maximum concentration was 60 mg/l.

DATA QUALITY

- **Reliabilities:** Klimisch Code 1 = Reliable without restrictions.
- **Remarks field for Data Reliability:** Experimental design and analytical procedure were well documented.

REFERENCES (Free Text)

Environment Agency of Japan (1997).

OTHER

• Last changed (administrative field for updating)
• Order number for sorting (administrative field)

ACUTE TOXICITY TO FISH (2)

TEST SUBSTANCE

- **Identity:** 3,4-Dichlorobut-1-ene (CAS No 760-23-6)

=> Remarks: Source: purity = unknown

METHOD

- **Method/guideline followed (experimental/calculated):** OECD TG203
- **Type (test type):** 96 h mortality
- **GLP (Y/N):** No
- **Year (study performed):** Not described
- **Species/Strain/Supplier:** *Pimephales promelas*
- **Analytical monitoring:** Yes
- **Exposure period (h):** 96
- **Statistical methods:** Not described

– Test fish (Age/length/weight, loading, pre-treatment): length = 4-10 cm
– Test conditions, e.g.
· Details of test (static, semi-static, flow-through): flow-through
· Dilution water source: Fresh water
· Dilution water chemistry (hardness, alkalinity, pH, DOC, TSS, salinity): soft water
· Stock and test solution and how they are prepared:
· Concentrations dosing rate, flow-through rate, in what medium:
· Vehicle/solvent and concentrations:
· Stability of the test chemical solutions:
·Exposure vessel type (e.g., size, headspace, sealed, aeration, lighting, # per treatment):
· Number of replicates, fish per replicate:
· Water chemistry in test (O2, pH) in the control and one concentration where effects were observed: dissolved oxygen 6.8 mg/l, hardness 46.5 mg/l calcium carbonate, alkalinity 43.5 mg/l calcium carbonate, and pH 7.7.
– Test temperature range: 25.1 deg C
– Method of calculating mean measured concentrations (i.e. arithmetic mean, geometric mean, etc.):

RESULTS

- **Nominal concentrations (as mg/L):**
- **Measured concentrations (as mg/L):**
- **Unit (results expressed in what unit):**
- **Element value:** LC50 at 96 hours=7.17 mg/l based on nominal concentrations
- **Statistical results, as appropriate:**

=> Remarks field for Results. Discuss if the effect concentration is greater than materials solubility. Describe additional information that may be needed to adequately assess data for reliability and use, including the following, if available:

– Biological observations:
– Table showing cumulative mortality:
– Lowest test substance concentration causing 100% mortality:
– Mortality of controls: 0 %
– Abnormal responses:
– Reference substances (if used) – results:
– Any observations, such as precipitation that might cause a difference between measured and nominal values.

CONCLUSIONS

The LC_{50} (96 hours) for *Pimephales promelas* exposed to 3,4-DCB is 7.17 mg/l from the concentration-response curve.

DATA QUALITY

- **Reliabilities:** Klimish Code 4 = not assignable. But this study is the lowest LC50 study.

REFERENCES (Free Text)

Geiger, D. L. et al, Acute Toxicity of Organic Chemicals to Pathead Winnows (Pimephales promelas) Vol. IV, EPA, US, Center for Lake Superior Environmental Studies, Superior, WI. ISBN 0-9614968-3-5 (1988)

OTHER

• Last changed (administrative field for updating)
• Order number for sorting (administrative field)

ACUTE TOXICITY TO DAPHNIA

TEST SUBSTANCE

- **Identity:** 3,4-Dichlorobut-1-ene (CAS No 760-23-6)
- **Remarks:** Kanto Chemical Industries - purity = 99.6 %

METHOD

- **Method/guideline:** OECD TG 202 (1984).
- **Test type:**
- **GLP (Y/N):** Yes.
- **Year (study performed):** 1997.
- **Analytical procedures:** Yes. Measured by GC-MS before and after the replacement of the test water.
- **Species/Strain:** *Daphnia magna*
- **Test details:** Static
- **Statistical methods:** Binomial method.

Remarks field for Test Conditions. Detail and discuss any significant protocol deviations and detail differences from the guideline followed including the following as appropriate:

– Test organisms:
  · Source, supplier, any pre-treatment, breeding method: Supplied by NIES (Japan).
  · Age at study initiation:
  · Control group: Yes.

– Test conditions
  · Stock solutions preparation and stability:
  · Test temperature range: 20 ± 1 °C (measured: 20.1-20.5 °C)
  · Exposure vessel type: 100 ml of tightly-closed glass vessel
  · Dilution water source: Dechlorinated tap water
  · Dilution water chemistry: Hardness: 69 mg/L as CaCO3, pH = 8.3.
  · Lighting: room light, 16h:8h light-darkness cycle
  · Water chemistry in test: DO= 7.7 - 8.7 mg/L; pH= 7.9 - 8.3.
  · Feeding: *Chlorella vulgaris*, 0.1-0.2 mgC/day/individual

– Element (unit) basis: Mean cumulative numbers of juveniles produced per adult (reproduction)
–Test design: Number of replicates=5; individuals per replicate=20; concentrations: 0, 1.8, 3.2, 5.6, 10, and 18 mg/L.
– Method of calculating mean measured concentrations (i.e. arithmetic mean, geometric mean, etc.): geometric mean.
– Exposure period: 48 h.
– Analytical monitoring: By GC analysis. 78-89% of the nominal concentration at preparation; 78-89 % just before the renewal of the test water (after 48 hours exposure).

RESULTS

- **Nominal concentrations:** 0, 1.8, 3.2, 5.6, 10, and 18 mg/l

- **Measured concentrations:** <0.1, 1.6, 2.8, 4.8, 8.4, and 14 mg/l
- **Measured concentrations after 48 hours:** <0.1, 1.6, 2.6, 4.5, 7.7, and 14 mg/l
- **Unit [results expressed in what unit]:**
- **Statistical results, as appropriate:** There was no statistically significant difference between data from the control and 4.6 mg/L test groups.

Remarks field for Results.

CONCLUSIONS

EiC50(24 h) = 13 mg/l
EiC50(48 h) = 10 mg/l
NOECi = 4.6 mg/l

DATA QUALITY

- **Reliabilities:** Klimisch Code: 1= Reliable without restrictions.
- **Remarks field for Data Reliability:** Experimental design and analytical procedure were well documented.

REFERENCES (Free Text)

Environment Agency of Japan (1997).

OTHER

• **Last changed (administrative field for updating)**
• **Order number for sorting (administrative field)**

Remarks field for General Remarks (Use for any other comments necessary for clarification.)

TOXICITY TO AQUATIC PLANTS (E.G., ALGAE)

TEST SUBSTANCE

- **Identity:** 3,4-Dichlorobut-1-ene (CAS No 760-23-6)

=>Remarks: Source: Kanto Chemical Industries - purity = 99.6 %

METHOD

- **Method/guideline followed (experimental/calculated):** OECD TG 201
- **Test type (static/other):** Static
- **GLP (Y/N):** Yes
- **Year (study performed):** 1997
- **Species/strain # and source:** *Selenastrum capricornutum* ATCC22662 (purchased from ATCC)
- **Element basis:** Area under the growth curve
- **Exposure period:** 72 h
- **Analytical monitoring:** Measured by gas chromatography at start and end of the test
- **Statistical methods:** Bartlett

=> Remarks field for Test Conditions. Detail and discuss any significant protocol deviations and detail differences from the guideline followed including the following as appropriate:

– Test organisms
  · Laboratory culture
  · Method of cultivation
  · Controls
– Test Conditions
  · Test temperature range: 23.1-23.3 °C (measured)
  · Growth/test medium: OECD medium
  · Shaking: 100 rpm
  · Dilution water source
  · Exposure vessel type: 100 ml medium in a 500 ml conical flask with a cap which allow ventilation
  · Water chemistry in test (pH) in at least one replicate of each concentration (at start and end of the test): pH=7.9 at start and 7.8 at end of the test (72 h)
  · Stock solutions preparation: DMF : Hydrogenated Castor oil(HCO-40) = 2:1
  · Light levels and quality during exposure: 4200-5000 lx, continuous

–Test design:
  · Number of replicates: Triplicate
  · Concentrations: 0, 10, 18, 32, 56, and 100 mg/l
  · Initial cell number in cells/ml: $1x10^4$
– Method of calculating mean measured concentrations (i.e. arithmetic mean, geometric mean, etc.): Not described

RESULTS

- **Nominal concentrations in mg/L:** 10, 18, 32, 56, and 100

- **Measured concentrations in mg/L:** 7.4, 14, 25, 46, and 86
- **Unit [results expressed in what unit]:** Cell density (cells/ml)
- **ErC50 (24-72 h);** EbC50(0-72 h)=49 mg/l;NOECb = 14 mg/l; ErC50(24-72h)=74 mg/l, NOECr (24-72h)=46 mg/l; calculated based on measured concentrations
- **Was control response satisfactory:** Yes: mean cell density increased to $5x10^5$ cells/ml after 72 h
- **Statistical results, as appropriate:**

=> Remarks field for Results. Discuss if effect concentration is not less than materials solubility. Describe additional information that may be needed to adequately assess data for reliability and use including the following:

– Biological observations
· Cell density at each flask at each measuring point: Control (cells/ml): 48300±7100 (24 h), 258000±20000 (48 h), 521000±40000 (72 h); 86 mg/l: 28200±1400 (24 h), 39500±4500 (48 h), 72100±3600 (72 h)
· Growth curves: Logarithmic growth until end of the test (72 h)
Percent biomass/growth rate inhibition per concentration
Observations

CONCLUSIONS

EC_{50}(72 h) =49 mg/l
NOEC(72 h)=14 mg/l

=> Remarks field with the ability to identify source of comment, i.e. author and/or submitter

DATA QUALITY

- **Reliabilities:** Klimisch Code: 1= Reliable without restrictions
- **Remarks field for Data Reliability:** Experimental design and analytical procedure were well documented.

REFERENCES (Free Text)

Environment Agency of Japan (1997).

OTHER

- **Last changed (administrative field for updating)**
- **Order number for sorting (administrative field)**

=> Remarks field for General Remarks (Use for any other comments necessary for clarification.)

CHRONIC TOXICITY TO AQUATIC INVERTEBRATES (E.G., DAPHNIA)

TEST SUBSTANCE

- Identity: 3,4-Dichlorobut-1-ene (CAS No 760-23-6)

=> Remarks: Source: Kanto Chemical Industries - purity = 99.6 %)

METHOD

- **Method/guideline:** OECD TG 202
- **Test type:** 21-d reproduction test
- **GLP (Y/N):** Yes
- **Year (study performed):** 1997.
- **Analytical procedures:** Measured by gas chromatography on 6, 8, 14, and 16-day.
- **Species/Strain:** *Daphnia magna*
- **Test details:** Semi-static (water renewal: every other day), closed-system
- **Statistical methods:** LC_{50}, ErC_{50}: Binomial method, NOEC: Student t-test

=> Remarks field for Test Conditions. Detail and discuss any significant protocol deviations and detail differences from the guideline followed including the following as appropriate:

–Test organisms:
- · source, supplier, any pre-treatment, breeding method: Supplied by NIES (Japan)
- · Age at study initiation: Juveniles within 24 h old.
- · Control group: Yes

–Test conditions
- · Stock solutions preparation and stability:Solubilizer control (DMF:HCO-40 = 2:1) , max. 10 mg/l.
- · Test temperature range: 19.8-21.0 °C
- · Exposure vessel type: 1000 ml glass beaker; 4 beakers per treatment
- · Dilution water source: Dechlorinated tap water
- · Dilution water chemistry: Hardness: 63 mg/l as $CaCO_3$
- · Lighting:16h:8h light-darkness cycle
- · Water chemistry in test: DO= 6.7-8.5 mg/l; pH=7.6-8.2
- · Feeding: *Chlorella vulgaris*, 0.1-0.2 mgC/day/individual

–Element (unit) basis: Mean cumulative numbers of juveniles produced per adult (reproduction)
–Test design: Number of replicates=4; concentrations: 0.10, 0.32, 1.0, 3.2, and 10 mg/l, because EC50 (48 h Immobilization test) was = 10 mg/l
–Method of calculating mean measured concentrations (i.e. arithmetic mean, geometric mean, etc.): Time Weighted Mean (10 mg/l, Geometric Mean)
–Exposure period: 21 d
–Analytical monitoring: 80-91% of the nominal concentration at preparation; 78-88% just before the renewal of the test water

RESULTS

- **Nominal concentrations:** 0.10, 0.32, 1.0, 3.2, and 10 mg/l
- **Measured concentrations:** 0.08, 0.28, 0.84, 2.9, and 8.5 mg/l six days after
- **Unit [results expressed in what unit]:** Mean cumulative numbers of juveniles produced per adult after 21 d
- NOEC (21 d, reproduction) =0.83 mg/l, ErC_{50} (21 d, reproduction) =4.0 mg/l ; LC_{50} for parental *Daphnia* (21 d) =4.5 mg/l; calculated based on measured concentrations.
- **Statistical results, as appropriate:** There was no statistically significant difference between data from the control and 0.83 mg/l test groups.

=> Remarks field for Results. Discuss if element effect concentration is not less than materials solubility. Describe additional information that may be needed to adequately assess data for reliability and use including the following as appropriate:

– Biological observations
· Cumulative numbers of dead parental *Daphnia*: Control: 0 (mortality: 0 %), 0.83 mg/l: 0 (mortality: 0 %), 2.8 mg/l: 2 (mortality: 5 %), 8.5 mg/l: 40 (mortality: 100 %)
· Time of the first production of young: 8 d
· Mean cumulative numbers of young produced per adult: Sol.Control: 5.5 (8 d), 28.5 (14 d), 77.1 (21 d); 0.83 mg/l: 5.9 (8 d), 30.1 (14 d), 77.1 (21 d); 2.8 mg/l: 0.2 (8 d), 12.5 (14 d), 54.7 (21 d); 8.5 mg/l: 0.0 (8 d), 0.0 (14 d), 0.0 (21 d).
· Was control response satisfactory: Yes

CONCLUSIONS

NOECr (21 d, reproduction) =0.83 mg/l
ErC50 (21 d, reproduction) =4.0 mg/l
LC50 for parental *Daphnia* (21 d) =4.5 mg/ l
=> Remarks field with the ability to identify source of comment, i.e. author and/or submitter calculated based on nominal concentrations

DATA QUALITY

- **Reliabilities:** Klimisch Code: 1= Reliable without restrictions
- **Remarks field for Data Reliability:** Experimental design and analytical procedure were well documented.

REFERENCES (Free Text)

Environment Agency of Japan (1997).

OTHER

- **Last changed (administrative field for updating)**
- **Order number for sorting (administrative field)**

=> Remarks field for General Remarks (Use for any other comments necessary for clarification.)

HEALTH ELEMENTS

ACUTE TOXICITY (Oral)

TEST SUBSTANCE

- 3,4-Dichlorobut-1-ene (CAS No 760-23-6)

Remarks: Source: Tokyo Kasei Kogyo, Lot No. FHD01, Purity: 99.7 %, Kept at 4 °C until use

METHOD

- **Method/guideline:** OECD TG 401
- **Test type:** OECD Single Dose Oral Toxicity Test
- **GLP:** Yes
- **Year:** 1995-1996
- **Species:** Rat
- **Strain:** Crj:CD (SD)
- **Route of administration:** oral (by single-dose gavage)
- **Doses/concentration levels:** 0 (vehicle), 670, 804, 965, 1158, 1389, 1667 mg/kg
- **Sex:** Male & Female
- **Route of administration (if inhalation- aerosol, vapor, gas, particulate):**
- **Remarks field for Test Condition:**

Test Subjects:

Age : 5 week old for males and females
Weight at study initiation: 125-138 g for males, 110-122 g for females
No. of animals per sex per dose: 5 per sex per dose group

Study Design:

Vehicle**:** Sesame oil
Volume administration or concentration:
Post dose observation period: 14 days
Exposure duration (for inhalation studies).
Clinical observations performed and frequency:

Each rat was weighed immediately prior to treatment, the day after 1, 3, 7, and 14 days. The rats were observed at least one time per day during this time for signs of toxicity. All rats were submitted for a gross pathological examination as they died spontaneously, or survivors two weeks post-treatment.

RESULTS

- **LD50**
  Male : 943 mg/kg (828-1068 mg/kg bw., 95% confidence interval).
  Female : 946 mg/kg (808-1085 mg/kg bw., 95% confidence interval).

REMARKS FIELD FOR RESULTS

Body weight: Body weight in the treated groups were lower than those of the control group on the day after dosing.
Food/water consumption: Not described
Clinical signs (description, severity, time of onset and duration): Clinical signs of decreased locomotor activity, deep respiration, ptosis, salivation, flaccidity, adoption of a prone position, piloerection and perinasal soiling with nasal discharge were observed in the treated groups.
At autopsy, lung enlargement, urine retention and crystalline materials in the urinary bladder, and hemorrhagic black spots in the glandular stomach mucosa were observed in animals.
Calculation of LD_{50}: Probit method based on the mortality on 14th days after dosing.

CONCLUSIONS

The LD_{50} values were 943 mg/kg for males and 946 mg/kg for females.

DATA QUALITY

- **Reliabilities:** Klimish Code 1 = Reliable without restrictions
- **Remarks field for Data Reliability**

Well conducted study, carried out by Research Institute for Animal Science in Biochemistry and Toxicology (Japan).

REFERENCES (Free Text)

Ministry of Health and Welfare: Japan, Toxicity Testing Reports of Environmental Chemicals 4, 535-536 (1996)

GENERAL REMARKS

ACUTE TOXICITY (Inhalation)

TEST SUBSTANCE

- 3,4-Dichlorobut-1-ene (CAS No 760-23-6)

Remarks: Source: Purity: 98 %, purified by gas chromatography

METHOD

- **Method/guideline:** Not described.
- **Test type:** Single Dose Inhalation Toxicity Test
- **GLP:** No
- **Year:** 1997
- **Species:** Rat
- **Strain:** ChR;CD (SD)
- **Route of administration:** Inhalation
- **Doses/concentration levels:** 1000, 2250, 3000 ppm
- **Sex:** Male
- **No. of animals per dose:** 6
- **Route of administration (if inhalation- aerosol, vapor, gas, particulate):** Vapor
- **Remarks field for Test Condition:**
- **Test Subjects:**

Age: No data available
Weight at study initiation: 246-295 g bw
Doses: The test material was metered by a stainless steel T-tube where it was vaporized at 120-150 centigrade. The resulting vapors were carried by a stream air into a 16-liter exposure chamber containing six rats. The chamber atmosphere was analyzed at least once every hour by a gas chromatographic method.
Doses per time period: four hours exposure
Volume administration or concentration: 1000, 2250, 3000 ppm
Post dose observation period: No data available
Exposure duration (for inhalation studies): No data available

Study Design:

Clinical observations performed and frequency:
Organs examined at necropsy: kidney, liver, trachea, lung, brain, testes, bone marrow, spleen, thymus, gastro intestinal tract were examined.

RESULTS

- **LC50:** 2100 ppm
- **Number of deaths and results of histopathologic examination of tissues at each dose level**

Rat No.	Exposure	Days killed /Died	Kidney	Liver	Trachea	Lung	Brain	Testes	Bone Marrow
89115	3000 ppm	D<1	2, 3	1	4	5	-	-	-
89154	3000 ppm	D<1	3	1	4	5	-	-	NS
89272	2250 ppm	K-14	6	-	4	-	-	-	-
89276	2250 ppm	K-14	2, 7	-	4	-	-	-	-
89811	1000 ppm	K-1	3	1	4	-	-	-	-
89831	1000 ppm	K-1	7, 3	1	4	-	-	-	-
89833	1000 ppm	K-2	-	-	-	-	-	-	-
89850	1000 ppm	K-2	3	-	-	-	-	-	NS
89852	1000 ppm	K-7	-	-	-	-	-	-	-
89857	1000 ppm	K-7	-	-	-	-	-	-	-

Lesier Code:

NS	No section
-	Not remarkable
1	Centrilobular hepatocellular degeneration
2	Focal nephritis
3	Tubular epithelial degeneration
4	Murine pneumonitis
5	Pulmonary congestion (acute)
6	Diffuse chronic nephritis
7	Hydronephrosis

- **REMARKS FIELD FOR RESULTS**

Statistical analysis by metod of Litchfield, J. T., Jr., and F. Wilcoxon, *J. Pharmacol. And Exper. Ther*., 96, 99 (1949).

CONCLUSIONS

Inhalation at both high and low dosage levels was followed by degenerative lesions of the livers and/or kidneys of rats which died or killed within two days of exposure. Observable lesions were not present in the tissues examined from rats killed at seven days following low level exposure or fourteen days following medium level exposure.

DATA QUALITY

- **Reliabilities:** Klimish Code 2 = Reliable with restrictions

- **Remarks field for Data Reliability**

Well conducted study, carried out by DU PONT Haskell Laboratory for Toxicology and Industrial Medicine

REFERENCES (Free Text)

Haskell Laboratory Report No. 96-67

GENERAL REMARKS

ACUTE SKIN IRRITATION

TEST SUBSTANCE

- 3,4-Dichlorobut-1-ene (CAS No 760-23-6)

Remarks: Source: Purity: 99 %

METHOD

- **Method/guideline:** OECD TG 404
- **Test type:** Acute skin irritation, Patch-Test
- **GLP:** Yes
- **Year:** 1999
- **Species:** Rabbit
- **Strain:** Himalayan
- **Route of administration:** dermal application to the shaved intact dorsal skin (semi-occlusive procedure)
- **Doses/concentration levels:** 0.5 ml/patch and animal, once epicutaneous.
- **Sex:** Male
- **No. of animals per dose:** 3
- **Route of administration (if inhalation- aerosol, vapor, gas, particulate):**
- **Remarks field for Test Condition:**
- **Test Subjects:**

Age: approx. 4 to 4.5 months.
Weight at study initiation: 2.0-2.5 kg bw
Doses: 0.5 ml
Doses per time period: four hours exposure
Volume administration or concentration: The undiluted test substance was applied to the site (area: approx. 6 cm^2, semiocclusive) and then covered with a gauze patch.
Post dose observation period: During the exposure the animals were kept in comfortable restrainers. After the 4-hour exposure period the patch was removed and the skin sites were evaluated. Scores were taken 60 minutes, 24, 48, 72 hours and 4 days after patch removal.

Study Design:

Clinical observations performed and frequency:
Organs examined at necropsy:

RESULTS

Under the present test conditions all three rabbits exposed for 4 hours of 0.5 ml 3,4-DCB and animal (semi-occlusive condition) showed an erythema:
animal no. 1: 60 minutes to 48 hours after patch remove grade 1;
animal no. 2: 60 minutes to 24 hours after patch remove 2 and 48 to 72 hours after patch remove grade 1;
animal no. 3: 60 minutes to 24 hours after patch remove 2 and 48 hours after patch remove grade 1.

- **REMARKS FIELD FOR RESULTS**

Examination schedule	**Skin irritation scores Animal no.**		
	1	**2**	**3**
Before dosing	**E0/Oe0**	**E0/Oe0**	**E0/Oe0**
Time after removal of the patch			
60 min	E1/Oe0	E2/Oe0	E2/Oe0
24 hrs	E1/Oe0	E2/Oe0	E2/Oe0
48 hrs	E1/Oe0	E1/Oe0	E1/Oe0
72 hrs	E0/Oe0	E0/Oe0	E0/Oe0
4 days	-	E0/Oe0	-

0: no pathological findings
E: erythema/eschar formation
Oe: oedema

CONCLUSIONS

All three rabbits showed an erythema (grade 1 or 2) for up to 72 hours after patch removal.

Based on the EC directive 67/548/EEC and its subsequent amendments (Annex VI (L110A, May 4 th, 1993) to Commission Directive 93/21/EEC) the test substance is classified as corrosive.

DATA QUALITY

- **Reliabilities:** Klimish Code 1 = Reliable without restrictions

- **Remarks field for Data Reliability**

Well conducted study, carried out by Laboratory of Pharmacology and Toxicology KG (Germany)

REFERENCES (Free Text)

Laboratory of Pharmacology and Toxicology KG, Germany, LPT Report No. 9300/382/95 (1999).

GENERAL REMARKS

ACUTE EYE IRRITATION

TEST SUBSTANCE

- 3,4-Dichlorobut-1-ene (CAS No 760-23-6)

Remarks: Source: Purity: approx. 99 %

METHOD

- **Method/guideline:** OECD TG 405
- **Test type:**
- **GLP:** Yes
- **Year:** 1999
- **Species:** Rabbit
- **Strain:** Himalayan
- **Route of administration:** single instillation into the conjunctival sac
- **Doses/concentration levels:** 0.1 ml/animal
- **Sex:** Male
- **No. of animals per dose:** 3
- **Route of administration (if inhalation- aerosol, vapor, gas, particulate):**
- **Remarks field for Test Condition:**
- **Test Subjects:**

Age: approx. 4.5 months
Weight at study initiation: 2.1-2.3g bw
Doses: A dose of 0.1 ml 3,4-DCB was administered into the conjunctival sac of the right eye of rabbits after gently pulling the lower lid away from the eyeball. The lid was then gently held together for about one second in order to prevent loss of test material.
The left eye, which remained untreated, served as control.
Doses per time period: four hours exposure
Volume administration or concentration: 0.1 ml of undiluted test substance.
Post dose observation period: The eyes were examined ophthalmoscopically with a slit lamp prior to the administration and also 1, 24, 48, and 72 hours after the administration. The eye reactions were observed and registered.
24 hours after administration the eyes were treated additionally with fluorescein and examined.

Study Design:

Clinical observations performed and frequency: Cornea, iris, and conjunctiva were examined and the reactions were scored according to the following scheme:

Cornea: 0: no ulceration of opacity
1: scattered or diffuse areas of opacity, details of iris clearly
2: easily discernible translucent area, details of iris slightly obscured
3: nacreous areas, no details of iris visible, size of pupil barely discernible
4: Opaque cornea, iris not discernible through the opacity

Iris: 0: normal
1: markedly deepened rugae, congestion, swelling, moderate circumcorneal hyperaemia, or injection, any of these or combination of any thereof, iris still reacting to light (sluggish reaction is positive)
2: no reaction to light, haemorrhage, gross destruction (any or all of these)

Conjunctiva:
Redness: 0: blood vessels normal
1: some blood vessels definitely hyperaemic (injected)
2: diffuse, crimson color, individual vessels not easily discernible
3: diffuse beefy red
Chemosis: 0: no swelling
1: any swelling above normal (including nictitating membranes)
2: obvious swelling with partial eversion of lids
3: swelling with lids about half-closed
4: swelling with lids more than half-closed

RESULTS

- **Corneal opacity / Conjunctival redness**

Corneal opacity (grade 1) was observed in animal no. tree 1 to 48 hours after instillation.
The fluorescein test performed after 24 hours revealed corneal staining in animal no. 3 (1/4 of the corneal surface).
An irritation of the iris (grade 1) was observed in animal no. three 1 to 48 hours after instillation.
Conjunctival redness (grade 1) was observed in all three animals 1 hour after instillation.
There was no systemic intolerance reaction.

- **REMARKS FIELD FOR RESULTS**

Right eye: 0.1 ml 3,4-DCB/animal

Time after administration	CORNEA	IRIS	CONJUNCTIVAE	
	Opacity		Redness	Chemosis
		Animal No. : 1/2/3		
Before dosing	0/0/0	0/0/0	0/0/0	0/0/0
1 hr	0/0/1	0/0/1	1/1/1	0/0/0
24 hrs	0/0/1	0/0/1	0/0/0	0/0/0
48 hrs	0/0/1	0/0/1	0/0/0	0/0/0
72 hrs	0/0/0	0/0/0	0/0/0	0/0/0

24 hrs fluorescein test: animal No. 3: corneal staining (1/4 of the surface)

Left eye: untreated

Time after administration	CORNEA	IRIS	CONJUNCTIVAE	
	Opacity		Redness	Chemosis
		Animal No. : 1/2/3		
Before dosing	0/0/0	0/0/0	0/0/0	0/0/0
1 hr	0/0/0	0/0/0	0/0/0	0/0/0
24 hrs	0/0/0	0/0/0	0/0/0	0/0/0
48 hrs	0/0/0	0/0/0	0/0/0	0/0/0
72 hrs	0/0/0	0/0/0	0/0/0	0/0/0

24 hrs fluorescein test: no pathological findings

CONCLUSIONS

This substance is classified as irritant based on the EC-directive 67/548/EEC.

DATA QUALITY

- **Reliabilities:** Klimish Code 1 = Reliable without restrictions

- **Remarks field for Data Reliability**

Well conducted study, carried out by Laboratory of Pharmacology and Toxicology KG (Germany).

REFERENCES (Free Text)

Laboratory of Pharmacology and Toxicology KG, Germany, LTP Report No. 9301/382/95 (1999).

GENERAL REMARKS

REPEATED DOSE TOXICITY

TEST SUBSTANCE

- 3,4-Dichlorobut-1-ene (CAS No 760-23-6)

Remarks: Source: Tokyo Kasei Kogyo, Lot No. FHD01, Purity: 99.7 %, Kept at 4 °C until use

METHOD

- **Method/guideline:** OECD TG 422
- **Test type:** OECD Combined Repeat Dose and Reproductive/Developmental Toxicity Screening Test
- **GLP:** Yes
- **Year:** 1995-1996
- **Species:** Rat
- **Strain:** Crj:CD (SD)
- **Route of administration:** oral (by gavage)
- **Doses/concentration levels:** 0, 0.4, 2, 10, 50 mg/kg/day (in distilled water)
- **Sex:** Male & Female
- **Exposure period:** Males; for 44 days, Females; for 41-46 days, from 14 days before mating to day 3 of lactation
- **Frequency of treatment:** Once daily
- **Control group and treatment:** Concurrent vehicle
- **Post exposure observation period:** none
- **Duration of test:** Male; for 44 days
  Female; for 41-46 days
- **Statistical methods:** Dunnett's or Scheffe's test for continuous data and Chi square test for quantal data

REMARKS FIELD FOR TEST CONDITIONS

– **Test Subjects:**

· ***Age at study initiation*:** 9 week old for males, 8 week old for females
· ***Weight at study initiation*:** 343-384 g for males, 192-222 g for females

· ***No. of animals per sex per dose*:** 10 per sex per dose group

– **Study Design:**

· ***Vehicle*:** Sesame oil
· ***Satellite groups and reasons they were added*:** none
· ***Clinical observations performed and frequency*:**
General condition was observed once a day, body wt. and food/water consumption were determined once a week.
Hematology and biochemistry for males were carried out only at time of necropsy after 44 days of chemical exposure. Urinalysis was carried out 38 or 40 days
· ***Organs examined at necropsy:***
organ weight: brain, heart, liver, kidney, spleen, adrenal, thymus, testes, epididymis
microscopic: all animals in control and 50 mg/kg, and males failed to cause pregnancy or non-pregnant females: brain, pituitary gland, eyeball, thyroid gland, parathyroid gland, thymus, heart, lung, liver, kidney, adrenal, spleen, stomach, small intestine, large intestine, pancreas, urinary bladder, bone marrow, testes, epididymis, prostate, seminal vesicle, ovary, uterus, vagina, mammary gland

RESULTS

- **NOAEL**
10 mg/kg/day

REMARKS FIELD FOR RESULTS

– ***Body weight:*** Significant differences from controls were not observed.
– ***Food/water consumption:*** Food consumption decreased on the first day of dose, but there was no sig. difference from controls after day-8.
– ***Clinical signs*** *(description, severity, time of onset and duration)**:***
Males: Ephemeral decreased locomotor activity (all rats, the first day of the study in the 50 mg/kg bw/day group, 1/10, day 5-12) and ephemeral slaver (50 mg/kg: 10/10, the first day of the study)
Females: Death(50 mg/kg: 1/10), ephemeral decreased locomotor activity (50 mg/kg: 10/10), and ephemeral slaver (50 mg/kg: 5/10, the first day of the study)
– ***Haematology*:**
– ***Biochem:***
Males: Increase of T. protein at 50 mg/kg *($p<0.01$).*

Dose level (mg/kg/day)	**0**	**0.4**	**2**	**10**	**50**
No. of animals	10	10	10	10	10
GOT (IU/l, Mean ± SD)	63 ± 11	60 ± 3	56 ± 5	62 ± 20	52 ± 7
GPT (IU/l, Mean ± SD)	28 ± 5	28 ± 3	28 ± 5	35 ± 16	31± 8
γ-GTTP(IU/l, Mean ± SD)	0.50± 0.66	0.64± 0.42	0.37 ± 0.19	0.32 ± 0.24	0.41± 0.25
Total protein (g/dl, Mean ± SD)	6.45 ± 0.19	6.47 ± 0.13	6.40 ± 0.26	6.63 ± 0.14	6.77 ± 0.27*
Urea nitrogen (mg/dl, Mean ± SD)	15.5 ± 1.6	14.2 ± 1.4	15.9 ± 1.4	15.0 ± 1.9	13.1 ± 1.7*

– ***Ophthalmologic findings:*** not examined
– ***Mortality and time to death:*** 1 female was dying 2 days after parturition.
– ***Gross pathology incidence and severity:*** Liver swelling (male: 2/10, female: 1/10) and kidney swelling (male: 3/10, female: 0/10) at 50 mg/kg.
– ***Organ weight changes:***
Male: increase in kidney weight at 10 mg/kg (absolute ($p<0.05$) and liver weight at 50

mg/kg (absolute ($p<0.01$) and relative ($p<0.01$))

Dose level (mg/kg/day)	0	0.4	2	10	50
Absolute weight					
Liver (g, Mean ± SD)	15.31 ± 1.50	15.13 ± 2.08	15.19 ± 2.17	16.58 ± 0.65	18.42 ± 2.23**
Kidneys (g, Mean ± SD)	3.24 ± 0.26	3.21 ±0.18	3.22 ± 0.29	3.57 ± 0.25 *	3.83 ± 0.36**
Relative weight					
Liver (g%, Mean ± SD)	3.03 ± 0.25	2.96 ± 0.27	2.96 ± 0.26	3.24 ± 0.15	3.74 ± 0.28**
Kidney (g, Mean ± SD)	0.64 ± 0.04	0.63 ± 0.05	0.63 ± 0.06	0.70 ± 0.05	0.78 ± 0.06**

Significant difference from group (*: $p<0.05$; **: $P<0.01$)

Female: increase in kidney weight at 50 mg/kg (relative ($p<0.01$))

Dose level (mg/kg/day)	0	0.4	2	10	50
Relative weight					
Kidney (g, Mean ± SD)	0.64 ± 0.04	0.57 ± 0.04	0.58 ± 0.04	0.61 ± 0.04	0.68 ± 0.04**

Significant difference from group (*: $p<0.05$; **: $P<0.01$)

– ***Histopathology*** *(incidence and severity)**:***

Male:

Liver: Hepatocellular hypertrophy (5/10) at 50 mg/kg.

Kidney: Increased deposition of hyaline droplets in the proximal tubular epithelium at 10 mg/kg.

Dose level (mg/kg/day)	degree*	0	0.4	2	10	50
No. of animals		10	10	10	10	10
Hepatocellular hypertrophy	+	0	0	0	0	5
Hyaline droplet in proximal tubule	+	9	10	10	5	1
	++	0	0	0	5	4
	+++	0	0	0	0	5
Basophilic tubules	+	4	3	4	4	5
	++	0	0	0	0	2

*degree: - negative, + slight, ++ moderate, +++ marked

Female:

Liver: Hepatocellular hypertrophy (3/10) at 50 mg/kg.

Dose level (mg/kg/day)	degree*	0	0.4	2	10	50
No. of animals		10	10	10	10	10
Hepatocellular hypertrophy	+	0	0	0	0	3

*degree: - negative, + slight, ++ moderate, +++ marked

CONCLUSIONS

The study was conducted at doses of 0, 0.4, 2, 10 and 50 mg/kg/day for at least 44 days. In males, absolute kidney weights were slightly increased with 10 mg/kg/day dose. Absolute and relative weights of the liver and kidneys were increased with 50 mg/kg/day dose. Blood chemical examination revealed an increase in total protein. The histopathological examination revealed increased hyaline droplets in the renal tubular epithelium with doses of 10 and 50 mg/kg/day and hepatocellular hypertrophy with dose of 50 mg/kg/day.

males, one female was sacrificed in a moribund condition on day 2 of lactation. An increase in relative kidney weights were observed at the dose of 50 mg/kg/day. However, no histopathological changes considered to be related to the change of the kidney weight were detected. Hepatocellular hypertrophy was observed at the dose of 50 mg/kg/day.

NOAELs in this r repeat dose study are 2 mg/kg/day for males and 10 mg/kg/day for females, but the renal toxicity in males is considered to be male rat specific, probably due to α_{2U}-globulin involvement. Therefore, the NOAEL for repeated dose toxicity is considered to be 10 mg/kg/day..

DATA QUALITY

- **Reliabilities:** Klimish Code 1 = Reliable without restrictions

Remarks field for Data Reliability

Well conducted study, carried out by Research Institute for Animal Science in Biochemistry and Toxicology (Japan).

REFERENCES (Free Text)

Ministry of Health and Welfare: Japan, Toxicity Testing Reports of Environmental Chemicals 4, 537-546 (1996)

GENERAL REMARKS

This study was conducted to examine both repeated dose toxicity and reproductive/developmental toxicity as an OECD screening combined study. Therefore, biochemical and haematological analysis, and urinalysis for females were not performed. Functional observation, estrous cycle length and pattern, and sperm examination were not performed because the test was conducted by the TG adopted in 1990.

TOXICITY TO REPRODUCTION/DEVELOPMENT

TEST SUBSTANCE

- 3,4-Dichlorobut-1-ene (CAS No 760-23-6)

Remarks: Source: Tokyo Kasei Kogyo, Lot No. FHD01, Purity: 99.7 %, Kept at 4 °C until use

METHOD

- **Method/guideline:** OECD TG 422
- **Test type:** OECD Combined Repeat Dose and Reproductive/Developmental Toxicity Screening Test
- **GLP:** Yes
- **Year:** 1995-1996
- **Species:** Rat
- **Strain:** Crj;CD (SD)
- **Route of administration:** oral (by gavage)
- **Doses/concentration levels:** 0, 0.4, 2, 10, 50 mg/kg/day (Vehicle: Sesame oil)
- **Sex:** Male & Female
- **Exposure period:** Male; for 44 days from 2 weeks prior to mating
  Female; for 41-46 days from 2 weeks prior to mating to day 3 postpartum throughout mating and pregnancy
- **Frequency of treatment:** Once daily
- **Control group and treatment:** Concurrent vehicle
- **Post exposure observation period:** none
- **Duration of test:** Male: for 44 days
  Female: for 41-46 days
- **Statistical methods:** Dunnett's or Scheffe's test for continuous data and Chi square test for quantal data

REMARKS FIELD FOR TEST CONDITIONS

– **Test Subjects:**

· ***Age at study initiation*:** 9 week old for males, 8 week old for females

· ***Weight at study initiation*:** 343-384 g for males, 192-222 g for females
· ***No. of animals per sex per dose*:** 10 per sex per dose group

– **Study Design:**
The animals were sacrificed on the day 4 of lactation for females. Females with no delivery were killed 4 days after the delivery expected date.

· ***Vehicle*:** Sesame oil
· ***Satellite groups and reasons they were added*:** none
· ***Mating procedures*:** Male/female per cage; 1/1, length of cohabitation; at the most 5 days, until proof of pregnancy (formation of vaginal closing or sperm detection in vagina)
· ***Clinical observations performed and frequency*:**
Parent: General appearance once a day
Foetus: General appearance once a day after birth
Hematology, biochemistry and urinalysis for males only at time of necropsy after 44 days of chemical exposure
· ***Organs examined at necropsy*:**
Parent: organ weight: brain, heart, liver, kidney, spleen, adrenal, thymus, testes, epididymis.
microscopic: all animals in control, 50 mg/kg group and unfertilised animals in other groups: brain, pituitary gland, eyeball, thyroid gland, parathyroid gland, thymus, heart, lung, liver, kidney, adrenal, spleen, stomach, small intestine, large intestine, pancreas, urinary bladder, bone marrow, ovary, uterus, vagina, mammary gland
Foetal: full macroscopic examinations on all of pups
· ***Parameters assessed during study*:**
Body wt. (once a week), food/water consumption (once a week), No. of pairs with successful copulation, copulation index (No. of pairs with successful copulation/No. of pairs mated x 100), pairing days until copulation, No. of pregnant females, fertility index = (No. of pregnant animals/No. of pairs with successful copulation x 100), No. of corpora lutea, No. of implantation sites, implantation index (No. of implantation sites/No. of corpora lutea x 100), No. of living pregnant females, No. of pregnant females with parturition, gestation length, No. of pregnant females with live pups on day 0, gestation index (No. of females with live pups/No. of living pregnant females x 100), No. of pregnant females with live pups on day 4, delivery index (No. of pups born/No. of implantation sites x 100), No. of pups alive on day 0 of lactation, live birth index (No. of live pups on day 0/No. of pups born x 100), sex ratio (Total No. of male pups/Total No. of female pups), No. of pups alive on day 4 of lactation, viability index (No. of live pups on day 4/No. of live pups on day 0 x 100), body wt. of live pups (on day 0 and 4)

RESULTS

- **NOAEL for reproductive performance:**

NOAEL: 50 mg/kg/day

- **NOAEL for offspring development:**

NOAEL: 50 mg/kg/day

- **Actual dose received by dose level by sex if available:**

0, 0.4, 2, 10, 50 mg/kg/day for both sexes

- **Maternal data with dose level (with NOAEL value):**

At 50 mg/kg, no statistically significant effects were observed.

Dose level (mg/kg/day)	**0**	**0.4**	**2**	**10**	**50**
No. of pairs mated	10	10	10	10	10
No. of pairs with successful copulation	10	10	10	10	10
Pairing days until copulation (Mean ± SD)	2.4 ± 1.2	2.1 ± 1.3	2.7 ± 0.9	2.4 ± 1.2	2.0 ± 1.2
No. of pregnant females	9	8	10	10	9
No. of corpora lutea (Mean ± SD)	18.3 ± 1.6	18.6 ± 2.1	17.4 ± 2.2	18.5 ± 2.8	17.2 ± 1.4
No. of implantation sites (Mean ± SD)	17.6 ± 1.4	18.1 ± 1.4	16.1 ± 3.1	17.3 ± 2.5	16.6 ± 1.3
No. of pregnant females with parturition	9	8	10	10	9
Gestation length (days, Mean ± SD)	22.6 ± 1.4	22.3 ± 0.5	22.5 ± 0.5	22.3 ± 0.5	22.4 ± 0.5
No. of pregnant females with live pups on day 0	9	8	10	10	9
Gestation index (%)	100	100	100	100	100
No. of pregnant died	0	0	0	0	1
No. of pregnant females with live pups on day 4	9	8	10	10	8

- **Foetal data with dose level (with NOAEL value):**

At 50 mg/kg, no statistically significant effects were observed.

Dose level (mg/kg/day)		**0**	**0.4**	**2**	**10**	**50**
No. of pups born (Mean ± SD)		16.7 ± 1.4	17.5 ± 2.2	15.4 ± 2.8	15.1 ± 3.3	15.3 ± 1.4
Delivery index (%)		95.0 ± 5.2	96.3 ± 7.0	96.0 ± 5.5	86.5 ± 14.6	92.9 ± 8.7
No. of pups alive on day 0 of lactation (Mean ± SD)		16.3 ± 1.4	17.3 ± 2.3	15.4 ± 2.8	14.9 ± 3.3	14.3 ± 3.1
Live birth index (%)		98.0 ± 4.0	98.6 ± 2.7	100 ± 0	98.8 ± 2.6	93.8 ± 18.7
Sex ratio (Male/Female)		0.88	1.06	1.11	0.99	0.79
No. of pups alive on day 4 of lactation (Mean ± SD)		16.2 ± 1.4	17.0 ± 2.0	15.4 ± 2.8	14.7 ± 3.3	13.6 ± 5.3
Viability index (%)		99.3 ± 2.0	98.7 ± 2.4	100 ± 0	98.7 ± 2.8	88.9 ± 33.3
Body weight of live pups (%) (Mean ± SD)						
on day 0	**Males**	7.1 ± 0.5	6.7 ± 0.6	7.0 ± 0.8	6.9 ± 0.4	6.8 ± 0.5
	Females	6.7 ± 0.6	6.3 ± 0.6	6.6 ± 0.6	6.5 ± 0.5	6.3 ± 0.5
on day 4	**Males**	11.2± 1.0	10.7 ± 1.1	11.3 ± 1.5	10.9 ± 1.5	11.1 ± 1.0
	Females	10.9 ± 1.1	10.2 ± 1.2	10.5 ± 1.4	10.3 ± 1.6	10.5 ± 0.8

REMARKS FIELD FOR RESULTS.

- ***Mortality and day of death*:** One female was sacrificed in a moribund condition on 2 day of lactation.
- ***Body weight*:** Low body weight gain during the pregnancy period in females at 50 mg/kg.
- ***Food/water consumption:*** In both sexes, food consumption were degreased on day 1, but there were not significant difference from controls after day 2.
- ***Reproductive data*:** There were no statistically significant differences from controls.
- ***Fetal data*:** There were no statistically significant differences from controls.
- ***Grossly visible abnormalities, external, soft tissue and skeletal abnormalities*:** no statistically significant effects

CONCLUSIONS

The NOAEL for both reproductive performance and offspring development are considered to be 50 mg/kg/day.

DATA QUALITY

- **Reliabilities:** Klimish Code 1 = Reliable without restrictions

Remarks field for Data Reliability

Well conducted study, carried out by Research Institute for Animal Science in Biochemistry and Toxicology (Japan).

REFERENCES (Free Text)

Ministry of Health and Welfare: Japan, Toxicity Testing Reports of Environmental Chemicals 4, 537-546 (1996)

GENERAL REMARKS

This study was conducted to examine both repeated dose toxicity and reproductive/developmental toxicity as an OECD screening combined study. Estrous cycle length and pattern, and anogenital distances were not performed because the test was conducted by the TG adopted in 1990.

GENETIC TOXICITY IN VITRO (BACTERIAL TEST)

TEST SUBSTANCE

- 3,4-Dichlorobut-1-ene (CAS No 760-23-6)

Remarks: Source: Tokyo Kasei Kogyo, Lot No. FBP01, Purity: 99 %, Kept in a refrigerator until use

METHOD

- **Method/guideline**: OECD TG 471
- **Test type**: Reverse mutation assay
- **GLP***:* Yes
- **Year**: 1996
- **Species/Strain:** *Salmonella typhimurium* TA100, TA1535, TA98, TA1537
  Escherichia coli WP2 *uvr*A
- **Metabolic activation:** S9 from rat liver, induced with phenobarbital and 5,6-benzoflavone
- **Statistical methods**: No statistic analysis

REMARKS FIELD FOR TEST CONDITIONS

– **Study Design:**

· ***Concentration*:**µg /plate

Reverse mutation test (I)

TA100, TA1535	-S9: 0, 500, 1000, 1500, 2000, 2500
	+S9: 0, 500, 1000, 1500, 2000, 2500, 3000(TA100 only)
WP2 *uvr*A,TA98, TA1537	-S9: 0, 156, 313, 625, 1250, 2500
	+S9: 0, 156, 313, 625, 1250, 2500, 5000(TA98 only)

Reverse mutation test (II)

TA100, TA1535	-S9: 0, 250, 400, 550, 700, 850, 1000
	+S9: 0, 1000, 1200, 1400, 1600, 1800, 2000, 2200
WP2 *uvr*A,TA98, TA1537	-S9: 0, 39, 78, 156, 313, 625, 1250, 2500(TA98 only)
	+S9: 0, 39, 78, 156, 313, 625, 1250

· ***Number of replicates*:** 2
· ***Plates/test*:** 3
· ***Procedure*:** Plate-incubation method
· ***Solvent*:** Acetone
· ***Positive controls*:** -S9 mix: 2-(2-Furyl)-3-(5-nitro-2-furyl) acrylamide (TA100, TA98, WP2), Sodium azide (TA1535) and 9-Aminoacridine (TA1537)
+S9 mix: 2-Aminoanthracene (five strains)

RESULTS

- **Cytotoxic concentration:**
  With metabolic activation: 1250 μg/plate(WP2, TA98, TA1537), 2000 μg/plate(TA1535), 2200 μg/plate(TA100)
  Without metabolic activation:625 μg/plate(TA98, TA1537), 850 μg/plate(TA100), 1000 μg/plate(TA1535), 1250 μg/plate(WP2)

- **Genotoxic effects:**

	TA1535			**TA100, TA98 TA1537**			**WP2 *uvr*A**		
	+	?	-	+	?	-	+	?	-
With metabolic activation:	**[X]**	**[ ]**	**[ ]**	**[ ]**	**[ ]**	**[X]**	**[ ]**	**[ ]**	**[X]**
Without metabolic activation:	**[X]**	**[ ]**	**[ ]**	**[ ]**	**[ ]**	**[X]**	**[ ]**	**[ ]**	**[X]**

REMARKS FIELD FOR RESULTS.

CONCLUSIONS

This chemical showed mutagenisity only in TA1353 at 1000 μg/plate, but not in other Salmonella typhimurium strains or Escherichia coil strain. In the case of TA1353, the number of induced colonies/plate, 20-30/mg-dose, indicates that this chemical was weakly mutagenic

DATA QUALITY

- **Reliabilities:** Klimish Code 1 = Reliable without restrictions

Remarks field for Data Reliability

Well conducted study, carried out by Research Institute for Animal Science in Biochemistry and Toxicology (Japan).

REFERENCES (Free Text)

Ministry of Health and Welfare: Japan, Toxicity Testing Reports of Environmental Chemicals 4, 547-556 (1996)

GENERAL REMARKS

GENETIC TOXICITY IN VITRO (NON-BACTERIAL IN VITRO TEST)

TEST SUBSTANCE

- 3,4-Dichlorobut-1-ene (CAS No 760-23-6)

Remarks: Source: Tokyo Kasei Kogyo, Lot No. FBP01, Purity: 99 %

METHOD

- **Method/guideline**: OECD TG 473
- **Test type**: Chromosomal aberration test
- **GLP***:* Yes
- **Year**: 1995
- **Species/Strain:** CHL/IU cell
- **Metabolic activation:** S9 from rat liver, induced with phenobarbital and 5,6-benzoflavone
- **Statistical methods**: Fisher's exact analysis

REMARKS FIELD FOR TEST CONDITIONS

– **Study Design:**

For continuous treatment, cells were treated for 24 or 48 hrs without S9. For short-term treatment, cells were treated for 6 hrs with and without S9 and cultivated with fresh media for 18 hrs.

- ***Concentration*****:** -S9 (continuous treatment): 0, 0.025, 0.050, 0.10 mg/ml
  -S9 (short-term treatment): 0, 0.050, 0.10, 0.20 mg/ml
  +S9 (short-term treatment): 0, 0.0025, 0.0050, 0.010 mg/ml
- ***Plates/test*****:** 2
- ***Solvent*****:** Acetone
- ***Positive controls*****:** Mitomycin C for continuous treatment
  Cyclophosphamide for short-term treatment

RESULTS

- **Cytotoxic concentration:**

Lowest concentration producing cytogenetic effects *in vitro*:

Without metabolic activation (continuous treatment):	0.05 mg/ml (clastogenicity)
	0.1 mg/ml (polyploid)
Without metabolic activation (short-term treatment):	0.2 mg/ml (clastogenicity)
With metabolic activation (short-term treatment):	0.01 mg/ml (clastogenicity)
	0.01 mg/ml (polyploidy)

- **Genotoxic effects:**

	clastogenicity			polyploidy		
	+	?	-	+	?	-
– With metabolic activation:	**[X]**	**[ ]**	**[ ]**	**[X]**	**[ ]**	**[ ]**
– Without metabolic activation:	**[X]**	**[ ]**	**[ ]**	**[X]**	**[ ]**	**[ ]**

REMARKS FIELD FOR RESULTS.

In comparison with historical solvent controls, polyploidy (1.00 and 1.75%) was increased significantly at 0.010 and 0.20 mg/ml on short-term treatment, with and without an exogenous metabolic activation system, respectively.

CONCLUSIONS

This chemical induced structural chromosome aberrations and polyploidy in chinese hamster lung cells (CHL/IU) with and without metabolic activation at the respective 50% growth inhibition - concentration, namely 0.01 and 0.2 mg/ml.

DATA QUALITY

- **Reliabilities:** Klimish Code 1 = Reliable without restrictions

Remarks field for Data Reliability

Well conducted study, carried out by Research Institute for Animal Science in Biochemistry and Toxicology (Japan).

REFERENCES (Free Text)

Ministry of Health and Welfare: Japan, Toxicity Testing Reports of Environmental Chemicals 4, 557-560 (1996)

GENERAL REMARKS

GENETIC TOXICITY IN VIVO

TEST SUBSTANCE

- 3,4-Dichlorobut-1-ene (CAS No 760-23-6)

Remarks: Source: 99.2%

METHOD

- **Method/guideline**: Unknown
- **Test type**: Cytogenetic assay
- **GLP***:* Unknown
- **Year**: 1985
- **Species/Strain:** rat
- **Route of administration:** inhalation – vapor
- **Doses/concentration levels:** 13.7 or 81.3 mg/m3
- **Exposure period**: 1, 30, 120 days, 4hrs/day, 5days/week

REMARKS FIELD FOR TEST CONDITIONS

– **Age at study initiation:** No data available
– **Weight at study initiation:** 140 – 180 g
No. of animals per dose: 36/group
· **Control groups and treatment:** Control rats were used in the same group as experimental rats and were treated in a similar way.
· **Clinical observations performed:** Not described
Organs examined at necropsy: Not described
Other: 50 well-spread and complete metaphase cells per animal were analysed. Aberrations were classified as general method.

RESULTS

- **Genotoxic effects:** positive, chromosome damage

The concentration of 13.7 mg/m3 caused chromosome damages in the bone marrow, mainly of the chromatid type. Other structural aberrations and numerical aberrations including polyploidy were not observed.

The number of aberrations increased in the increasing of concentration and exposure period.

- **Statistical results, as appropriate:**

Concentration Mg/l	Time of exposure days	Frequencies of cells with aberrations %
0	1	1.03±0.34
0	30	1.36±0.70
0	120	2.77±0.70
13.7	1	1.36±0.33
13.7	30	3.84±0.70*
13.7	120	4.54±0.35*
0	1	1.73±0.30
0	30	1.30±0.34
0	120	2.77±0.70
81.3	1	3.11±0.70*
81.3	30	8.33±1.12*
81.3	120	11.6+0.69*

*P>0.05

REMARKS FIELD FOR RESULTS.
Chromosome damage was mainly chromatid-tipe, not chromosome-tipe. Other structural aberrations and numerical aberrations including polyploidy were not observed.

CONCLUSIONS

This chemical induced chromosomal aberrations, mainly of the chromatid type, in rat bone marrow cells.

DATA QUALITY

- **Reliabilities:** Klimish Code 2 = Reliable with restrictions
- **Remarks field for Data Reliability**

REFERENCES (Free Text)

Nalbandyan, T.I. et al., Zh. Eksp. Klin. Med., 25, 335 – 339 (1985)

GENERAL REMARKS