

FOREWORD

INTRODUCTION

1,2-DICHLOROBENZENE

CAS N°: 95-50-1

SIDS Initial Assessment Report

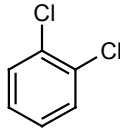
For

SIAM 13

Bern, Switzerland, 6-9 November 2001

1. **Chemical Name:** 1,2-Dichlorobenzene
2. **CAS Number:** 95-50-1
3. **Sponsor Country:** Australia:
Dr Sneha Satya
National Industrial Chemicals Notification and Assessment Scheme
GPO Box 58
Sydney 2001, Australia
Fax: 61 2 85778880
Email: Sneha.satya@nicnas.gov.au
4. **Shared Partnership with:**
5. **Roles/Responsibilities of the Partners:**
 - Name of industry sponsor /consortium
 - Process used
6. **Sponsorship History**
 - How was the chemical or category brought into the OECD HPV Chemicals Programme ?
SIAM 13 will be first time the chemical has been discussed.
7. **Review Process Prior to the SIAM:**
8. **Quality check process:**
9. **Date of Submission:** 14 September 2001 (to the OECD Secretariat)
10. **Date of last Update:**
11. **Comments:**

SIDS INITIAL ASSESSMENT PROFILE

CAS No.	95-50-1
Chemical Name	1,2-Dichlorobenzene
Structural Formula	
RECOMMENDATIONS	
<p>Health: The chemical is not a candidate for further work. Environment: The chemical is a candidate for further work.</p>	
SUMMARY CONCLUSIONS OF THE SIAR	
Human Health	
<p>1,2-Dichlorobenzene has been shown to cause eye and respiratory irritation in humans at exposure levels above 100 ppm. Skin irritation has been observed following dermal application in humans and animals.</p> <p>1,2-Dichlorobenzene is absorbed via the oral route. Absorption via the dermal or inhalation routes is poorly characterized. Inhalation is expected to be the major route for human exposure. The available toxicological data indicate that metabolic profiles and effects from 1,2-dichlorobenzene exposure are similar in rats, mice and humans. Animal studies with rats and mice have shown 1,2-dichlorobenzene to induce acute hepatotoxic effects. The LD₅₀ for a single oral exposure to 1,2-dichlorobenzene for the rat ranges from 1516 to 2138 mg/kg bw. The LC₁₀₀ for the rat is ≤ 977 ppm (5.9 mg/L) for a 10 hour exposure. During a 4 hour exposure, 1 of 20 rats died at 941 ppm (5.6 mg/L). In humans, the acute effects of 1,2-dichlorobenzene by ingestion or inhalation are reported to be headache, nausea, vomiting, vertigo, malaise and unconsciousness.</p> <p>Several oral studies of rats and mice ranging from 10 days to 2 years duration indicate that the adverse effects include increases in liver and kidney weights and hepatotoxicity. From these repeat dose studies, the NOAEL for non-neoplastic effects was 60 mg/kg bw, while the LOAEL was 120 mg/kg bw due to increased renal tubular regeneration in male mice.</p> <p>In several microbial organisms and mammalian systems, 1,2-dichlorobenzene tested negative <i>in vitro</i>. However, it did induce sister chromatid exchanges in Chinese Hamster ovary cells and increased mutation frequency in mouse lymphoma cells, both in the presence of metabolic activation. 1,2-dichlorobenzene was negative in several <i>in vivo</i> mammalian tests, except one of two micronuclei assays in mouse bone marrow was positive. In a two-year oral study in rats and mice, 1,2-dichlorobenzene was considered not to be carcinogenic (maximum dose of 120 mg/kg bw). In an inhalation 2-generation reproduction study in rats, no fertility effects were observed and reduced pup weight during lactation occurred at doses toxic to adults. The NOAEL and LOAEL (kidney and liver effects) for adult rats were 50 (0.3 mg/L) and 150 ppm (0.6 mg/L) respectively. In developmental studies in rats and rabbits, developmental effects were only seen in rats at maternally toxic doses (400 ppm, 2.4 mg/L). No human epidemiological studies have been conducted.</p>	
Environment	
<p>1,2-Dichlorobenzene has a water solubility of 155.8 mg/L; vapour pressure of 0.196 kPa; and Log Kow of 3.4. It is expected to partition mainly to the atmospheric compartment where its primary removal mechanism will be through reaction with hydroxyl radicals (half life <50 days). Where released to either soil or water compartments, a major removal mechanism being volatilisation up into the surrounding atmosphere. However, adsorption to sediment may also be a major fate process. Biodegradation studies (generally following non-standard procedures) show 1,2-</p>	

dichlorobenzene to be biodegradable under aerobic conditions where bacterial populations have been acclimatised to the chemical. However, where bacterial populations are not acclimatised, the chemical can not be regarded as readily biodegradable. The chemical is not degraded under anaerobic conditions. 1,2-Dichlorobenzene has a high potential for bioconcentration in the fatty tissue of aquatic species with BCFs based on lipid content up to 8710 for fish, and 28840 for a crab species. However, depuration from exposed organisms is expected to be rapid once exposure ceases.

1,2-Dichlorobenzene has been tested on a wide range of aquatic organisms under acute exposure, although chronic data are scarce. Results for fish ranged from 96 h LC50=1.58 mg/L for rainbow trout to 57 mg/L for fathead minnow. Both acute and chronic toxicity to aquatic invertebrates were obtained with two results showing high acute toxicity, namely EC50's of 0.78 mg/L and 0.66 mg/L to *Daphnia* and *Ceriodaphnia* respectively. Results from exposure to algae showed EC50 values in the 1-100 mg/L range for 1,2-dichlorobenzene. Toxicity to micro-organisms can be considered slight.

Although the major compartment expected to be exposed to 1,2-dichlorobenzene is the atmosphere, there are no ecotoxicity results available for organisms exposed through the gas phase. The chlorine substituents on the chemical suggest a potential for effects on stratospheric ozone. However, the chemical is unlikely to persist long enough to escape the troposphere, although it may persist long enough to undergo long range atmospheric transport.

While there are a large number of acute data covering all trophic levels, chronic data are scarce. Therefore, an assessment factor of 100 has been chosen. The result used for determining the PNEC was the lowest chronic value obtained, i.e. 21 d NOEC = 0.63 mg/L for *Daphnia magna*. The PNEC_{aquatic} was therefore determined to be 6.3 µg/L.

Exposure

1,2-Dichlorobenzene is manufactured in Europe, the USA, Canada, Mexico and China. Production figures were reported to be approximately 16,500 tonnes for Western Europe in 1983 and approximately 23,680 tonnes produced by the USA in 1984. More recent data indicates that in 1999 production in the Western World was 54,000 tonnes, with the predominant uses being chemical synthesis and use as a solvent.

The main industrial use of 1,2-dichlorobenzene in Australia is as a solvent with approximately 86% used in the agricultural sector for wool branding products. The chemical is also used as an automotive and marine degreaser/decarboniser and in industrial paint strippers, industrial deodorants and a small amount in a single pharmaceutical preparation.

Occupational exposure to 1,2-dichlorobenzene can occur during manufacture and end use, with inhalation the major route of exposure. Potential for consumer exposure from the use of products and human exposure via the environment is expected to be low.

NATURE OF FURTHER WORK RECOMMENDED

Environment: 1,2-Dichlorobenzene is toxic and bioconcentrates. Additionally, it may be considered persistent due to its lack of biodegradation where microbial communities are not acclimatised. Member countries may wish to undertake a more in-depth exposure analysis and if then indicated, a risk assessment may be considered.

FULL SIDS SUMMARY

CAS NO: 95-50-1	SPECIES	PROTOCOL	RESULTS
PHYSICAL-CHEMICAL			
Melting Point			-16.7 °C (1.94°F)
Boiling Point			180.3 °C (356°F)
Density			1.3007 kg/L (@25 °C)
Vapour Pressure			0.196 kPa (@ 25°C)
Vapour Density			5.05 g/cm ³ (@ 20°C)
Partition Coefficient (Log P_{ow})			3.4
Water Solubility			155.8 mg/L (@ 25°C)
Solubility in organic solvents			Miscible with most organic solvents
Henry's Law Constant (25°C)			193 Pa.m ³ /mol
Flash Point (closed cup)			66 °C (150°F)
Ignition Temperature			648 °C (1198°F)
Flammability Limits			Upper 9.2% Lower 2.2%
ENVIRONMENTAL FATE/BIODEGRADATION			
Fugacity model		level I	<i>At equilibrium</i> , partition mainly as: 94.6% to atmosphere 2.8% to soil 2.5% to water
Atmospheric fate			Direct photolysis unlikely. Will react with photochemically produced hydroxyl radicals with troposphere global hydroxyl radical concentration of 5X10 ⁵ molecules/cm ³ , calculated half-life is 38±2 days. Atmospheric wash out accounts for <i>o</i> -DCB in rainwater.

Aquatic fate			<p>Readily volatile with a Henry's Law constant of 193Pa.m³/mol. at 25°C. Volatilisation main removal mechanism from surface water and soil. Volatilisation half-life in shallow stream <1 hour and up to 60 days for deep slow moving river.</p> <p>Adsorption to sediments is a major fate process.</p> <p>Photolytic degradation due to hydroxyl radicals likely – estimated half-life 12.8 days.</p> <p>Mineralisation likely – produce CO₂ and HCl.</p> <p>Persistent and slightly mobile in groundwater. Estimated half-life in groundwater 30-300 days.</p>
Terrestrial fate			<p>Medium to slight mobility in soils – Log K_{oc}= 2.5 in soil with OC of 1.9%; Log K_{oc}= 3.76 and 4.62 in aquifer soil with OC of 0.02 or 0.018%.</p> <p>Two-step first order kinetic model accounts for decrease in DCB in soil – 80% removal in first 35 days, additional 4.3% over the next 224 days.</p>
Biodegradation			<p><i>Aerobic biodegradation:</i></p> <p>If inoculum unacclimatised then very small degradation. Degradation with acclimatised inoculum 93-100%.</p> <p><i>Anaerobic/Anoxic biodegradation:</i></p> <p>No degradation in soil column under anaerobic conditions.</p> <p>Unlikely to be extensively degraded under anaerobic conditions in aquatic compartment.</p>
Bioaccumulation			<p>Some tendency to bioaccumulate – BCF_(whole organism) fish 142-560, crab 144, algae 6212-19700; BCF_(Lipid content) fish 3240-8710, crab 28840. Elimination expected to be rapid when transferred to clean environment.</p> <p>Some uptake by benthic worms but eliminated quickly in clean environment.</p>
ECOTOXICOLOGY			
Toxicity to micro-organisms	Bacillus (TL 81) – from activated sludge		30 min exposure EC50 = 169±13 mg/L

Acute toxicity to Aquatic Plants	Activated sludge bacteria	OECD TG 210	3 hr EC50 = 100 mg/L	
	<i>Photobacterium phosphoreum</i>	Microtox test	5 min exposure, EC50 = 10.25±0.35 mg/L	
	<i>Photobacterium phosphoreum</i>	Microtox test	30 min exposure EC50 = 4.0 mg/L 5 min exposure EC50 = 2.7 mg/L	
	<i>Tetrahymena pyriformis</i> (Ciliate)		24 hr, static, LC50 = 51 mg/L	
	<i>Selenastrum capricornutum</i>		96 hr ErC50 = 2.2, NOEC = 0.88 mg/L 96 hr EC50 = 71.1 mg/L 96 hr EC50 = 76.1 mg/L, NOEC <10 mg/L 96 hr ErC50 = 98 mg/, EC50 = 91.6 mg/L (chlorophyll impairment)	
	<i>Scenedesmus pannanicus</i>		EC50 = 17 mg/L	
	<i>Scenedesmus subspicatus</i> (green algae)		48 hr, static, EC50 = 14 mg/L	
	<i>Skeletonema costatum</i> (marine algae)		96 hr EC50 = 44.2 mg/L (Chlorophyll impairment)	
	Acute Toxicity to Aquatic Invertebrates	<i>Daphnia magna</i>		24 hr, closed, IC50 = 0.78 mg/L (measured) 24 hr, EC50 = 1.7 mg/L 48 hr, closed, EC50 = 2.35 mg/L 48 hr, closed, IC50 = 3.77 mg/L 48 hr, static, LC50 = 2.2 mg/L 48 hr, static, EC50 = 2.4 mg/L
		<i>Ceriodaphnia dubia</i>		48 hr, static, EC50 = 0.66 mg/L
<i>Artemia</i> (Brine Shrimp)			24 hr EC50 = 15 mg/L	
<i>Palaemonetes pugio</i> (Salt water grass shrimp)			96 hr LC50 = 10 mg/L 96 hr LC50 = 9.4 mg/L	

	<i>Mercenaria mercenaria</i> (Hard clam)	48 hr, static, EC50 >100 mg/L
	<i>Mysidopsis bahia</i> (Opossum shrimp)	96 hr LC50 = 1.97 mg/L
	<i>Tanytarsus dissimilis</i> (Midge)	48 hr, static, LC50 = 12 mg/L
Chronic Toxicity to Aquatic Invertebrates	<i>Daphnia magna</i>	14 days EC50 = 0.55 mg/L 16 days IC50 = 1.5 mg/L 21 days, semi static, NOEC = 0.63 mg/L
	<i>Mercenaria mercenaria</i> (Hard clam)	12 days, flow-through, EC50 = 0.25-10 mg/L (growth), LC50 >100 mg/L
Acute/Prolonged Toxicity to Fish	<i>Brachydanio rerio</i> (zebra fish)	48 hr LC50 = 6.8 mg/L 96 hr LC50 = 5.2 mg/L
	<i>Oncorhynchus mykiss</i> (Rainbow trout)	48 hr LC50 = 2.3 mg/L 96 hr LC50 = 1.61 mg/L 96 hr LC50 = 1.58 mg/L 144 hr LC50 = 1.54 mg/L
	<i>Cyprinodon variegatus</i> (Sheepshead minnow)	48 hr LC50 = 9.3 mg/L 96 hr LC50 = 9.7 mg/L
	<i>Lepomis macrochirus</i> (Bluegill sunfish)	24 hr LC50 = 6.3 mg/L 96 hr LC50 = 5.6 mg/L 96 hr LC50 = 27 mg/L
	<i>Menidia beryllina</i> (Inland silverside)	96 hr LC50 = 7.3 mg/L
	<i>Pimephales promelas</i> (Fathead minnow)	96 hr LC50 = 57 mg/L
	<i>Oryzias latipes</i> (Japanese rice fish)	48 hr LC50=9.3 mg/L
Chronic Toxicity to Fish	<i>Brachydanio rerio</i> (zebra fish)	14 day NOEC = 0.37 mg/L
	<i>Pimephales promelas</i> (fry)	28 days (?) NOEC = 2 mg/L

TOXICOLOGY			
Acute Oral Toxicity	Rat	OECD 401	LD ₅₀ = 1516 - 2138 mg/kg bw
Acute Intraperitoneal Toxicity	Rat Mouse		LD ₅₀ (rat) = 840 mg/kg bw LD ₅₀ (mouse) = 1228 mg/kg bw
Acute Inhalation Toxicity	Rat	OECD 403	LC ₁₀₀ ≤ 5885 mg/m ³ (10h)
Skin Irritation	Rabbit		Slight to moderate irritation
Eye Irritation	Rabbit		Slight irritation
Respiratory Irritation	Mouse		RD ₅₀ = 163 and 182 ppm
Repeat Dose Toxicity: Oral			
	Rat		90 days NOAEL = 25 mg/kg bw 90 days LOAEL = 100 mg/kg bw
	Rat		13 weeks NOAEL = 60 mg/kg bw LOAEL = 125 mg/kg bw
	Mouse		13 weeks NOAEL = 125 mg/kg bw LOAEL = 250 mg/kg bw
	Rat		103 weeks NOAEL = 120 mg/kg bw LOAEL = nd
	Mouse		103 weeks: NOAEL = 60 mg/kg bw (males) NOAEL = 120 mg/kg bw (females) LOAEL = 120 mg/kg bw (males)
Genetic Toxicity (<i>in vitro</i>)			
Bacterial assays:			
- Gene mutation	<i>S. typhimurium</i> <i>Saccharomyces cerevisiae</i>	OECD 471	negative with & without metabolic activation
- DNA damage	<i>S. typhimurium</i>		negative with & without metabolic activation
- Recombination assay	Bacillus subtilis		One study positive and one negative without metabolic activation; negative with metabolic activation

- DNA damage & repair	<i>Escherichia coli</i>	negative with & without metabolic activation
- Differential toxicity	<i>Escherichia coli</i>	positive without metabolic activation; metabolic activation not tested
- Reverse mutation	<i>Escherichia coli</i>	negative with & without metabolic activation
- Mitotic recombination	<i>Saccharomyces cerevisiae</i>	negative with & without metabolic activation
Non-Bacterial assays:		
- Chromosomal aberrations	CHO cells	negative with & without metabolic activation
- HGPRT assay	CHO cells	negative with & without metabolic activation
- SCE	CHO cells	positive with & negative without metabolic activation
- DNA damage & repair	Rat liver	negative without metabolic activation; metabolic activation not tested
- Mouse lymphoma assay	Mouse L5178Y cells	positive with & negative without metabolic activation
- Inhibition of DNA synthesis	Lymphocytes (human)	negative with & positive without metabolic activation
Genetic Toxicity (<i>in vivo</i>)		
- Sex-linked recessive mutation	<i>Drosophila melanogaster</i>	Negative
- Eye mosaic assay		Negative
- Chromosomal aberration	Rat bone marrow (male and female)	Negative
- DNA damage	Rat (female)	Negative
- Micronucleus	Mouse bone marrow (male)	1 study positive and 1 study negative
Toxicity to Reproduction		
Developmental: Inhalation	Rat & Rabbit	NOAEL of 400 ppm for developmental effects in rabbits. Developmental effects in rats at maternally toxic dose of 400 ppm.

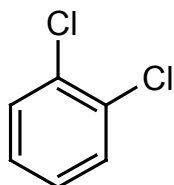
<p>2-generation reproduction: Inhalation</p> <p>EXPERIENCE WITH HUMAN EXPOSURE</p>	Rat	<p>No fertility effects. Reduced pup weight during lactation at 400 ppm. NOAEL of 50 ppm and LOAEL of 150 ppm for adult toxicity.</p> <p>Eye and respiratory irritation reported at atmospheric levels estimated to be no greater than 100 ppm. At high doses, 1,2-dichlorobenzene produces central nervous system effects in humans.</p>
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SIDS Initial Assessment Report

1 IDENTITY

1.1 Identification of the Substance

CAS Number: 95-50-1
 IUPAC Name: 1,2-Dichlorobenzene
 Molecular Formula: C₆H₄Cl₂
 Structural Formula:



Synonyms: 1,2-Dichlorobenzol; Benzene, 1,2-Dichloro-; Chloroben o-Dichlorobenzene; Benzene, o-Dichloro-; o-DCB ortho-dichlorobenzene

1.2 Purity/Impurities/Additives

Composition of technical grade product:
 65-85 % 1,2-dichlorobenzene, < 0.05 % chlorobenzene, < 0.5 % trichlorobenzene, remainder 1,4- and 1,3-dichlorobenzene.

Pure grade: > 99.8 % 1,2-dichlorobenzene, < 0.05 % chlorobenzene, < 0.1 % trichlorobenzene, < 0.1 % 1,4-dichlorobenzene.

1.3 Physico-Chemical properties

Table 1: Summary of physico-chemical properties

Property	Value	Reference:
Melting point	-16.7 °C	Carswell (1928)
Boiling point	180.3 °C	Carswell (1928)
Density (at 25 °C)	1.3007 kg/L	Curry and Gilkerson (1957)
Vapour pressure (at 25 °C)	0.196 kPa	Mackay and Shiu (1981)
Water solubility	155.8 mg/L	Banerjee <i>et al</i> (1980)
Partition coefficient n-octanol/water (log value)	3.4	Banerjee <i>et al</i> (1980) Miller <i>et al</i> (1985)
Henry's law constant	193 Pa.m ³ /mol	Mackay and Shiu (1981)
Autoignition temperature	648°C	Sax (1996)
Log K _{oc}		
	2.5 (O M 1.9%)	Chiou <i>et al</i> (1983)
	3.76 (Freundlich distribution)	Curtis <i>et al</i> (1986)
Flash point, closed cup	66 °C	Sax (1996)

2 GENERAL INFORMATION ON EXPOSURE

1,2-Dichlorobenzene is manufactured in Europe, the USA, Canada, Mexico and China. Production figures were reported to be approximately 16,500 tonnes for Western Europe in 1983 and approximately 23,680 tonnes produced by the USA in 1984 (BUA, 1990). More recent figures indicate that in 1999 a production volume of about 54,000 per year of 1,2-dichlorobenzene was manufactured by only a few producers in the Western world. The manufacture was shared by Western Europe (37%), USA (27%), Brazil (6%), Japan (24%) and other Asia (6 %). Of this, about 67% was used in chemical synthesis, about 11% as a solvent (e.g. about 7 % for TDI processing) and 22 % for other applications not known (Bayer AG Leverkusen, personal communication, September 2001). Additional uses cited in the literature are: in the production of dyes and pesticides following conversion to 1,2-dichloro-4-nitrobenzene; to produce disinfectants and deodorants; and some small use as a heat transfer fluid. Several products containing 1,2-dichlorobenzene are listed in the Danish Product Register for use as lubricants and additives, and as cleaning/washing agents.

In 1998, less than 100 tonnes of 1,2-dichlorobenzene were imported into Australia with similar volumes being imported in previous years. The main use of 1,2-dichlorobenzene in Australia is as a solvent with approximately 86% used in the agricultural sector for wool branding products. The chemical finds a number of industrial uses as an automotive and marine degreaser/decarboniser and in industrial paint strippers and accounts for approximately 12% of use. Another 0.3% is formulated into an industrial deodorant with a further 0.3% used in a single pharmaceutical preparation.

2.1 Environmental Exposure and Fate

2.1.1 Sources of Environmental Exposure

The following table summarises environmental monitoring data available in published literature.

Further information on the occurrence of 1,2-dichlorobenzene in the environment, including, air and water monitoring data, is available in the BUA Report (BUA, 1990).

Differences in the median 1,2-dichlorobenzene concentration in air are dependent on the macroenvironment in which it is found. Throughout urban United States this value may vary in excess of 10 fold depending on the degree of industrialisation. For example, levels as high as 61 ng/m³ have been recorded in highly industrialised areas in New Jersey (Bozzilli *et al*, 1982).

Several water measurements in the North American Great Lakes recorded concentrations from below the detection limit to 0.007 µg/L (Oliver and Nicol, 1982). In Europe documented concentrations of 1,2-dichlorobenzene in river waters rarely exceed 0.5 µg/L. Typically, measured concentrations in North American rivers are at least two orders of magnitude lower than this (Govt. Canada, 1993).

Table 2.1.1: Monitoring data regarding the presence of 1,2-dichlorobenzene in the environment.

REFERENCE	LOCATION	MEDIUM	CONCENTRATION
BUA (1990)	The Rhine	Sediments	<5-227 µg/g
	Niagara River	Suspended particles	75-110 µg/g
	Europe and USA	Rainwater	0.03-110 ng/L
Oliver (1984)	Lake Ontario (near Niagara river)	Sediment	27 ng/g
	Lake Ontario (central basin)	Sediment	19 ng/g
	Lake Ontario (eastern basin)	Sediment	20 ng/g
	Hamilton Harbour	Sediment	5.7 ng/g
Pereira <i>et al</i> (1988)	Calcasieu River and Bayou d'Inde	Biota	0.08 µg/g
		Biota	0.26 µg/g
		Biota	0.06 µg/g
Ligocki <i>et al</i> (1985)	Portland Oregon	Rain water	0.00013-0.00062 µg/L
		Atmospheric gas phase	0.0033-0.01 µg/L
Oliver and Nicol (1982)	Grand River	Surface water	<0.001-0.03 µg/L
	Lake Erie	Sediment	1-4 ng/g
		Biota	1 ng/g
	Lake Huron	Sediment	<5-56 ng/g
		Biota	1 ng/g
		Surface water	<0.001 µg/g
	Lake Ontario	Sediment	4-27 ng/g
		Biota 6 ⁺ yrs	1 ng/g
		Biota 4 ⁺ yrs	1 ng/g
		Sediment 0-1 cm	14 ng/g
		Sediment 1-2 cm	16 ng/g
		Sediment 2-3 cm	19 ng/g
		Sediment 3-4 cm	16 ng/g
		Sediment 4-5 cm	26 ng/g
		Sediment 5-6 cm	13 ng/g
		Sediment 6-7 cm	2 ng/g
Sediment 7-8cm		<5 ng/g	
Surface water	0.002-0.007 µg/L		
Lake Superior	Sediment	<5-1 ng/g	
	Biota 6 yrs	0.3 ng/g	

Within Australia, no 1,2-dichlorobenzene was detected in the receiving waters (detection limit 0.5 ppb) when effluent was discharged from 16 sewage treatment plants (Sydney Water, 1996).

Readily available information on exposure to the chemical from production and processing is available from the largest producer, for a site in Germany. In 2000, 83.5 kg of 1,2-dichlorobenzene were emitted into the atmosphere from the site. Waste water leaving the production and processing

facilities are treated in an industrial biological waste water treatment plant. While influent concentrations of 1,2-dichlorobenzene are not available, monitoring of the effluent of the waste water treatment plant indicated that all values from January 2000 to May 2001 for the substance were equal to or less than 2 µg/l, except one value of 17 µg/l. As worst case for the receiving water a PEC of ≤ 0.003 µg/l is calculated, taking the 10 percentile of the river flow into account (Bayer AG Leverkusen, personal communication, September 2001).

Indirect entry of 1,2-dichlorobenzene into the environment is possible by metabolic breakdown of lindane and higher chlorinated benzenes.

2.1.2 Biodegradation

A variety of data on biodegradation of 1,2-dichlorobenzene is summarised by Howard (1989) and in BUA (1990). Overall, it appears that 1,2-dichlorobenzene is not readily biodegradable.

Aerobic biodegradation

There is a great deal of variation in the reported results, with some studies indicating almost zero biodegradation, while others report almost complete degradation. For example, Canton *et al* (1985) observed no degradation in a repetitive die-away test. Alternatively, Hoechst (1985) reported results for a closed bottle test (OECD 301 D) where 1,2-dichlorobenzene, initially present at a concentration of 4 mg/L and inoculated with bacteria from a municipal sewer plant, was progressively degraded by 18, 35, 77 and 93% after 5, 14, 21 and 28 days respectively.

Results in table 2.1.2 are only where aerobic biodegradability was studied using acclimatised microorganism populations.

Table 2.1.2: Aqueous Aerobic Biodegradation Data

TEST	RESULT	SOURCE/REFERENCE; NOTES
Closed Bottle – OECD 301 D	93 % after 28 days	Hoechst (1985); <i>o</i> -DCB initially present at 4 mg/L
Not Specified	100 %	Worne (1972); adapted <i>Pseudomonas</i> in sewage
Simulated Activate Sludge Plant	> 97 %	Goltz <i>et al</i> (1983)
Simulated Activated Sludge Plant	100 % removal (75% attributed to biodeg.)	Kincannon <i>et al</i> (1983b)
Simulated Activated Sludge Plant	> 99 % removal (75% attributed to biodeg.)	Stover and Kincannon (1982, 1983b); test run over 60 days
Simulated Activated Sludge Plant	94 % removal (35% attributed to biodeg.)	Weber <i>et al</i> (1987)
Biofilm on glass beads	96±2 %	Bouwer (1985); Test duration 2 years

Tests reported with respect to aerobic degradation generally appeared to follow non-standard conditions. Bacteria, including strains of *Pseudomonas*, are capable of aerobic degradation of the compound.

Anaerobic/Anoxic Degradation

In their studies of degradation of 1,2-dichlorobenzene in soil columns, Kuhn *et al* (1985) found no evidence of biodegradation under anaerobic conditions. Similarly, Bouwer (1985) reported no

evidence of anaerobic degradation in a reactor filled with glass beads on which bio-films had been allowed to form.

Kirk *et al* (1989) found that 66% of 1,2-dichlorobenzene (present initially at 710 µg/L) was eliminated after 32 days incubation with digested sludge under anaerobic conditions. However, this elimination was attributed to a chemical conversion or physical removal process other than sorption, rather than biodegradation, since similar elimination rates were observed in a system in which all biological activity had been suppressed through addition of sodium azide. Similarly, Garrison (1969) recorded 20% removal of 1,2-dichlorobenzene in 7 days using digested sludge from a municipal sewage plant, but the sludge was not analysed for adsorbed chemical.

1,2-Dichlorobenzene therefore appears unlikely to be extensively degraded under anaerobic conditions in the environmental water compartment. The persistence over several decades of 1,2-dichlorobenzene in the sediments of the North American Great Lakes supports this conclusion (Oliver and Nicol, 1982).

In a study by Nowak *et al* (1996), using a methanogenic mixed culture enriched from Saale river sediment, all chlorobenzenes present were transformed by reductive dechlorination via monochlorobenzene to unsubstituted benzene. This occurred after a one week lag phase, which could not be explained. It was found that the dechlorination process was dependent on the biological activity. Reductive dechlorination was stimulated when the mixed cultures were supplemented with pyruvate and methanol.

2.1.3 Bioaccumulation

Results of various bioaccumulation experiments are summarised in the table 2.1.3.

Table 2.1.3: Bioconcentration of 1,2-dichlorobenzene in Aquatic Organisms

ORGANISM	BCF (Whole Organism)	BCF (Lipid Content)	REFERENCE
FISH			
Rainbow Trout (<i>Salmo gairdneri</i>)	270±21 [o-DCB]=0.047 µg/L	3240 ^a	Oliver and Niimi (1983) ^b
Rainbow Trout (<i>Salmo gairdneri</i>)	560±130 [o-DCB]=0.940 µg/L	6720 ^a	Oliver and Niimi (1983) ^b
Spotted Sea Trout (<i>Cynoscion nebulosis</i>)	142 ^c	6166	Pereira <i>et al</i> (1988)
Blue Cat Fish (<i>Ictalurus furcatus</i>)	218 ^c	6607	Pereira <i>et al</i> (1988)
Atlantic Croaker (<i>Micropogonias undulatus</i>)	192 ^c	8710	Pereira <i>et al</i> (1988)
Carp (<i>Cyprinus carpio</i>)	90-260	-	CITI (1992)
OTHER ORGANISMS			
Blue Crab (<i>Callinectes sapidus</i>)	144 ^c	28840	Pereira <i>et al</i> (1988)
Cyanobacteria/Green Algae	6212		Davis <i>et al</i> (1983)
Green Algae (<i>Selenastrum capricornutum</i>)	19700		Cassery <i>et al</i> (1983)

^a The lipid BCF calculated by multiplying the whole organism BCF by 12 (Oliver and Niimi, 1983)

^b In this study a chlorobenzene mixture was used, thus the BCF values may be influenced by breakdown of higher chlorobenzenes.

^c The BCF (whole organism) is calculated by multiplying the BCF (lipid content) by the percentage lipid content in the organism given in the reference.

The conclusion from these data is that 1,2-dichlorobenzene has the potential to bioaccumulate, and in the fatty tissue of aquatic species 1,2-dichlorobenzene may be considered highly concentrating (Mensink *et al*, 1995). However, once the exposed organisms are transferred to a clean environment, elimination is expected to be fairly rapid based on research from Barrows *et al* (1980) and Veith *et al* (1980) where a half-life for elimination from the tissues of bluegill sunfish was less than one day.

Oliver (1984) investigated the bioavailability of 1,2-dichlorobenzene incorporated in lake sediments contaminated with a number of chlorobenzenes to benthic worms, including *Limnodrilus hoffmeisteri* and *Tubifex tubifex*. In this study, no uptake of 1,2-dichlorobenzene by these organisms was observed, but when the contaminant loading of the chlorobenzene mixture contaminated sediment was increased by a factor of 10 in a later experiment (Oliver, 1987), transfer to the worms was detected. However, although transfer was observed, once transferred to an uncontaminated environment the 1,2-dichlorobenzene was quickly eliminated and could not be detected in the worms after 5 days.

The impact of sediment organic carbon content was investigated in Knezovich and Harrison (1988). They showed that 1,2-dichlorobenzene sorbed on sediments was bioavailable to the sediment dwelling midge larvae (*Chironomus decorus*), when exposed under flow through conditions using different levels of organic carbon content. *Chironomus decorus* (fourth instar larvae) in 20 g lake sediment composed of 51% sand, 47% silt, 2% clay, organic matter of 14.5% and pH 4.4, spiked with 1 µg/l radiolabeled 1,2-dichlorobenzene (200 ml) for 5 days showed, bioconcentration factors (BCF) of 0.23±0.07, 49±10 and 29±5 under non-equilibrium conditions and 0.22±0.04, 31±5 and 29±5 in equilibrium conditions in sediment, overlying water and interstitial water respectively. When the sediment was modified to lower the organic matter (3.6%), the BCFs were 1.08±0.53, 1,071±881 and 31±18 in sediment, overlying water and interstitial water respectively, however, very little of any test substance was detectable in the overlying water. No firm conclusions can be drawn from these values as no concentrations of 1,2-dichlorobenzene in the experiment were found in the paper, and the organisms were exposed to the chemical within the whole system (sediment, overlying water and interstitial water). The authors concluded that 'the accumulation of sediment-sorbed chlorobenzenes by midge larvae was mediated by the uptake of the compounds in interstitial water'. They also discuss the indication that sediment characteristics have an effect on the bioavailability of sediment sorbed chemicals in aquatic ecosystems. Specifically, a sediment's organic carbon content is likely to be the main determinant of chemical bioavailability for neutral organic compounds.

Casserly *et al* (1983) studied the sorption of selected organics, including 1,2-dichlorobenzene, by *Selenastrum capricornutum* (green algae). There were two series of tests done: firstly the organic compounds were added separately, secondly they were added simultaneously. The first series gave a BCF for 1,2-dichlorobenzene of 19700, while in the second series it was 10080. While, this would indicate that it is highly concentrating in algae, unfortunately the fraction adsorbing to the cells was not determined.

2.1.4 Other Information on Environmental Fate

The Trent University, Level 1, Fugacity – based, Environmental Equilibrium Partitioning Model, 1999, predicts that, at equilibrium, 1,2-dichlorobenzene will predominantly partition to the atmosphere (94.6%) with in the order of 2.8% partitioning to soil and 2.5% to water. Negligible amounts are expected to partition directly to other media such as aerosols and sediments (Trent University, 1999). Default settings were used in the modeling which included air, water and soil compartments of $1 \times 10^{14} \text{ m}^3$, $2 \times 10^{11} \text{ m}^3$ and $9 \times 10^9 \text{ m}^3$ respectively with a release of 100,000 kg of chemical. Chemical properties used were those reported in Section 1.

Atmospheric fate

1,2-Dichlorobenzene absorbs radiation weakly at wavelengths greater than 300 nm, so direct photolysis in the atmosphere is not likely (Bunce *et al*, 1987). However, reaction with photochemically produced hydroxyl radicals in the atmosphere will occur. Wahner and Zetzsch (1983) calculated a rate constant for the reaction between hydroxyl radicals and 1,2-dichlorobenzene in the atmosphere at room temperature of $4.2 \times 10^{-13} \text{ cm}^3/\text{molecule}/\text{sec}$. When allowance is made for the mean global hydroxyl radical concentration in the troposphere of $5 \times 10^5 \text{ molecules}/\text{cm}^3$ (Calamari, 1993), the half-life computes to 38 ± 2 days.

The presence of 1,2-dichlorobenzene in rainwater indicates that it persists long enough to be returned to the earth's surface by atmospheric wash out (Ligocki *et al*, 1985).

Aquatic fate

The Henry's Law Constant at 25°C is $193 \text{ Pa}\cdot\text{m}^3/\text{mol}$., indicating 1,2-dichlorobenzene is readily volatile from aqueous solution. Volatilisation is expected to be the dominant mechanism for removal from surface water and soil (Slimak *et al*, 1980; Smith *et al*, 1980; and Thomas, 1982).

1,2-Dichlorobenzene is expected to have a short residence time in water, with the half-life decreasing as the degree of agitation increases. The US EPA (1987) reports volatilisation half-lives ranging from less than 1 hour for a shallow stream, up to 60 days for a deep slow moving river (US EPA, 1987). Adsorption to sediment in water will attenuate volatilisation. Monitoring data conducted in the Great Lakes area of North America indicate that adsorption to sediment and volatilization accounted for the low concentrations found in the water (Oliver and Nicol, 1982). Its detection in Lake Ontario sediment cores by Oliver and Nicol (1982) indicates that the chemical has persisted in these sediments for decades.

Photolytic degradation in water is also possible, again through the agency of hydroxyl radicals. Russi *et al* (1982) have estimated the half-life for photochemical oxidation in water (the river Goldach in Germany) as 12.8 days. It is unlikely that hydrolytic degradation would be a significant mechanism for degradation in the aquatic environment.

1,2-Dichlorobenzene was reported to be persistent and slightly mobile during field studies of groundwater contaminated by sewage effluent and municipal and industrial wastes (Govt. of Canada, 1993), with Zoeteman *et al* (1980) estimating that the half-life in ground water ranged from 30 to 300 days.

Terrestrial fate

Using Chiou *et al* (1983), it can be seen that 1,2-dichlorobenzene has medium to slight mobility in soils with an organic matter content of 1.9%, with a Log Koc value of 2.5. In an aquifer soil (organic carbon content is 0.02%), Curtis *et al* (1986) found that the Freundlich distribution coefficient for 1,2-dichlorobenzene to be 1.16, which can be used to determine a Log Koc of 3.76. Mackay *et al* (1986) could not explain all the observed sorption properties in a Borden aquifer soil (OCC 0.02%) by either an OCC/SA two-phase model or a multiple regression analysis using K_d . It was determined that the sorption properties may be related to the amount and distribution of unidentified mineral phases in the soil.

Stauffer and MacIntyre (1986) found that adsorption to soils and oxide minerals was very dependent on the ambient pH, with adsorption strongly suppressed under basic conditions. However, in a recent study of adsorption/desorption to peat soils, Deitsch and Smith (1999) found that after an adsorption time greater than 2 days, subsequent desorption of the compound was incomplete, and some of the chemical appeared to be irreversibly sorbed to the soil, and could consequently persist in this media.

Medium mobility is supported by the laboratory results of Bouwer *et al* (1981) which indicated that water percolating through a column of soil previously contaminated with 1,2-dichlorobenzene removed the chemical. Further evidence for mobility is provided by the field results of Demirjian *et al* (1987) who found that four months after applying sludge contaminated with 1,2-dichlorobenzene to the upper layer of a sandy soil (depth 0-15 cm), the chemical was detected in the lower layers at depths between 15 and 48 cm.

Wang and Jones (1994) investigated the behaviour and fate of a series of chloro substituted benzenes when spiked into soil (both “standard” soil and sewage sludge amended soil) using kinetic techniques over a 259 day test period. They found that, in general, the decrease in the chlorobenzene content of the soil could be described by a two-step first order kinetic model, indicating two elimination mechanisms. In the case of 1,2-dichlorobenzene, around 80% was removed after 35 days with a process half-life of 8.6 days, while only an additional 4.3% was removed in the ensuing 224 days. The corresponding data in sewage sludge amended soil were 80% removal over the first 19 days (half-life = 13.2 days) followed by an additional 14 % removal over 240 days. While the half-life for the second stage of the elimination process is significantly longer than that of the first stage, the second stage elimination is pertinent to only a fraction of the initial load in the soil (around 25%), and the overall half-lives in “standard” soil and sewage amended material were 10.5 and 14.4 days respectively. It was concluded that volatilisation was the major elimination process and that biodegradation and other removal processes were of significantly less importance.

In a separate study of 8 archived samples of sewage sludge amended soil collected between 1942 and 1991, Wang *et al* (1995) compared them to soil from a control plot that had never been treated with either sewage sludge or other organic manures. It was found that the level of chlorobenzene compounds (including 1,2-dichlorobenzene) in the sludge amended samples was elevated over those of the control. The range of 1,2-dichlorobenzene applied in the sewage sludge was not detected to 126 µg/kg, however during the 50 years the residue of 1,2-dichlorobenzene was found to be the lowest of the dichlorobenzene compounds at 6-9%. This result supports the relatively rapid elimination of 1,2-dichlorobenzene from soils. Volatilisation was identified by microcosm as the main mechanism of loss.

2.2 Human Exposure

2.2.1 Occupational Exposure

Occupational exposure to 1,2-dichlorobenzene can occur during its manufacture, conversion to intermediate products (for pesticides or dyes) and formulation into products or during the use of products containing the chemical. The major route of occupational exposure is by inhalation of the vapour, although dermal exposure may also occur due to the vapour or the liquid.

In the sponsor country, the main sources of occupational exposure are during the formulation and use of products. 1,2-Dichlorobenzene is formulated into a limited number of products for industrial use, including degreasing/decarbonising agents and paint-stripper/paint removal products. The percentage of 1,2-dichlorobenzene in these products can vary from 2.5 to 70 % (w/v). There are no occupational exposure monitoring data for Australia and no data available in the published literature.

Occupational exposures levels were estimated by use of the UK EASE model. For formulation, levels were estimated to be 0.5 to 3 ppm (8 hour TWA) at 20oC, assuming a non-dispersive pattern of use with local exhaust ventilation present. Dermal exposure is unlikely to contribute significantly. Exposure values of 10 to 50 ppm (8 hour TWA) at 25oC were obtained for end-use,

assuming a non-dispersive pattern of use and no aerosol formation. Dermal exposure is likely to be incidental during an 8-hour day.

Information on workplace exposure to the chemical from production and processing is presented by way of example of the largest producer for a site in Germany. During the past five years (1997 - 2001) 21 samples were taken. All measurements were less than 15 mg/m³ (Bayer AG Leverkusen, personal communication, September 2001).

2.2.2 Consumer Exposure

Potential exposure to 1,2-dichlorobenzene from drinking water, food and ambient air is expected to be negligible. Public exposure to 1,2-dichlorobenzene in Australia is unlikely, as there are no products available to the public with the exception of one pharmaceutical for topical use that contains 14% (v/v) 1,2-dichlorobenzene.

3 HUMAN HEALTH HAZARDS

3.1 Effects on Human Health

3.1.1 Toxicokinetics, Metabolism and Distribution

Studies in Animals

1,2-Dichlorobenzene is well absorbed via the oral route. In rats, absorption of 1,2-dichlorobenzene from the gastrointestinal tract was considered complete at doses of 5 and 50 mg/kg bw but incomplete (83% absorption) at 250 mg/kg bw (Hissink et al., 1996). There are no quantitative data for the dermal and inhalation absorption of 1,2-dichlorobenzene in animals or absorption of the chemical via any route in humans.

Studies with rats have shown that 1,2-dichlorobenzene is distributed primarily to the adipose tissue with lesser amounts detected in the kidneys, liver and plasma. 1,2-Dichlorobenzene equivalents were bound to the kidneys, liver and plasma with covalent binding accounting for a substantial proportion of bound material. In particular, Charbonneau et al. (1989) observed non-specific covalent binding to the $\alpha_2\mu$ -globulin fraction of the rat kidney.

Several studies have found that the administration of a single dose of 1,2-dichlorobenzene by either the oral, intraperitoneal or intravenous route results in high initial tissue levels of 1,2-dichlorobenzene equivalents. Peak tissue levels occur within 1 and 6 hours, depending on the method of administration, followed by rapid decline thereafter (Hissink et al., 1996; Stine et al., 1991; Kato and Kimura, 1997).

The metabolism of 1,2-dichlorobenzene has been well studied in rats, mice and humans and found to be similar. The major site for the biotransformation of 1,2-dichlorobenzene is the liver. Metabolism proceeds predominately by cytochrome P450-mediated aromatic hydroxylation to dichlorophenol derivatives. Several studies have shown the major cytochromes involved in the metabolism of 1,2-dichlorobenzene to be CYP2B1/2 and CYP2E1 resulting in the formation, via their intermediate epoxides, of 3,4-dichlorophenol (3,4-DCP) and 2,3-dichlorophenol (2,3-DCP) as the primary metabolites respectively (Den Besten et al., 1992; Valentovic et al., 1993). Secondary oxidation of the dichlorophenols produces the corresponding dichlorohydroquinones and lesser amounts of 3,4- and 4,5-dichlorocatechol. The hydroquinone and catechol species undergo autoxidation yielding the corresponding dichlorobenzoquinones (Den Besten et al., 1992).

Following the administration of 1,2-dichlorobenzene to rabbits and rats, the major urinary metabolites identified were 2,3-DCP, 3,4-DCP and their glucuronide, sulfate and mercapturic acid derivatives (Azouz et al., 1955; Hissink et al., 1996).

Studies in Humans

Human exposure to 1,2-dichlorobenzene resulted in the following urinary metabolites being detected: 2,3-DCP, 3,4-DCP, 3,4-dichlorocatechol and 4,5-dichlorocatechol. Each of the metabolites was also present in conjugated form (Kumagi and Matsunaga, 1995).

3.1.2 Acute Toxicity

Studies in Animals

The acute toxicity of 1,2-dichlorobenzene is low by the oral and inhalation routes.

The oral LD₅₀ (rat) = 1516 - 2138 mg/kg; inhalation (10h) LC₁₀₀ (rat) ≤ 5885 mg/m³; intraperitoneal LD₅₀ (rat) = 840 mg/kg bw; intraperitoneal LD₅₀ (mouse) = 1228 mg/kg bw (Dura *et al.*, 1985; Murakami and Fukami, 1986; Mohtashampur *et al.*, 1987; RTECS, 1989).

The main acute effects in animals following inhalation exposure (≥ 539 ppm) are drowsiness, unsteady gait, eye irritation, difficulty breathing and anesthesia. Also observed were increases in liver and kidney weights with histopathological lesions of the liver and kidneys (Hollingsworth *et al.*, 1958).

Several well-conducted studies have shown hepatotoxicity, characterized by elevated plasma alanine aminotransferase and aspartate aminotransferase levels, to be the major systemic effect occurring at doses of 172 mg/kg bw (oral) or 147 mg/kg bw (intraperitoneal) or greater (Den Besten *et al.*, 1991; Stine *et al.*, 1991; Allis *et al.*, 1992; Umemura *et al.*, 1996). An increase in hepatic cell proliferation was observed following a single oral dose (300 mg/kg bw) along with hepatocyte swelling and necrosis (Umemura *et al.*, 1996).

Studies in Humans

There have been no fatalities reported following acute exposure to 1,2-dichlorobenzene. Twenty-six laboratory workers consisting of 8 males (range 26 to 46 years, mean 36 years) and 18 females (range 20 to 60 years, mean 30.9 years) were accidentally exposed to 1,2-dichlorobenzene vapour, estimated by the study authors to be no greater than 100 ppm (602 mg/m³), for 4 days (8hr/day). Reported clinical symptoms included headache, vertigo, nausea, malaise and most individuals reported eye, nose and throat irritation with one individual developing a partial facial oedema (Zapata-Gayon *et al.*, 1982).

3.1.3 Irritation

Studies in Animals

Rabbits exhibited pain and conjunctival irritation, described as slight, after direct application of two drops of undiluted 1,2-dichlorobenzene to the eye with the inflammatory response resolving within one week (Hollingsworth *et al.*, 1958). 1,2-Dichlorobenzene caused slight to moderate erythema and oedema up to 72 h post exposure, on the intact skin of rabbits following application of 0.5 mL of undiluted sample for 4 hours (no further data available) (Younger Laboratories, 1972).

Studies with Swiss OF₁ mice indicate that 1,2-dichlorobenzene induces respiratory irritation, with a 50% reduction in respiratory rate (RD₅₀) reported at 163 ppm (Zissu, 1995) and 182 ppm (De Ceaurriz *et al.*, 1981).

Studies in Humans

The application of 1,2-dichlorobenzene to human skin for 15 minutes resulted in a burning sensation and the development of erythema and blistering within 24 hours. Subsequent hyperpigmentation of the affected area developed and persisted for a number of months (Riedel, 1941).

Exposure to 1,2-dichlorobenzene vapour at 100 ppm has been reported to cause some respiratory irritation in humans (Elkins, 1959). Eye and upper respiratory tract irritation was reported by laboratory workers following exposures estimated to be no greater than 100 ppm (602 mg/m³) for 8 h (Zapata-Gayon *et al.*, 1982).

3.1.4 Sensitisation

Studies in Animals

No animal studies addressing sensitisation were identified.

Studies in Humans

One case report of an individual experiencing dermatitis and giving a positive patch test to 1,2-dichlorobenzene has been described (Downing, 1939).

3.1.5 Repeated Dose Toxicity

The results of subchronic and chronic studies (NOAELs, LOAELs and associated effects) are summarised in Table 3.1.5.

Studies in Animals

Inhalation

Male mice (strain Swiss OF₁) were exposed to 1,2-dichlorobenzene vapour at 64 and 163 ppm (385 and 980 mg/m³ respectively) for 4, 9 and 14 days (6 hours/day 5 days/week) and their respiratory tracts examined. Lesions to the olfactory epithelium were observed at 64 ppm after 4 days and were classified as very severe. On increasing the exposure time the severity of the lesions diminished so that on day 9 epithelial damage was classified as severe and on day 14 as moderate. The author concluded that epithelial regeneration may occur in order to replace the damaged epithelium. The respiratory epithelium remained unaffected, as did the trachea and lungs (Zissu, 1995).

In a study of the effects of 1,2-dichlorobenzene (49 ppm; 295 mg/m³), rats and guinea pigs (strains not specified) were exposed for 7 hours/day, 5 days/week for 6.5 months. No adverse effects were observed based on gross appearance, behaviour, growth, mortality, organ-weight studies and gross and histopathological examination of unspecified tissues. Further studies were conducted at (93 ppm; 577 mg/m³) for 7 hours/day, 5 days/week for 6 to 7 months with rats, guinea pigs, rabbits and monkeys (strains not specified). Under these conditions, the final average body weight of male rats was significantly lower ($p \leq 0.05$) compared to control males. No significant difference was observed in the final body weights of female rats or both sexes of guinea pigs. The average organ weights (lung, heart, liver, kidneys, spleen and testes) of rats and guinea pigs did not differ with treatment with the exception of the spleens of male guinea pigs which were significantly lower ($p \leq 0.01$) than control animals. However, histopathological examination revealed no splenic abnormalities. No other adverse effects, as determined by gross appearance, behaviour, growth, mortality, organ-weight studies, haematology or urinalysis, were observed in the species tested. Gross and histopathological examination of unspecified tissues proved negative (Hollingsworth *et al.*, 1958). The value of this study is limited due to inadequate reporting of the experimental conditions and results obtained.

In a 2-generation reproduction study with rats, liver hypertrophy and kidney effects were observed in F0 and F1 adult males. The corresponding NOAEL and LOAEL were 50 and 150 ppm (see also section 3.8).

Oral

Charbonneau *et al.* (1989) studied renal protein droplet formation and cell proliferation in a short-term repeat dose study. Treatment of male rats (strain F344) by gavage daily for 7 days with *o*-DCB (0.8 or 2.0 mmol/kg bw; 118 and 294 mg/kg bw) did not lead to an increase in protein droplet

formation. When treated for 6 days in a similar manner there was no evidence of increased cell proliferation (assessed by incorporation of [³H]-thymidine) compared to controls.

To examine the oral toxicity of 1,2-dichlorobenzene, male and female rats (strain Sprague-Dawley) were administered 0, 37.5, 75, 150 or 300 mg/kg bw per day for 10 days. At 300 mg/kg bw/day a decrease in male total body weight gain and absolute organ weight (heart, kidneys, spleen, testes and thymus) were observed. A significant increase ($p \leq 0.05$) in absolute and relative liver weights and the development of hepatocellular necrosis was evident. Plasma ALT levels were significantly elevated after treatment with 300 mg/kg bw for both sexes while for females, cholesterol levels were elevated at all doses compared with controls. Leukocytosis was present in males at 150 and 300 mg/kg bw while the absolute and relative weights of female livers increased at these doses. Spleen weights decreased only at 300 mg/kg bw. Histopathological findings were the presence of hepatocellular lesions (40% of males treated with 300 mg/kg bw) which were judged by the authors to be slight in severity (Robinson *et al.*, 1991).

In a 14-day study of rats (strain F344), 1,2-dichlorobenzene was administered orally at 0, 60, 125, 250, 500 or 1000 mg/kg bw. The highest dose resulted in 100% mortality by day 5 while 500 mg/kg bw resulted in reduced body weight gain (-12%) (NTP, 1985).

In a 14-day study of mice (strain B6C3F₁), 1,2-dichlorobenzene was administered orally at 0, 250, 500, 1,000, 2,000 or 4,000 mg/kg bw. Only one mouse (250 mg/kg bw) survived the treatment and one control animal died. Hepatic necrosis was observed in 3/3 males dosed at 500 mg/kg bw and 1/3 females at 250 mg/kg bw when examined for histological lesions. Hepatocellular degeneration was observed in 1/3 males at 250 mg/kg bw (NTP, 1985).

In a second 14-day study of mice (strain B6C3F₁), 1,2-dichlorobenzene was administered orally at 0, 30, 60, 125, 250 or 500 mg/kg bw. Two mice died during the course of the study, one male in the 500 mg/kg bw group and one female in the 125 mg/kg group. There were no changes in body weight. Hepatocellular necrosis (described as mild) was observed in 2/4 males at 500 mg/kg bw while moderate focal hepatic necrosis was observed in 1/4 females at 500 mg/kg bw, mild multifocal hepatitis in 1/4, mild cytomegaly and karyomegaly in 2/4 and hepatocellular degeneration in 1/4 (NTP, 1985).

The toxicity of 1,2-dichlorobenzene was examined during a 13-week study of male and female rats (F344) and mice (strain B6C3F₁) administered 1,2-dichlorobenzene (0, 30, 60, 125, 250 or 500 mg/kg bw) 5 days/week by gavage. A decreased survival time for both sexes of mice and female rats at 500 mg/kg bw was observed with pathological findings of hepatic centrilobular necrosis and hepatocellular degeneration, depletion of lymphocytes in the thymus and spleen of both species. High-dose male rats showed renal tubular degeneration while mice exhibited multifocal mineralisation of myocardial fibres and skeletal muscle. A dose of 250 mg/kg bw induced necrosis of individual hepatocytes in both sexes of rats and male mice. Mice were unaffected by 125 mg/kg bw while rats displayed minimal hepatocellular necrosis. The spleen weight/body weight ratio at all doses decreased relative to controls in female mice. Haematological changes were observed at 500 mg/kg bw in rats, which included a slight decrease in haematocrit and haemoglobin, and in the erythrocyte count for male rats (NTP, 1985).

In a two-year study, rats (strain F344) were administered 1,2-dichlorobenzene (0, 60 or 120 mg/kg bw) for 5 days/week. At the highest dose, males exhibited a significant decrease ($p < 0.001$) in survival, however, three of these deaths were accidental and several others were attributed to handling/gavage errors. High-dose males also exhibited a slightly reduced body weight gain while females experienced an increase in weight gain at the same dose level. Histological examination revealed no non-neoplastic lesions. Treatment of mice (B6C3F₁) under the same conditions

produced no change in body weight compared to control animals and survival rates were similar. A dose-dependent increase in renal tubular regeneration was observed in males (NTP, 1985).

The oral toxicity of 1,2-dichlorobenzene for male and female rats (strain Sprague-Dawley) was assessed by administering 0, 25, 100 or 400 mg/kg bw per day for 90 days by gavage. At 400 mg/kg bw per day a significant decrease ($p \leq 0.05$) in total body weight gain was observed for males but not females. Significant increases ($p \leq 0.05$) in absolute and relative liver weights occurred for both sexes at 100 and 400 mg/kg bw and absolute and relative kidney weights were increased at 400 mg/kg bw for both sexes and absolute kidney weights increased for females at 100 mg/kg bw. Plasma ALT levels were elevated at 100 and 400 mg/kg bw in the male but the female levels did not reach significance. In both sexes, an increase in bilirubin occurred at the highest dose. There was no evidence of leukocytosis or other haematological changes for either sex. Histopathological findings included centrilobular degeneration, centrilobular hypertrophy and evidence of apoptosis at 400 mg/kg bw for both genders (Robinson *et al.*, 1991).

Hollingsworth *et al.* (1958) investigated the effect of 1,2-dichlorobenzene (0, 18.8, 188 and 376 mg/kg bw) on female rats (strain not specified) administered by gavage five days/week over 192 days (a total of 138 doses). No treatment-related effects were observed with respect to growth or mortality. At 188 and 376 mg/kg bw significant increases in average liver and kidney weights were observed. No changes in haematological parameters were found. Exposure to 18.8 mg/kg bw produced no adverse effects. The value of this study is limited due to inadequate reporting of the experimental conditions and results obtained.

Table 3.1.5 – Summary of NOAEL and LOAEL values for 1,2-dichlorobenzene in SubChronic and Chronic Studies (non-carcinogenic)

Species (strain)	Study type and duration	Sex	NOAEL (mg/kg bw per day)	LOAEL and associated pathologies	Reference
Rat (SD)	Oral 90 days	Male	25	100 mg/kg bw; increased absolute and relative liver weight ^a . Increased absolute kidney weights for females ^a . Increased plasma ALT levels in males ^a .	Robinson <i>et al.</i> , 1991
		Female			
Rat (F344)	Oral 13 week	Male	60	125 mg/kg bw; hepatocellular necrosis.	NTP, 1985
		Female			
Mice (B6C3F ₁)	Oral 13 week	Male	125	250 mg/kg bw; hepatocellular necrosis.	
		Female	NI	30 mg/kg bw; decreased spleen weight to body weight ratio ^a .	
Rat (strain not specified)	Oral 192 days	Female	18.8	188 mg/kg bw; increase in average liver ^c and kidney weights ^d .	Hollingsworth <i>et al.</i> , 1958
Rat (F344)	Oral 2 years	Male	120	No treatment-related pathologies observed.	NTP, 1985
		Female			
Mice (B6C3F ₁)	Oral 2 years	Male	60	120 mg/kg bw; increased renal tubular regeneration.	
		Female	120	No treatment-related pathologies observed.	
Rat (strain not specified)	Inhalation 26 weeks	Male	49 ppm	93 ppm; decreased male body weight ^a .	Hollingsworth <i>et al.</i> , 1958
		Female	93 ppm	No treatment-related pathologies observed.	
Guinea pig	Inhalation 26 weeks	Male	49 ppm	93 ppm; decreased male spleen weight ^b .	Hollingsworth <i>et al.</i> , 1958
		Female	93 ppm	No treatment-related pathologies observed.	
Rat (Crj: CD(SD))	Inhalation 2-generation reproduction	Male	50 ppm	150 ppm; F0 and F1 adults showed liver hypertrophy and kidney effects in males.	Bio/dynamics Inc., 1989
		Female			

^a, $p \leq 0.05$; ^b, $p \leq 0.01$; ^c, $p = 0.003$; ^d, $p = 0.002$; NI = not identified (i.e. effects seen at the lowest dose).

3.1.6 Mutagenicity

1,2-Dichlorobenzene has been investigated in a number of *in vitro* and *in vivo* assays for a number of genetic endpoints. Details of studies are summarised in the Annex Table A1.

Genotoxicity testing with several microbial species produced negative results with the exception of one recombination assay with *Bacillus subtilis* (Matsui *et al.*, 1989) and a differential toxicity assay with *Escherichia coli* (Waters *et al.*, 1982). *In vitro* testing with mammalian cells produced negative results with the chromosomal aberration assay and the HGPRT assay using Chinese hamster ovary (CHO) cells. However, two sister chromatid exchange assays performed with CHO cells (Tennant *et al.*, 1987; Loveday *et al.*, 1990) and two mouse lymphoma assays (Tennant *et al.*, 1987; Myhr and Caspary, 1991) were positive in the presence of, and negative in the absence of, metabolic activation. A DNA synthesis inhibition assay performed with human lymphocytes was positive without metabolic activation and negative with metabolic activation (Perocco *et al.*, 1983).

In vivo testing of 1,2-dichlorobenzene yielded negative results with the *Drosophila* sex-linked recessive mutation (Bioassay Systems, 1983 (cited in BUA, 1990 and NTP, 1989)) and eye mosaic assays (Vogel and Nivard, 1993). Chromosomal aberration assays with rat bone marrow (Reustle and Scriber, 1979 and Bioassay Systems, 1983 (cited in BUA, 1990)) and DNA damage studies in rats were negative (Kitchin *et al.*, 1992). A positive micronucleus assay in mouse bone marrow (Mohtashampur *et al.*, 1987) was not confirmed in a more recent, well-conducted study (Shelby *et al.*, 1993).

The role of 1,2-dichlorobenzene as an inducer of DNA synthesis was assessed using an *in vivo-in vitro* replicative DNA synthesis assay with hepatocytes derived from male B6C3F₁ mice. The animals were administered 1,2-dichlorobenzene (1000 or 2000 mg/kg bw) by the oral route and hepatocytes prepared 24, 39 or 48 hours later. Replicative DNA synthesis was assessed after the addition of [methyl-³H]-thymidine followed by autoradiography. Results were negative for both doses at all time points (Miyagawa *et al.*, 1995).

Following accidental exposure to 1,2-dichlorobenzene vapour, estimated by the study authors to be no greater than 100 ppm (602 mg/m³), the mean value of chromosomal aberrations in peripheral blood leukocytes from exposed individuals was 8.92% compared to 2.02% for a control group (Zapata-Gayon *et al.*, 1982). Due to the relatively low number of cells examined, little confidence can be attributed to findings of this study.

3.1.7 Carcinogenicity

Studies in Animals

In a two-year study of both sexes of rats (F344/N) and mice (B6C3F₁), 1,2-dichlorobenzene (0, 60 or 120 mg/kg bw) was administered by gavage (5 days/week). A dose-related increased incidence of renal tubular regeneration was observed in male rats (control, 8/48; low dose, 12/50; high dose 17/49 animals). Although the incidence of pheochromocytoma in male rats was increased in the low-dose group (16/50 animals), the high-dose incidence (6/49 animals) was lower than the control group (9/50 animals) with no significant dose-response trend being evident. The incidence of malignant histiocytic lymphoma in male (control, 0/50; low-dose, 1/50; high-dose 4/50 animals) and female (control, 0/49; low-dose, 0/50; high-dose, 3/49 animals) mice was significantly increased ($p < 0.05$). However, the findings were considered not biologically significant, as the number of animals with all types of lymphomas (combined), which is considered to be a better indicator, had not increased. Under the conditions of the study, 1,2-dichlorobenzene was not considered to be carcinogenic in rats or mice (NTP, 1985).

Tumour initiation or promotion by 1,2-dichlorobenzene was investigated using the γ -glutamyltranspeptidase-positive foci assay as an indicator of carcinogenicity. Male and female rats (Sprague-Dawley) were treated with diethylnitrosamine (0.5 mmol/kg), a tumour initiator, one day after a two-thirds hepatectomy followed, by intraperitoneal injections 1 and 5 weeks later of 1,2-dichlorobenzene (1 mmol/kg bw; 147 mg/kg bw). The number of positive foci from treated rats was not significantly different from control animals (Herren-Freund and Pereira, 1986).

Studies in Humans

There are no well-conducted epidemiological studies for 1,2-dichlorobenzene. Five cases of haematological disorders including two cases of acute myeloblastic leukaemia, two cases of chronic lymphoid leukaemia and a myeloproliferative syndrome, have been attributed to 1,2-dichlorobenzene (Girard *et al*, 1969). However, the cases were poorly characterized with respect to the chemicals involved, the level and duration of exposure and other confounding influences.

3.1.8 Toxicity for Reproduction

Studies in Animals

Effects on Fertility

In an inhalation, 2-generation reproduction study in rats, animals were exposed to 0, 50, 150 or 400 ppm 1,2-dichlorobenzene for 6 hours/day, 7 days per week. At the highest dose, F0 and F1 adults had significantly lower terminal body weights and increased absolute and relative liver weights and liver hypertrophy. Males in the high dose group also had increased relative kidney weights and kidney effects were observed. Liver hypertrophy was also observed in some mid-dose F0 and F1 adults and kidney effects were observed to a lesser extent in mid-dose F0 and F1 adult males. No fertility effects, as indicated by mating indices, pregnancy rates or fertility indices, were noted. For F0 and F1 pups, gestation length, parturition, litter and pup survival were unaffected. A significantly lower pup weight during lactation at the highest dose was observed in both the F0 and F1 litters. No treatment related effects were observed in adults or pups at the lowest dose (Bio/dynamics Inc., 1989). The NOAEL and LOAEL for adults were 50 ppm and 150 ppm respectively and for reproductive toxicity and offspring growth and development were 150 ppm and 400 ppm respectively.

1,2-Dichlorobenzene has been reported to induce morphological changes in rat sperm. Doses ranging from 50 to 800 mg/kg body weight (i.p.) resulted in dose-dependent acrosomal, head and tail abnormalities (Murthy and Holovack 1985, abstract only).

Developmental Toxicity

The developmental effects of 1,2-dichlorobenzene for rabbits and rats have been investigated. Inseminated rabbits were exposed to 1,2-dichlorobenzene (0, 100, 200 or 400 ppm) for 6 hr/day on days 6 to 18 of gestation. Maternal toxicity was observed, described as slight, and based on a decrease in body weight gain during the first three days of exposure at all dose levels. At doses up to 400 ppm (2404 mg/m³) 1,2-dichlorobenzene did not prove to be embryotoxic, fetotoxic or teratogenic in the rabbit based on observations of the number of pregnancies, litter size, resorption rate, foetal body measurements or foetal malformations. Rats treated with 1,2-dichlorobenzene (0, 100, 200 or 400 ppm) for 6 hr/d on days 6 to 15 of gestation showed maternal toxicity at all dose levels as judged by a significant decrease in body weight gain from gestation days 6 through to 20. A significant increase in maternal liver weights occurred with rats exposed to 400 ppm. The only developmental treatment-related effect was a significant increase in the occurrence of delayed ossification of cervical vertebral centra in the highest dose group (Hayes, 1985). For the rabbit, a

NOAEL of 400 ppm was determined for developmental effects and for the rat developmental effects were only seen at maternally toxic doses (400 ppm).

In a briefly reported study, no teratogenic effects were observed following the oral administration of 1,2-dichlorobenzene (50, 100 or 200 mg/kg bw) to rats. Foetuses were examined for litter size, body weight, deciduoma, and skeletal and visceral variations (Ruddick *et al*, 1983, abstract only).

Studies in Humans

There are no data on the reproductive or developmental effects of 1,2-dichlorobenzene in humans.

3.2 Initial Assessment for Human Health

1,2-Dichlorobenzene is absorbed via the oral route. Absorption via the dermal or inhalation routes is poorly characterized. Inhalation is expected to be the major route for human exposure. The available toxicological data indicate that metabolic profiles and effects from 1,2-dichlorobenzene exposure are similar in rats, mice and humans.

The critical effects from acute exposure to 1,2-dichlorobenzene in animals and humans are eye and respiratory irritation, reported at atmospheric levels at 100 ppm (602 mg/m³) in humans. 1,2-Dichlorobenzene has also been shown to cause skin irritation in one human study and in a study with rabbits. At high doses, 1,2-dichlorobenzene produces central nervous system effects in humans and test animals.

Animal studies with rats and mice have shown 1,2-dichlorobenzene to induce acute hepatotoxic effects. The LD₅₀ for a single oral exposure to 1,2-dichlorobenzene for the rat ranges from 1516 to 2138 mg/kg bw. The LC₁₀₀ for the rat is ≤ 977 ppm (5.9 mg/L) for a 10 hour exposure. During a 4 hour exposure, 1 of 20 rats died at 941 ppm (5.6 mg/L). In humans, the acute effects of 1,2-dichlorobenzene by ingestion or inhalation are reported to be headache, nausea, vomiting, vertigo, malaise and unconsciousness.

Several oral studies of rats and mice ranging from 10 days to 2 years duration indicate that the adverse effects include increases in liver and kidney weights and hepatotoxicity. In these repeat dose studies, the NOAEL for non-neoplastic effects was 60 mg/kg bw while the LOAEL was 120 mg/kg bw, due to increased renal tubular regeneration in male mice.

In an inhalation, 2-generation reproduction study in rats, no fertility effects were observed and the only effect on the pups was a significantly lower body weight during lactation at doses causing adult toxicity (kidney and liver effects). The NOAEL and LOAEL for adult toxicity were 50 ppm and 150 ppm respectively.

In several microbial organisms and mammalian systems, 1,2-dichlorobenzene tested negative in vitro. However, it did induce sister chromatid exchanges in Chinese Hamster ovary cells and increased mutation frequency in mouse lymphoma cells, both in the presence of metabolic activation. 1,2-dichlorobenzene was negative in several in vivo mammalian tests, except one of two micronuclei assays in mouse bone marrow was positive.

In a two-year oral study in rats and mice, 1,2-dichlorobenzene was considered not to be carcinogenic. No human epidemiological studies have been conducted.

4 HAZARDS TO THE ENVIRONMENT

4.1 Aquatic Effects

1,2-Dichlorobenzene has been tested in a wide variety of aquatic species (micro-organisms, plants, invertebrates and fish). Results are summarised in Table 4.1.

These results indicate that under acute exposure conditions, 1,2-dichlorobenzene is toxic to fish (LC₅₀ range 1-10 mg/L), very toxic to aquatic invertebrates (LC₅₀ range <1-10 mg/L) and toxic to moderately toxic to algae (1-100 mg/L).

Table 4.1: Summary of Effects of 1,2-Dichlorobenzene on Aquatic Organisms

ORGANISM	TEST DURATION	RESULT (mg/L)	Conc. #	REFERENCE
<i>Micro-organisms</i>				
Bacillus (TL 81) – from activated sludge	30 min exposure	EC50 = 169±13	X	Liu and Thomson (1984)
Activated sludge bacteria	3 hours (OECD TG 210)	EC50 = 100	X	Yoshioka <i>et al</i> (1986b)
<i>Photobacterium phosphoreum</i>	5 min exposure (Microtox test)	EC50 = 10.25±0.35	X	McFeters <i>et al</i> (1983)
<i>Photobacterium phosphoreum</i>	30 min exposure (Microtox test)	EC50 = 4.0		Kaiser and Ribo (1985)
	5 min exposure (Microtox test)	EC50 = 2.7		Ribo and Kaiser (1983)
<i>Tetrahymena pyriformis</i> (Ciliate)	24 hours, static	LC50=51	X	Yoshioka <i>et al</i> (1985)
<i>Algae</i>				
<i>Selenastrum capricornutum</i>	96 hours	ErC50 = 2.2 NOEC = 0.88	N	Calamari <i>et al</i> (1983)
	96 hours	EC50=71.1		US EPA (1978)
	96 hours	EC50=76.1 NOEC <10		US EPA (1978)
	96 hours	ErC50=98 EC50=91.6 (chlorophyll impairment)		US EPA (1978)
<i>Scenedesmus pannonicus</i>		EC50=17	M	Canton <i>et al</i> (1985)
<i>Scenedesmus subspicatus</i> (green algae)	48 hours, static	EC50=14	N	Kuhn and Pattard (1990)
<i>Skeletonema costatum</i> (marine algae)	96 hours	EC50=44.2 (Chlorophyll impairment)		US EPA (1978)

Table 4.1: Summary of Effects of 1,2-Dichlorobenzene on Aquatic Organisms (cont.)

ORGANISM	TEST DURATION	RESULT (mg/L)	Conc.#	REFERENCE
<i>Invertebrates</i>				
<i>Daphnia magna</i>	24 hours, closed	IC50=0.78	M	Calamari <i>et al</i> (1983)
	24 hours	EC50=1.7	N	Kuhn <i>et al</i> (1989)
	48 hours, closed	EC50=2.35	N	Abernathy <i>et al</i> (1986)
	48 hours, closed	IC50=3.77	N	Hermens <i>et al</i> (1984)
	48 hours, static	LC50=2.2	M	Canton <i>et al</i> (1985)
		EC50=0.74	M	
48 hours, static	EC50=2.4	N	LeBlanc (1980)	
<i>Ceriodaphnia dubia</i>	48 hours, static	EC50=0.66	N	Rose <i>et al</i> (1998)
<i>Artemia</i> (Brine Shrimp)	24 hours	EC50=15	N	Abernathy <i>et al</i> (1986)
<i>Palaemonetes pugio</i> (Salt water grass shrimp)	96 hours	LC50=10	N	Curtis and Ward (1981)
	96 hours	LC50=9.4	N	Curtis <i>et al</i> (1979)
<i>Mercenaria mercenaria</i> (Hard clam) eggs and larval stage	48 hours, static	EC50 >100	X	Davis and Hidu (1969)
<i>Mysidopsis bahia</i> (Opossum shrimp)	96 hours	LC50=1.97		US EPA (1978)
<i>Tanytarsus dissimilis</i> (Midge)	48 hours, static	LC50=12	M	Call <i>et al</i> (1983)
Chronic Toxicity				
<i>Daphnia magna</i>	14 days	EC50= 0.55	N	Calamari <i>et al</i> (1983)
	16 days	IC50=1.5	N	Hermens <i>et al</i> (1984)
	21 days, semi static	NOEC = 0.63	N	Kuhn <i>et al</i> (1989)
<i>Mercenaria mercenaria</i> (Hard clam)	12 days, flow-through	EC50=0.25-10 (growth) LC50 >100	X	Davis and Hidu (1969)

Table 4.1: Summary of Effects of 1,2-Dichlorobenzene on Aquatic Organisms (cont.)

ORGANISM	TEST DURATION	RESULT (mg/L)	Conc. [#]	REFERENCE
<i>Fish</i>				
<i>Brachydanio rerio</i> (zebra fish)	48 hours	LC50=6.8	N	Calamari <i>et al</i> (1983)
	96 hour	LC50=5.2		Roederer (1990)
<i>Oncorhynchus mykiss</i> (Rainbow trout)	48 hours	LC50=2.3	N	Calamari <i>et al</i> (1983)
	96 hours	LC50=1.61	M	Ahmad <i>et al</i> (1984)
	96 hours	LC50=1.58	M	Call <i>et al</i> (1983)
	144 hours	LC50=1.54	M	Call <i>et al</i> (1983)
<i>Cyprinodon variegatus</i> (Sheepshead minnow)	48 hour	LC50=9.3	N	Heitmuller <i>et al</i> (1981)
	96 hours	LC50=9.7	N	Heitmuller <i>et al</i> (1981)
<i>Lepomis macrochirus</i> (Bluegill sunfish)	24 hour	LC50=6.3	N	Buccafusco <i>et al</i> (1981)
	96 hours	LC50=5.6	N	Buccafusco <i>et al</i> (1981)
	96 hours	LC50=27	X	Dawson <i>et al</i> (1977)
<i>Menidia beryllina</i> (Inland silverside)	96 hours	LC50=7.3	X	Dawson <i>et al</i> (1977)
<i>Pimephales promelas</i> (Fathead minnow)	96 hours	LC50=57	N	Curtis and Ward (1981)
	96 hours	LC50=57	N	Curtis <i>et al</i> (1979)
<i>Oryzias latipes</i> (Japanese rice fish)	48 hours	LC50=9.3	X	Yoshioka <i>et al</i> (1986a)
Chronic				
<i>Brachydanio rerio</i>	14 day	NOEC= 0.37		Roederer (1990)

[#] - this column indicates if the result is based on a nominal (N) or measured (M) concentration, or if this cannot be determined from the literature (X).

4.2 Terrestrial Effects

Walton *et al* (1989) studied the effects of 1,2-dichlorobenzene at 1000 µg/g on the respiration of soil bacteria. The study was undertaken in the dark at 20°C for 6 days. Although the rate of CO₂ evolution was depressed for the first few days of the experiment, the rate was not significantly different from the untreated controls at the end of the 6 day period.

Meharg *et al* (1998) found that 1,2-dichlorobenzene had no deleterious effects on soil microorganisms up to levels of 50 µg/g, and also found that the metabolic activity of the biomass shifted to enhance degradation of 1,2-dichlorobenzene.

Thompson *et al* (1999) found that although 1,2-dichlorobenzene levels of 65 µg/g and above caused significant decrease in hyphal fungal length, soil bacteria were significantly more tolerant, with observable population decreases only at 1,2-dichlorobenzene levels of 3.25 mg/g (dry weight). Further, there was evidence that 1,2-dichlorobenzene at levels up to 325 µg/g stimulated counts of *Pseudomonas*.

Yukimoto (1983) investigated the phytotoxicity of a series of chlorinated benzenes to photosynthesis in spinach leaves. It has not been possible to locate the original paper, so the

method of exposure of the leaves to the chemical is unclear. This worker found that these compounds had some inhibitory effect on photosynthesis, and for 1,2-dichlorobenzene obtained the following results: IC7 = 10.3 mg/L, IC46 = 59 mg/L and IC85 = 103 mg/L.

4.3 Initial Assessment for the Environment

The majority (>90%) of 1,2-dichlorobenzene is expected to partition to the atmospheric compartment where reaction with photochemically produced hydroxyl radicals provides the most significant removal mechanism. Where release is to water or soil, the chemical is expected to volatilise to the surrounding atmosphere.

No experimental data on environmental organisms exposed through the gas phase are available. However, abiotic effects can be assessed. While direct photolysis is not considered likely, the atmospheric half-life is relatively short due to reaction with photochemically produced hydroxyl radicals ($t_{1/2}$ 38 \pm 2 days). The chemical contains chlorine substituents which suggest a potential effect on stratospheric ozone. However, with half-lives for migration to the stratosphere of 3 to 10 years (Bunce, 1994), this chemical would not be expected to persist long enough in the troposphere to be of concern.

Nonetheless, Webster *et al* (1998) state that transport times to the Arctic can be measured in weeks. Therefore, it could be expected that 1,2-dichlorobenzene could undergo significant transport in the atmosphere and may migrate to the poles. No measurements appear to be available from these regions.

1,2-Dichlorobenzene has been tested on a wide range of aquatic organisms under acute exposure, although chronic data are scarce. Results for fish ranged from 96 h LC50=1.58 mg/L for rainbow trout to 57 mg/L for fathead minnow. Both acute and chronic toxicity to aquatic invertebrates were obtained with two results showing high toxicity, namely EC50's of 0.78 mg/L and 0.66 mg/L to *Daphnia* and *Ceriodophnia* respectively. Results from exposure to algae showed EC50 values in the 1-100 mg/L range for 1,2-dichlorobenzene. Toxicity to micro-organisms can be considered slight.

While there are a large number of acute data covering all trophic levels, chronic data are scarce. Therefore, an assessment factor of 100 has been chosen. The result used for determining the PNEC was the lowest chronic value obtained, i.e. 21 d NOEC = 0.63 mg/L for *Daphnia magna*. The PNEC_{aquatic} was therefore determined to be 6.3 μ g/L.

No PNEC_{soil} was determined, as the data are considered insufficient for realistic estimations of this parameter for terrestrial life.

5 RECOMMENDATIONS

1,2-Dichlorobenzene is toxic and bioconcentrates. Additionally, it may be considered persistent due to its lack of biodegradation where microbial communities are not acclimatised. Member countries may wish to undertake a more in-depth exposure analysis and if then indicated, a risk assessment may be considered.

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ANNEX

Table A1: Summary of genotoxicity studies

Type of test	Test system	Result	Reference
GENE MUTATION ASSAYS			
<i>In vitro</i>			
Ames test (reverse mutation)	<i>S. typh.</i> (8 strains not specified)	Negative (- MA Only)	Andersen <i>et al</i> , 1972
Ames test (reverse mutation)	<i>S. typh.</i> (strains TA98; TA100; TA1535; TA1537; TA1538)	Negative (+ & - MA)	Litton Bionetics, 1976
Ames test (reverse mutation)	<i>S. typh.</i> (strains TA98; TA100; TA1535; TA1537; TA1538)	Negative (+ & - MA)	Lawlor <i>et al</i> , 1979
Ames test (reverse mutation)	<i>S. typh.</i> (strain TA100)	Negative (+ & - MA)	Rohm & Hass Co, 1979
Ames test (reverse mutation)	<i>S. typh.</i> (strains TA98; TA100; TA1535; TA1537; TA1538)	Negative (+ & - MA)	Waters <i>et al</i> , 1982
Ames test (reverse mutation)	<i>S. typh.</i> (strains TA98; TA100; TA1535; TA1537)	Negative (+ & - MA)	Haworth <i>et al</i> , 1983
Ames test (reverse mutation)	<i>S. typh.</i> (strains TA98; TA100; TA1535; TA1537; TA1538)	Negative (+ & - MA)	Shimizu <i>et al</i> , 1983
Ames test (reverse mutation)	<i>S. typh.</i> (strains TA98; TA100; UTH8414; UTH8413)	Negative (+ & - MA)	Connor <i>et al</i> , 1985
Ames test (reverse mutation)	<i>S. typh.</i> (strains TA97; TA98; TA100; TA102; TA1535; TA1537; TA1538)	Negative (+ & - MA)	Koch <i>et al</i> , 1985
Ames test (reverse mutation)	<i>S. typh.</i> (strains TA98; TA100; TA2637)	Negative (+ & - MA)	Nohmi <i>et al</i> , 1985
Ames test (reverse mutation)	<i>S. typh.</i> (strains TA98; TA100; TA1535; TA1537)	Negative (+ & - MA)	NTP, 1985 (Tennant <i>et al</i> , 1986)
DNA damage	<i>S. typh.</i> (strain TA1535/pSK1002)	Negative (+ & - MA)	Nakamura <i>et al</i> , 1987
DNA damage	<i>S. typh.</i> (strain TA1535/pSk1002)	Negative (+ & - MA)	Ono <i>et al</i> , 1992
Reverse mutation	<i>Escherichia coli</i>	Negative (+ & - MA)	Waters <i>et al</i> , 1982
Reverse mutation	<i>Aspergillus nidulans</i>	Negative (- MA only)	Prasad and Pramer, 1968 & Prasad, 1970
Gene mutation	<i>Saccharomyces cerevisiae</i>	Negative (+ & - MA)	Litton Bionetics, 1976
Mouse lymphoma assay	Mouse L5178Y cells	Negative (- MA) Positive (+ MA)	Tennant <i>et al</i> , 1987
Mouse lymphoma assay	Mouse L5178Y cells	Negative (- MA) Positive (+ MA)	Myhr & Caspary, 1991

In vivo

Sex-linked recessive mutation	<i>Drosophila melanogaster</i>	Negative	Bioassay Systems, 1983
Eye mosaic assay	<i>Drosophila melanogaster</i>	Negative	Vogel and Nivard, 1993

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Recombination assay	<i>Bacillus subtilis</i>	Positive (- MA) Negative (+ MA)	Matsui <i>et al</i> , 1989
Recombination assay	<i>Bacillus subtilis</i>	Negative (- MA only)	Waters <i>et al</i> , 1982
DNA damage & repair	<i>Escherichia coli</i>	Negative (+ & - MA)	DeMarini and Brooks, 1992
Differential toxicity	<i>Escherichia coli</i>	Positive (- MA only)	Waters <i>et al</i> , 1982
Mitotic recombination	<i>Saccharomyces cerevisiae</i>	Negative (+ & - MA)	Waters <i>et al</i> , 1982
DNA damage & repair	Primary hepatocytes (rat)	Negative (- MA only)	Shimada <i>et al</i> , 1983
DNA damage & repair	Primary hepatocytes (rat)	Negative (- MA only)	Williams <i>et al</i> , 1989
DNA synthesis - inhibition	Lymphocytes (human)	Positive (- MA) Negative (+ MA)	Perocco <i>et al</i> , 1983

ASSAYS FOR CHROMOSOMAL ABERRATIONS

In vitro

SCE	CHO	Negative (- MA) Positive (+ MA)	Loveday <i>et al</i> , 1990
SCE	CHO	Negative (- MA) Positive (+ MA)	Tennant <i>et al</i> , 1987
Chromosomal aberration	CHO	Negative (+ & - MA)	Loveday <i>et al</i> , 1990
Chromosomal aberration	CHO	Negative (+ & - MA)	Tennant <i>et al</i> , 1987
Chromosomal aberration	CHO	Negative (+ & - MA)	Bioassay Systems, 1983
Chromosomal aberration	CHO	Negative (+ & - MA)	Waters <i>et al</i> , 1982

In vivo

Chromosomal	Rat bone marrow (male)	Negative	Reustle and Scriber,
-------------	------------------------	----------	----------------------

aberration			1979
Chromosomal aberration	Rat bone marrow (male and female)	Negative	Bioassay Systems, 1983
ASSAYS FOR CHROMOSOMAL ABERRATIONS (cont.)			
Micronucleus (bone marrow)	Mouse (male)	Positive	Mohtashamipur <i>et al</i> , 1987
Micronucleus (bone marrow)	Mouse (male)	Negative	Shelby <i>et al</i> , 1993
OTHER			
HGPRT assay	CHO	Negative (+ & - MA)	Bioassay Systems, 1984

+MA = *with* metabolic activation

-MA = *without* metabolic activation

CHO = Chinese hamster ovary

E. coli = *Escherichia coli*

RDS = replicative DNA synthesis

SCE = sister chromatid exchange

S. cerevisiae = *Saccharomyces cerevisiae*

S. typh. = *Salmonella typhimurium*

TWA = time weighted average

UDS = Unscheduled DNA synthesis

I U C L I D

D a t a S e t

Existing Chemical ID: 95-50-1
CAS No. 95-50-1
EINECS Name 1,2-dichlorobenzene
EINECS No. 202-425-9
TSCA Name Benzene, 1,2-dichloro-
Molecular Formula C6H4Cl2

Producer Related Part

Company: NICNAS
Creation date: 23-AUG-2001

Substance Related Part

Company: NICNAS
Creation date: 23-AUG-2001

Printing date: 10-JUL-2003
Revision date:
Date of last Update: 09-JUL-2003

Number of Pages: 187

Chapter (profile): Chapter: 1, 2, 3, 4, 5, 7
Reliability (profile): Reliability: without reliability, 1, 2, 3, 4
Flags (profile): Flags: without flag, confidential, non confidential, WGK
(DE), TA-Luft (DE), Material Safety Dataset, Risk
Assessment, Directive 67/548/EEC, SIDS

1.0.1 OECD and Company Information

Name: Atochem
Street: 4, Cours Michelet
Town: 92080 Paris la Defense
Country: France
Source: EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
11-FEB-2000

Name: BASF AG
Street: Karl-Bosch-Str
Town: 67056 Ludwigshafen
Country: Germany
Source: EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
11-FEB-2000

Name: Bayer AG
Town: 51368 Leverkusen
Country: Germany
Source: EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
11-FEB-2000

Name: DALTRADE LTD
Street: 16 DEVONSHIRE STREET
Town: W1N 1FS LONDON
Country: United Kingdom
Phone: 0171 4365454
Telefax: 0171 4361445
Source: EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
11-FEB-2000

Name: Enichem Synthesis
Street: VIA MEDICI VASCELLO, 40
Town: 20138 Milan
Country: Italy
Source: EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
11-FEB-2000

Name: ESAR S.A.
Street: 89-91 Rue du Faubourg Saint-Honore
Town: 75370 PARIS
Country: France
Phone: (1) 42.66.15.66
Telefax: (1) 42.66.11.92
Telex: 285 144F
Cedex: PARIS 08
Source: EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
11-FEB-2000

Name: VOS B.V.
Street: Ondernemingsweg 1A
Town: 2404 HM Alphen aan den Rijn
Country: Netherlands
Phone: 31-172-431601
Telefax: 31-172-432494
Source: EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
11-FEB-2000

1.0.2 Location of Production Site

1.0.3 Identity of Recipients

1.1 General Substance Information

Substance type: organic
Physical status: liquid
Source: EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
11-FEB-2000

1.1.0 Details on Template

1.1.1 Spectra

1.2 Synonyms

1,2-DCB
23-AUG-2001

1,2-Dichloorbenzeen
02-JUN-1998

1,2-DICHLOROBENZENE
25-JUN-1993

1.2-DICHLORBENZOL
25-JUN-1993

BENZENE, 1,2-DICHLORO-
25-JUN-1993

Benzene, 1,2-dichloro- (9CI)
30-AUG-1996

BENZENE, O-DICHLORO-
25-JUN-1993

Benzene, o-dichloro- (8CI)
30-AUG-1996

CHLOROBEN
23-AUG-2001

Cloroben
23-AUG-2001

Dilatin DB
30-AUG-1996

Dowtherm E
30-AUG-1996

O-DICHLORBENZOL
23-AUG-2001

o-DICHLOROBENZENE
02-JUN-1994

ODCB
02-JUN-1994

ORTHO-DICHLOROBENZENE
02-JUN-1994

1.3 Impurities

CAS-No:
EINECS-No:
EINECS-Name:
Contents: = 15 - 35 % w/w
Remark: Commercial 1,2-DCB: 15-35% para and meta-dichlorobenzene,
with lesser amounts of chlorobenzene & trichlorobenzene
03-SEP-2001

1.4 Additives

1.5 Quantity

Quantity
23-AUG-2001

1.6.1 Labelling

Labelling: as in Directive 67/548/EEC
Symbols: Xn
N
C
Specific limits: yes
R-Phrases: (22) Harmful if swallowed
(36/37/38) Irritating to eyes, respiratory system and skin
(50/53) Very toxic to aquatic organisms, may cause long-term
adverse effects in the aquatic environment
S-Phrases: (2) Keep out of reach of children
(23) Do not breathe ...
(60) This material and/or its container must be disposed of
as hazardous waste
(61) Avoid release to the environment. Refer to special
instructions/Safety data sets
Source: EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
11-FEB-2000

1.6.2 Classification

Classification: as in Directive 67/548/EEC
Class of danger: corrosive
R-Phrases: (22) Harmful if swallowed
Source: EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
11-FEB-2000

Classification: as in Directive 67/548/EEC

Class of danger: dangerous for the environment
R-Phrases: (50) Very toxic to aquatic organisms
(53) May cause long-term adverse effects in the aquatic
environment

1. GENERAL INFORMATION

DATE: 10-JUL-2003

ID: 95-50-1

Source: EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
11-FEB-2000

Classification: as in Directive 67/548/EEC
Class of danger: irritating
R-Phrases: (36/37/38) Irritating to eyes, respiratory system and skin
Source: EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
11-FEB-2000

1.7 Use Pattern

Type: type
Category: Non dispersive use
Source: EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
11-FEB-2000

Type: type
Category: Use in closed system
Source: EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
11-FEB-2000

Type: industrial
Category: Basic industry: basic chemicals
Source: EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
11-FEB-2000

Type: industrial
Category: Chemical industry: used in synthesis
Source: EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
11-FEB-2000

Type: industrial
Category: Paints, lacquers and varnishes industry
Source: EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
11-FEB-2000

Type: use
Category: Intermediates
Source: EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
11-FEB-2000

Type: use
Category: Solvents
Source: EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
11-FEB-2000

1.7.1 Technology Production/Use

1.8 Occupational Exposure Limit Values

1.9 Source of Exposure

Remark: Chlorination of benzene (catalyst FeCl_3)
Separation of chlorobenzene by distillation.
One production site.
Source: Atochem Paris la Defense
24-AUG-2001

1. GENERAL INFORMATION

DATE: 10-JUL-2003

ID: 95-50-1

Remark: MANUFACTURING
Source: ESAR S.A. PARIS
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
02-JUN-1994

1.10.1 Recommendations/Precautionary Measures

1.10.2 Emergency Measures

1.11 Packaging

1.12 Possib. of Rendering Subst. Harmless

1.13 Statements Concerning Waste

1.14.1 Water Pollution

1.14.2 Major Accident Hazards

1.14.3 Air Pollution

1.15 Additional Remarks

1.16 Last Literature Search

1.17 Reviews

1.18 Listings e.g. Chemical Inventories

2.1 Melting Point

Value: -16.7 degree C
Method: other: not specified
GLP: no data
Source: NICNAS
23-AUG-2001 (61)

2.2 Boiling Point

Value: 180.3 degree C
Method: other: not specified
GLP: no data
Source: NICNAS
03-SEP-2001 (61)

2.3 Density

Type: density
Value: 1.3007 g/cm³ at 25 degree C
Method: other: not specified
GLP: no data
Source: NICNAS
14-MAY-2003 (70)

2.3.1 Granulometry

2.4 Vapour Pressure

Value: 1.96 hPa at 25 degree C
Source: NICNAS
03-SEP-2001 (160)

2.5 Partition Coefficient

log Pow: = 3.4 at 25 degree C
Method:
Year:
Remark: experimentally measured
Source: NICNAS
Test substance: 14C-orthodichlorobenzene
24-AUG-2001 (18) (172)

log Pow: 3.4
Method: other (calculated): Leo, A., CLOGP-3.63 (1991) Daylight,
Chemical Information Systems, Inc. Irvine, CA USA
Year:
Source: Bayer AG Leverkusen
24-AUG-2001 (55)

log Pow: 3.43
Method:
Year:
Remark: experimentally measured
Source: Bayer AG Leverkusen

24-AUG-2001 (256)

log Pow: = 3.49
 Method: other (measured): Chiou et al , M. Environ. Sci. Technol.,
 1982, 16:4-10.

Year:
 Remark: Distilled water used
 Source: NICNAS
 03-SEP-2001 (203)

log Pow: = 3.56
 Method: other (measured): Chiou et al , M. Environ. Sci. Technol.,
 1982, 16:4-10.

Year:
 Remark: Bayou d'Inde water used
 Source: NICNAS
 03-SEP-2001 (203)

2.6.1 Water Solubility

Value: .13 g/l at 20 degree C
 Source: Bayer AG Leverkusen
 24-AUG-2001 (24)

Value: = 155.8 mg/l at 25 degree C
 Remark: Experimentally measured
 Source: NICNAS
 Test substance: 14C-orthodichlorobenzene
 03-JUL-2002 (18)

2.6.2 Surface Tension

2.7 Flash Point

Value: 66 degree C
 Type: other
 Method: other: closed cup, DIN 51758
 Year:
 Source: Bayer AG Leverkusen
 24-AUG-2001 (24)

Value: = 66 degree C
 Type:
 Method: other: closed cup
 Year:
 Source: NICNAS
 23-AUG-2001 (230)

Value: 68 degree C
 Type: closed cup
 Method: other
 Year:
 GLP: no data
 Remark: Method: NFT 60-103
 Source: ELF ATOCHEM S.A., France
 Bayer AG Leverkusen
 EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)

10-MAY-1994 (226)

2.8 Auto Flammability

Value: 648 degree C
Source: NICNAS
03-SEP-2001 (230)

2.9 Flammability

2.10 Explosive Properties

Result: other
Remark: explosive limits:
upper: 9.2% by vol
lower: 2.2% by vol
Source: NICNAS
24-AUG-2001 (230)

2.11 Oxidizing Properties

2.12 Additional Remarks

Remark: Thermal decomposition products: toxic chlorinated substances
such as hydrogen chloride, phosgene
Source: ELF ATOCHEM S.A., France Bayer AG Leverkusen (227)
24-AUG-2001
Remark: Odour threshold : 1.8 mg/m3
Source: NICNAS
24-AUG-2001 (9)

3.1.1 Photodegradation

Type: air
 INDIRECT PHOTOLYSIS
 Sensitizer: OH
 Conc. of sens.: 1000000 molecule/cm3
 Rate constant: .0000000000003 cm3/(molecule * sec)
 Degradation: 50 % after 27 day
 Method:
 Year: GLP: no data
 Test substance: no data
 Remark: Method: not specified
 Source: Bayer AG Leverkusen
 EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
 10-MAY-1994 (238)

Type: air
 INDIRECT PHOTOLYSIS
 Sensitizer: OH
 Conc. of sens.: 500000 molecule/cm3
 Rate constant: .0000000000003 cm3/(molecule * sec)
 Degradation: 50 % after 53 day
 Method:
 Year: GLP: no data
 Test substance: no data
 Remark: Method: not specified
 Source: Bayer AG Leverkusen
 EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
 10-MAY-1994 (238)

Type: air
 INDIRECT PHOTOLYSIS
 Sensitizer: OH
 Conc. of sens.: 500000 molecule/cm3
 Method: other (calculated)
 Year: GLP: no
 Test substance: no data
 Remark: Rate of Constant: 4.2 +/- 0.2 E-13 cm3/(molecule .sec)
 Degradation: 50 % after 38 +/- 2 day at 292 degree K.
 Source: Bayer AG Leverkusen
 EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
 02-JUL-2003 (278) (279)

Type: air
 Light source: other: wavelength 254 nm
 Light spect.: 254 nm
 Conc. of subst.: at 23 degree C
 Quantum yield: .63
 Method:
 Year: GLP:
 Test substance:
 Remark: "direct photolysis is not a degradation pathway of any consequence in the environment since 1,2-DCB does not absorb enough in the wavelength range encountered in tropospheric sunlight."
 Source: NICNAS
 14-MAY-2003 (52)

Type: water
 INDIRECT PHOTOLYSIS
 Sensitizer: OH

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Method: other (measured): Photochemical degradation in presence of H2O2 on indication with light of wave length > 290 nm
 Year: GLP: no data
 Test substance: no data
 Remark: Concentration of sensitizer: e-16 to e17 mol/l
 Rate of constant: 3.0e9 l/molxsec
 Degradation: 50 % after 642 - 6418 hour of sunshine
 According to the author degradation proceeds via intermediates (chlorobenzene, chlorophenol) as far as mineralization to CO2 and HCl
 Source: Bayer AG Leverkusen
 EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
 10-MAY-1994 (163) (164)

Type: water
 INDIRECT PHOTOLYSIS
 Sensitizer: OH
 Method: other (measured): water was sampled at a depth of 8 cm beneath the surface of the river Goldbach 440 m above sea level under cloudless sky
 Year: GLP: no data
 Test substance: no data
 Remark: Conc. of sensitizer: 0.0000000000000001 mol/l
 Rate of Constant: no data
 Degradation: 50 % after 12.8 days (10 h sunshine/d)
 Source: Bayer AG Leverkusen
 EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
 01-JUL-2003 (224)

3.1.2 Stability in Water

Type: abiotic
 Method: other: Hydrolysis
 Year: GLP:
 Test substance:
 Result: o-dichlorobenzene is stable in aqueous solution (15 mg/l) for 2 months at 4 degree C.
 Hydrolysis of o-dichlorobenzene under conditions obtaining in the environment is improbable.
 Source: Bayer AG Leverkusen
 EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
 17-MAY-1994 (50) (150)

Type:
 Method:
 Year: GLP:
 Test substance:
 Remark: VOLATILE FROM WATER COLUMN-ESTIMATED HALF LIFE 4.4 HOURS
 FROM 1 METER RIVER FLOWING 1M/SEC WIND VELOCITY 3M/SEC.
 PERSISTANT HALF LIFE EST 0.3-3 DAYS-RIVERS
 3-30 LAKES
 30-300 GROUND WATERS
 Source: DALTRADE LTD LONDON
 EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
 07-SEP-2001 (97)

Type:
 Method:
 Year: GLP:
 Test substance:

Remark: With an approximate value of Henry's constant of 200 Pa/mol at
25 C, 1,2-DCB would be considered readily volatile from water.

Source: NICNAS
14-MAY-2003 (253)

3.1.3 Stability in Soil

Type: field trial Radiolabel:
Concentration:
Cation exch.
capac.
Microbial
biomass:
Method:
Year: GLP:
Test substance:
Remark: MODERATELY-TIGHTLY ABSORBED IN SOIL.CHEMICAL TRANSFORMATION
PROCESSES SUCH AS HYDROLYSIS,OXIDATION OR DIRECT PHOTOLYSIS
ON SOIL SURFACES ARE NOT EXPECTED TO OCCUR.

Source: DALTRADE LTD LONDON
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
16-MAY-2003 (97)

3.2 Monitoring Data (Environment)

Type of
measurement: background concentration
Medium: sediment
Method:
Concentration
Remark: O-dichlorobenzene levels from < 5 to 227 ug/kg were found in
Rhine sediments.
In USA, the concentrations of o-dichlorobenzene collected
from the vicinity of industrial discharges were found to be
7.1 mg/kg (express as organic carbon content) and 1.3 mg/kg
(dry weight), surficial sediments collected from great lakes
yielded concentrations up to 56 ug/kg.
Investigations of suspended particles of the Niagara river
revealed that the concentrations of o-dichlorobenzene in
larger particles were greater than in smaller ones (75ug/kg,
dry weight) for particles of 75 um and 110 ug/kg (dry
weight) for particles of > 500 um.
The lipid content of the suspended particles could be the
reason for the difference.
Measured concentrations of o-dichlorobenzene in benthic
sediments at the vicinity of a discharge of municipal waste
water were up to 750 ug/kg (dry weight) at a sediment depth
of 0-2 cm and up to 800 ug/kg at depth of 0-5 cm.
The concentration in the sediments decreased sharply with
increasing distance from discharge zones.

Source: Bayer AG Leverkusen
24-AUG-2001 (50)

Type of
measurement: background concentration
Medium: other: rainwater
Method:
Concentration

Remark: In Europe and USA concentrations in rainwater were found to range from 0.03 ng/l to 110 ng/l

Source: Bayer AG Leverkusen
24-AUG-2001 (50)

Type of measurement: background concentration
Medium: drinking water
Method:
Concentration

Remark: In the USA, in a monitoring survey in 113 cities, measured concentrations of o-dichlorobenzene was 0.01 ug/l (1977). Systematic studies in New Jersey revealed from 0.3 to 0.5 ug/l of o-dichlorobenzene in 6 out of 750 potable water samples submitted by 600 water works (June 1985). In December again 6 out of 750 samples contained from 0.3 to 25 ug/l of o-dichlorobenzene.

Source: Bayer AG Leverkusen
24-AUG-2001 (50)

Type of measurement: background concentration
Medium: ground water
Method:
Concentration

Remark: In the USA a nation wide study did not revealed any o-dichlorobenzene in the samples of ground water submitted by 466 water works (limit of detection 0.5 ug/l).

Source: Bayer AG Leverkusen
24-AUG-2001 (50)

Type of measurement: background concentration
Medium: drinking water
Method: capillary gas chromatography with and electron capture detector
Concentration < .001 - .007 µg/l
Remark: in the paper the reported units are ppt. They have been converted to ug/L

Source: NICNAS
03-SEP-2001 (196)

Type of measurement: background concentration
Medium: surface water
Method: capillary gas chromatography with and electron capture detector
Concentration < .001 - .007 µg/l
Remark: in the paper the reported units are ppt. They have been converted to ug/L

Source: NICNAS
03-JUL-2002 (196)

Type of measurement: background concentration
Medium: sediment
Method:
Concentration 27
Remark: Lake Ontario - in the vicinity of the Niagara River. Results in ng/g.

Source: NICNAS

03-SEP-2001 (195)

Type of

measurement: background concentration
 Medium: sediment
 Method:
 Concentration 19
 Remark: Lake Ontario - central basin of lake. Results in
 Source: NICNAS
 03-SEP-2001 (195)

Type of

measurement: background concentration
 Medium: sediment
 Method:
 Concentration 20
 Remark: Lake Ontario - eastern basin of lake. Results in ng/g.
 Source: NICNAS
 03-SEP-2001 (195)

Type of

measurement: background concentration
 Medium: sediment
 Method:
 Concentration 5.7
 Remark: Hamilton Harbour. Results in ng/g.
 Source: NICNAS
 03-SEP-2001 (195)

Type of

measurement: background concentration
 Medium: other: biota Atlantic croakers (*Micropogonias undulatus*)
 Method:
 Concentration .08
 Remark: Units in ug/g of lipid. Site is junction of Calcasieu River
 and Bayou d'Inde
 Source: NICNAS
 03-SEP-2001 (203)

Type of

measurement: background concentration
 Medium: other: biota blue crabs (*Callinectes sapidus*)
 Method:
 Concentration .26
 Remark: Units in ug/g of lipid. Site is junction of Calcasieu River
 and Bayou d'Inde
 Source: NICNAS
 03-SEP-2001 (203)

Type of

measurement: background concentration
 Medium: other: biota spotted trout (*Cynoscion nebulosus*)
 Method:
 Concentration .06
 Remark: Units in ug/g of lipid. Site is junction of Calcasieu River
 and Bayou d'Inde
 Source: NICNAS
 03-SEP-2001 (203)

Type of measurement: background concentration
 Medium: other: rain water
 Method:
 Concentration .00013 - .00062 µg/l
 Country: Portland, Oregon, USA.
 Remark: Data in paper given in ng/L
 Source: NICNAS
 03-SEP-2001 (156)

Type of measurement: background concentration
 Medium: other: atmospheric gas phase
 Method:
 Concentration .0033 - .01 µg/l
 Country: Portland, Oregon, USA.
 Remark: Data in paper given in ng/L
 Source: NICNAS
 03-SEP-2001 (156)

Type of measurement: background concentration
 Medium: other: receiving waters taking effluent from sewage treatment plants
 Method:
 Concentration < .5 - µg/l
 Remark: No DCB was detected in receiving waters for the effluent from 16 sewage treatment plants in the Sydney region, Australia. The detection limit of the equipment was 0.5 ppb (ug/L).
 Source: NICNAS
 02-JUL-2003 (249)

Type of measurement: concentration at contaminated site
 Medium: ground water
 Method:
 Concentration
 Remark: In a nation wide study in the USA, 2 out of 479 water works which had been contaminated in the past were found to contain o-dichlorobenzene concentrations of 2.2 ug/l and 2.7 ug/l (1984).
 In New Jersey, 3 % of both ground water from 685 wells and surface water from 463 sampling stations were found to be contaminated by o-dichlorobenzene with a maximum concentration of 6800 ug/l and 8.2 ug/l respectively (1981).
 In the USA in ground water contaminated by waste water o-dichlorobenzene concentrations of from 0.01 to 0.67 ug/l were measured in Massachusetts and of 77 ug/l and 85 ug/l in Michigan.
 Ground water in the immediate vicinity of a chemical factory in Ohio, was found to contain up to 4370 ug/l of o-dichlorobenzene (1982-1987).
 A remote well still contained 372 ug/l.
 In USA investigation of ground water contaminated by domestic and industrial landfill revealed o-dichlorobenzene concentrations ranging from 5 ug/l to 130 ug/l.
 In Canada ground water near an abandoned landfill contained a o-dichlorobenzene mean concentration of 0.038 ug/l.
 The maximum o-dichlorobenzene concentration in leachate from 44 hazardous landfills in the USA was 670 ug/l.
 Source: Bayer AG Leverkusen

24-AUG-2001 (50)

Type of measurement: concentration at contaminated site
 Medium: other: waster water effluent
 Method: capillary gas chromatography with and electron capture detector
 Concentration: .006 - .022 µg/l
 Remark: in the paper the reported units are ppt. They have been converted to ug/L
 Source: NICNAS

03-SEP-2001 (196)

Type of measurement: concentration at contaminated site
 Medium: surface water
 Method: capillary gas chromatography with and electron capture detector
 Concentration: .009 - µg/l
 Remark: in the paper the reported units are ppt. They have been converted to ug/L
 Source: NICNAS

03-SEP-2001 (196)

Type of measurement: concentration at contaminated site
 Medium: surface water
 Method: capillary gas chromatography with and electron capture detector
 Concentration: .056 - µg/l
 Remark: in the paper the reported units are ppt. They have been converted to ug/L
 Source: NICNAS

03-SEP-2001 (196)

Type of measurement: concentration at contaminated site
 Medium: surface water
 Method: capillary gas chromatography with and electron capture detector
 Concentration: 12 - µg/l
 Remark: in the paper the reported units are ppt. They have been converted to ug/L
 Source: NICNAS

03-SEP-2001 (196)

Type of measurement: concentration at contaminated site
 Medium: sediment
 Method: used a Finnigan TSQ-46B computerised capillary gc/ms/ms.
 Concentration: 7.1
 Remark: Units are ug/g of organic carbon
 Source: NICNAS

03-SEP-2001 (203)

Type of measurement: concentration at contaminated site
 Medium: surface water
 Method: used a Finnigan TSQ-46B computerised capillary gc/ms/ms.
 Concentration: .009 - µg/l
 Source: NICNAS

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(203)

Type of measurement: concentration at contaminated site
 Medium: other: biota blue catfish (*Ichталurus furcatus*)
 Method:
 Concentration .11
 Remark: units ug/g of lipid. Site is Bayou d'Inde industrial outfall
 Source: NICNAS

03-SEP-2001

(203)

Type of measurement: concentration at contaminated site
 Medium: other: biota blue catfish (*Ichталurus furcatus*)
 Method:
 Concentration .06
 Remark: Units in ug/g of lipid. Site is junction of Calcasieu River and Bayou d'Inde
 Source: NICNAS

03-SEP-2001

(203)

Type of measurement: other: Grand River
 Medium: surface water
 Method: capillary gas chromatography with an electron capture detector
 Concentration < .001 - .031 µg/l
 Remark: in the paper the reported units are ppt. They have been converted to ug/L
 Source: NICNAS

03-JUL-2002

(196)

Type of measurement: other: Lake Erie
 Medium: sediment
 Method: capillary gas chromatography with an electron capture detector
 Concentration 1 - 4
 Remark: Units are ng/g (ppb)
 Source: NICNAS

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(196)

Type of measurement: other: Lake Erie
 Medium: other: biota rainbow trout age 6+ years
 Method: capillary gas chromatography with and electron capture detector
 Concentration 1
 Remark: Units are ng/g (ppb)
 Source: NICNAS

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(196)

Type of measurement: other: Lake Huron
 Medium: sediment
 Method: capillary gas chromatography with and electron capture detector

Concentration < 5 - 56
 Remark: Units are ng/g (ppb)
 Source: NICNAS

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(196)

Type of

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measurement:	other: Lake Huron	
Medium:	other: biota lake trout age 6+ years	
Method:	capillary gas chromatography with and electron capture detector	
Concentration	1	
Remark:	Units are ng/g (ppb)	
Source:	NICNAS	
03-SEP-2001		(196)
Type of		
measurement:	other: Lake Huron water	
Medium:	surface water	
Method:	capillary gas chromatography with and electron capture detector	
Concentration	< .001 - µg/l	
Remark:	in the paper the reported units are ppt. They have been converted to ug/L	
Source:	NICNAS	
03-SEP-2001		(196)
Type of		
measurement:	other: Lake Ontario	
Medium:	sediment	
Method:	capillary gas chromatography with and electron capture detector	
Concentration	4 - 27	
Remark:	Units are ng/g (ppb)	
Source:	NICNAS	
03-SEP-2001		(196)
Type of		
measurement:	other: Lake Ontario	
Medium:	other: biota lake trout age 6+years	
Method:	capillary gas chromatography with and electron capture detector	
Concentration	1	
Remark:	Units are ng/g (ppb)	
Source:	NICNAS	
03-SEP-2001		(196)
Type of		
measurement:	other: Lake Ontario	
Medium:	other: biota lake trout age 4+years	
Method:	capillary gas chromatography with and electron capture detector	
Concentration	1	
Remark:	Units are ng/g (ppb)	
Source:	NICNAS	
03-SEP-2001		(196)
Type of		
measurement:	other: Lake Ontario	
Medium:	other: sediment core 0-1 cm	
Method:	capillary gas chromatography with and electron capture detector	
Concentration	14	
Remark:	units are ng/g (ppb)	
Source:	NICNAS	
03-SEP-2001		(196)

Type of measurement:	other: Lake Ontario	
Medium:	other: sediment core 1-2 cm	
Method:	capillary gas chromatography with and electron capture detector	
Concentration	16	
Remark:	Units are ng/g (ppb)	
Source:	NICNAS	
03-SEP-2001		(196)
Type of measurement:	other: Lake Ontario	
Medium:	other: sediment core 2-3 cm	
Method:	capillary gas chromatography with and electron capture detector	
Concentration	19	
Remark:	Units are ng/g (ppb)	
Source:	NICNAS	
03-SEP-2001		(196)
Type of measurement:	other: Lake Ontario	
Medium:	other: sediment core 3-4 cm	
Method:	capillary gas chromatography with and electron capture detector	
Concentration	16	
Remark:	Units are ng/g (ppb)	
Source:	NICNAS	
03-SEP-2001		(196)
Type of measurement:	other: Lake Ontario	
Medium:	other: sediment core 4-5 cm	
Method:	capillary gas chromatography with and electron capture detector	
Concentration	26	
Remark:	Units are ng/g (ppb)	
Source:	NICNAS	
03-SEP-2001		(196)
Type of measurement:	other: Lake Ontario	
Medium:	other: sediment core 5-6 cm	
Method:	capillary gas chromatography with and electron capture detector	
Concentration	13	
Remark:	Units are ng/g (ppb)	
Source:	NICNAS	
03-SEP-2001		(196)
Type of measurement:	other: Lake Ontario	
Medium:	other: sediment core 6-7 cm	
Method:	capillary gas chromatography with and electron capture detector	
Concentration	2	
Remark:	Units are ng/g (ppb)	
Source:	NICNAS	
03-SEP-2001		(196)

Type of measurement: other: Lake Ontario
 Medium: other: sediment core 7-8 cm
 Method: capillary gas chromatography with and electron capture detector
 Concentration: < 5
 Remark: Units are ng/g (ppb)
 Source: NICNAS
 03-SEP-2001 (196)

Type of measurement: other: Lake Ontario water
 Medium: surface water
 Method: capillary gas chromatography with and electron capture detector
 Concentration: .002 - .007 µg/l
 Remark: in the paper the reported units are ppt. They have been converted to ug/L
 Source: NICNAS
 03-SEP-2001 (196)

Type of measurement: other: Lake Superior
 Medium: sediment
 Method: - capillary gas chromatography with and electron capture detector
 Concentration: < 5 - 1
 Remark: Units are ng/g (ppb)
 Source: NICNAS
 03-SEP-2001 (196)

Type of measurement: other: Lake Superior
 Medium: other: biota lake trout age 6+years
 Method: capillary gas chromatography with and electron capture detector
 Concentration: .3
 Remark: Units are ng/g (ppb)
 Source: NICNAS
 03-SEP-2001 (196)

Type of measurement: other: heavily industrialised, municipal and rural
 Medium: air
 Method:
 Concentration: ca. 1.3 - 61
 Remark: This range is the range of the maximum values taken across all sites and are in ug/cubic metre. The overall mean was 3 ug/cubic metre (mean range was 1.2-11.6 ug/cubic metre).
 Source: NICNAS
 01-JUL-2003 (39)

3.3.1 Transport between Environmental Compartments

Type: adsorption
 Media: other

Air (Level I):
 Water (Level I):
 Soil (Level I):
 Biota (L.II/III):

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Soil (L.II/III):
Method: other: adsorption to soil
Year:
Result: Experimental determination of soil/water coefficients in various soils and coefficients of soil sorption coefficient (KOC = carbon organic content) showed value ranging from 0.02 to 250 and 286 to 4654 respectively
Source: Bayer AG Leverkusen
01-JUL-2003 (50)

Type: adsorption
Media: other
Air (Level I):
Water (Level I):
Soil (Level I):
Biota (L.II/III):
Soil (L.II/III):
Method: other: adsorption to soil
Year:
Result: The soil sorption coefficient KOC expressed in terms of the content of organic carbon was 383 for a surface soil after 24 h exposure at 22.5 +/- 1 degree C with an unadjusted pH of 6.3.
The soil sorption coefficient was significantly reduced under basic conditions.
Source: Bayer AG Leverkusen
24-AUG-2001 (50) (242)

Type: adsorption
Media: other
Air (Level I):
Water (Level I):
Soil (Level I):
Biota (L.II/III):
Soil (L.II/III):
Method: other: adsorption to soil
Year:
Result: The elimination rate for o-dichlorobenzene was found during bank filtration in the lower Rhine to be 75 - 80 %.
Source: Bayer AG Leverkusen
24-AUG-2001 (40) (50)

Type: adsorption
Media: other
Air (Level I):
Water (Level I):
Soil (Level I):
Biota (L.II/III):
Soil (L.II/III):
Method: other: adsorption to soil
Year:
Result: Elimination through soil is severely impaired by the high desorption power of o-dichlorobenzene
Source: Bayer AG Leverkusen
03-SEP-2001 (50) (114)

Type: adsorption
Media: other: soil
Air (Level I):
Water (Level I):
Soil (Level I):

Biota (L.II/III):
 Soil (L.II/III):
 Method: other: calculation
 Year:
 Result: Koc = 977. calculated using the equation $\log Koc = 1.377 + 0.544$
 Source: NICNAS
 03-SEP-2001 (54)

Type: adsorption
 Media: other: soil - water
 Air (Level I):
 Water (Level I):
 Soil (Level I):
 Biota (L.II/III):
 Soil (L.II/III):
 Method: other: adsorption to soil
 Year:
 Result: o-dichlorobenzene was desorbed from contaminated soil columns by elution with distilled water
 Source: Bayer AG Leverkusen
 24-AUG-2001 (37) (50)

Type: adsorption
 Media: other: soil - water
 Air (Level I):
 Water (Level I):
 Soil (Level I):
 Biota (L.II/III):
 Soil (L.II/III):
 Method: other
 Year:
 Result: constant resuspensions of soil sediment from lake Ontario could result in more than 98 % desorption over the course a year.
 The calculated release of 2 kg per year is however very low compared with the 2.6 t/a of o-dichlorobenzene via the Niagara.
 Source: Bayer AG Leverkusen
 24-AUG-2001 (50) (199)

Type: adsorption
 Media: water - soil
 Air (Level I):
 Water (Level I):
 Soil (Level I):
 Biota (L.II/III):
 Soil (L.II/III):
 Method: other: adsorption to soil
 Year:
 Result: Elimination efficiencies from 15 % to 53 % during infiltration and soil percolation of o-dichlorobenzene containing waste water from a waste water treatment plant
 Source: Bayer AG Leverkusen
 24-AUG-2001 (38) (50)

Type: adsorption
 Media: water - soil
 Air (Level I):
 Water (Level I):
 Soil (Level I):

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Biota (L.II/III):
 Soil (L.II/III):
 Method: other: adsorption to soil
 Year:
 Result: No detection of o-dichlorobenzene in the water pumped out of aquifer after the passage through the soil
 Source: Bayer AG Leverkusen
 24-AUG-2001 (50) (258)

Type: adsorption
 Media: water - soil
 Air (Level I):
 Water (Level I):
 Soil (Level I):
 Biota (L.II/III):
 Soil (L.II/III):
 Method: other: adsorption to soil
 Year:
 Result: Four month after sludge containing o-dichlorobenzene had been incorporated into the upper layer of the soil (0-15 cm) which was subsequently irrigated, it was detected in the lower layer (15-48 cm).
 Source: Bayer AG Leverkusen
 24-AUG-2001 (50) (86)

Type: adsorption
 Media: water - soil
 Air (Level I):
 Water (Level I):
 Soil (Level I):
 Biota (L.II/III):
 Soil (L.II/III):
 Method:
 Year:
 Remark: Woodburn silt loam soil used: 1.9% OM, 68% silt, 21% clay and 9% sand.
 Result: log Kom = 2.27 (Kom is Soil-organic matter-water distribution coefficient).
 Source: NICNAS
 03-SEP-2001 (66)

Type: volatility
 Media: other: surface water and soil to air
 Air (Level I):
 Water (Level I):
 Soil (Level I):
 Biota (L.II/III):
 Soil (L.II/III):
 Method:
 Year:
 Remark: Dominant removal mechanism from surface water and soil is expected to be volatilisation
 09-JUL-2003 (240)

Type: volatility
 Media: other: water - air and water - soil
 Air (Level I):
 Water (Level I):
 Soil (Level I):
 Biota (L.II/III):
 Soil (L.II/III):

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Method: other: Henry's constant
 Year:
 Result: calculated:
 H = 193 Pa m³/mol at 25 degree C
 H = 190 - 198 Pa m³/mol at 25 degree C
 H = 172 Pa m³/mol at 20 degree C
 H = 121.6 Pa m³/mol at 20 degree C
 H = 219 Pa m³/mol at 20 degree C
 Source: Bayer AG Leverkusen
 24-AUG-2001 (50)

Type: volatility
 Media: water - air
 Air (Level I):
 Water (Level I):
 Soil (Level I):
 Biota (L.II/III):
 Soil (L.II/III):
 Method: other: Henry's constant
 Year:
 Result: experimental values:
 H = 165 Pa m³/mol at 10 degree C
 H = 145 Pa m³/mol at 15 degree C
 H = 170 Pa m³/mol at 20 degree C
 H = 159 Pa m³/mol at 25 degree C
 H = 240 Pa m³/mol at 30 degree C
 Source: Bayer AG Leverkusen
 24-AUG-2001 (14)

Type: volatility
 Media: water - air
 Air (Level I):
 Water (Level I):
 Soil (Level I):
 Biota (L.II/III):
 Soil (L.II/III):
 Method: other: Henry's constant
 Year:
 Result: 290 +/- 30 Pa m³/mol at 37 degree C
 based on an experimental water/air coefficient = 9.0 +/- 1
 Source: Bayer AG Leverkusen
 10-SEP-2001 (228)

Type: volatility
 Media: water - air
 Air (Level I):
 Water (Level I):
 Soil (Level I):
 Biota (L.II/III):
 Soil (L.II/III):
 Method: other
 Year:
 Result: 40 % decrease in concentration of o-dichlorobenzene in waste
 water due to evaporation to the atmosphere
 Source: Bayer AG Leverkusen
 Test condition: Secondary treated waste water contaminated with the
 substance flowed through basis in which the residence time
 was 8 hours
 24-AUG-2001 (38)

Type: volatility

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Media: water - air
 Air (Level I):
 Water (Level I):
 Soil (Level I):
 Biota (L.II/III):
 Soil (L.II/III):
 Method: other
 Year:
 Result: 50 % evaporation from ponds into the atmosphere within
 14.6 h
 Source: Bayer AG Leverkusen
 Test condition: Model experiment to investigate the distribution of
 o-dichlorobenzene in waste stabilisation ponds during waste
 water treatment.

24-AUG-2001 (78) (79)

Type: volatility
 Media: water - air
 Air (Level I):
 Water (Level I):
 Soil (Level I):
 Biota (L.II/III):
 Soil (L.II/III):
 Method: other
 Year:
 Result: Half lives for evaporation of o-dichlorobenzene from
 solution were found to be 1.17 and 2.5 minutes for depth of
 0.75 and 1.6 cm respectively
 Source: Bayer AG Leverkusen

24-AUG-2001 (104)

Type: volatility
 Media: water - air
 Air (Level I):
 Water (Level I):
 Soil (Level I):
 Biota (L.II/III):
 Soil (L.II/III):
 Method: other
 Year:
 Result: 19.82 and 85 % evaporation from aqueous solution after 2, 4
 and 8 d at room temperature without aeration
 Source: Bayer AG Leverkusen

20-MAY-2003 (60)

Type: volatility
 Media: water - air
 Air (Level I):
 Water (Level I):
 Soil (Level I):
 Biota (L.II/III):
 Soil (L.II/III):
 Method: other
 Year:
 Result: In a closed system under addition of 2 % methanol to aqueous
 phase, 25 % of o-chlorobenzene had evaporated within 25 min.
 and 90 % within 3.5 h without aeration
 Source: Bayer AG Leverkusen

24-AUG-2001 (120)

Type: volatility

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Media: water - air
 Air (Level I):
 Water (Level I):
 Soil (Level I):
 Biota (L.II/III):
 Soil (L.II/III):
 Method: other
 Year:
 Result: 50 % of the initial concentration within 4 h and a 90 % reduction within 24 h has a solution of Rhine water slowly stirred and containing 0,05 ug/l of o-dichlorobenzene
 Source: Bayer AG Leverkusen
 24-AUG-2001 (205)

Type: volatility
 Media: water - air
 Air (Level I):
 Water (Level I):
 Soil (Level I):
 Biota (L.II/III):
 Soil (L.II/III):
 Method:
 Year:
 Remark: This paper discusses the volatilisation rates of high-volatility compounds, and the transport of such chemicals from water bodies to air as important pathways.
 Source: NICNAS
 07-SEP-2001 (50) (241)

Type: volatility
 Media:
 Air (Level I):
 Water (Level I):
 Soil (Level I):
 Biota (L.II/III):
 Soil (L.II/III):
 Method: other: calculated
 Year:
 Result: Henry's constant, $H = 0.0013 \text{ atm m}^3/\text{moles}$
 Source: NICNAS
 03-SEP-2001 (54)

Type: other: sorption and distribution coefficient (Kd)
 Media: other: solute-sorbent system (aquifer soil-artificial groundwater)
 Air (Level I):
 Water (Level I):
 Soil (Level I):
 Biota (L.II/III):
 Soil (L.II/III):
 Method:
 Year:
 Remark: Real Borden aquifer material, synthetic groundwater and carbon 14 labelled 1,2-DCB were used. Sorption was analysed at times ranging from 2-144 hours. The initial aqueous concentration was approximately 30 ug/L. Initial sorption was rapid, with approximately 50% of the total sorption occurring in the first 2 hours and then a gradually declining sorption rate over a period of days.
 Result: Isotherm data:
 Linear Kd (95% CI), with intercept = 0.76 ± 0.03

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Linear Kd (95% CI), with suppressed intercept = 0.81 +/- 0.03
 Freundlich distribution coefficient, Kf = 1.16 +/- 0.0.

Source: NICNAS
 16-MAY-2003 (73)

Type: other: sorption/desorption
 Media: soil - air
 Air (Level I):
 Water (Level I):
 Soil (Level I):
 Biota (L.II/III):
 Soil (L.II/III):
 Method:
 Year:
 Result: desorption rate slower than sorption rate for contact times
 of 7,14,49,and 99 days. Rates of sorption and desorption for
 2 days contact not statistically different.

Source: NICNAS
 16-MAY-2003 (83)

3.3.2 Distribution

Media: other: transport in an unconfined sand aquifer
 Method: other (measurement): field
 Year:
 Result: Initial one-point partition coefficient results indicated that
 the sorption distributionof coefficients for four halogenated
 organic solutes (including 1,2-DCB) varied proportionally
 among core strata. On this basis one solute
 (tetrachloroethylene) was used to further investigate the
 distribution sorption coefficients. The observation could not
 be explained by organic carbon content or specific surface
 area. It is possible that unidentified minerals phases may
 account for the observations.

Source: NICNAS
 19-MAY-2003 (161)

3.4 Mode of Degradation in Actual Use

3.5 Biodegradation

Type: aerobic
 Inoculum: predominantly domestic sewage, adapted
 Concentration: 4 mg/l related to Test substance
 Degradation: 58 % after 20 day
 Method: OECD Guide-line 301 D "Ready Biodegradability: Closed Bottle
 Test"
 Year: 1977 GLP: no
 Test substance:
 Source: Bayer AG Leverkusen
 24-AUG-2001 (50)

Type: aerobic
 Inoculum: other: wastewater from a municipal wastewater treatment plant
 Concentration: 4 mg/l related to Test substance
 Contact time: 28 day
 Degradation: 93 % after 28 day
 Testsubstance: 5 day 18 %

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	14 day	35 %	
	21 day	77 %	
	28 day	93 %	
Method:	OECD Guide-line 301 D "Ready Biodegradability: Closed Bottle Test"		
Year:		GLP:	
Test substance:			
Source:	NICNAS		
01-JUL-2003			(127)
Type:	aerobic		
Inoculum:	activated sludge		
Concentration:	100 mg/l		
Degradation:	0 % after 28 day		
Result:	under test conditions no biodegradation observed		
Method:	other: see remarks		
Year:		GLP:	
Test substance:			
Remark:	"Biodegradation test of chemical substance by microorganisms etc." stipulated in the Order Prescribing the Items of the Test Relating to the New Chemical Substance (1974, Order of the Prime Minister, Minister of Health and Welfare, the MITI No. 1). This guideline corresponds to "301C, Ready Biodegradability: Modified MITI Test I" stipulated in the OECD Guidelines for Testing of Chemicals (May 12, 1981). Sludge conc. : 30 mg/l		
Source:	Bayer AG	Leverkusen	
24-AUG-2001			(31)
Type:	aerobic		
Inoculum:	activated sludge, adapted		
Concentration:	83 mg/l related to Test substance		
Contact time:	8 hour(s)		
Degradation:	99.9 %		
Method:			
Year:		GLP:	
Test substance:			
Remark:	The wastewater treatment pilot plant was operated for 60 days and had a residence time of 8 hours. 24% of the elimination was due to stripping during aeration and 75% was due to biodegradation.		
Source:	NICNAS		
09-JUL-2003			(248)
Type:	aerobic		
Inoculum:	Pseudomonas sp. (Bacteria)		
Concentration:	200 mg/l related to Test substance		
Contact time:	72 hour(s)		
Degradation:	100 %		
Method:			
Year:		GLP:	
Test substance:			
Remark:	Degradation was via ring cleavage.		
Source:	NICNAS		
14-MAY-2003			(293)
Type:	aerobic		
Inoculum:	Pseudomonas sp. (Bacteria)		
Concentration:	200 mg/l		
Contact time:	26 hour(s)		
Degradation:	100 %		

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Inoculum:	anaerobic microorganisms	
Concentration:	83 mg/l	
Degradation:	99.9 %	
Method:		
Year:		GLP:
Test substance:		
Remark:	means of removal 22% due to stripping and 78% due to biodegradation.	
Source:	NICNAS	
03-SEP-2001		(141)
Type:		
Inoculum:	other bacteria: wastewater purification simulating pilot plant	
Concentration:	38.6 µg/l	
	405 µg/l	
Degradation:	97 - 99 %	
Method:		
Year:		GLP:
Test substance:		
Remark:	Influent concentration range was 38.6 and 495 ug/L. The result is based on the limit of detection of DCB in the effluent. The type of inoculum used in the plant and the retention time were not specified.	
Source:	NICNAS	
14-MAY-2003		(109)
Type:		
Inoculum:	other bacteria:simulated biological wasterwater treatment plant	
Concentration:	50 µg/l	
	150 µg/l	
Contact time:	5.5 hour(s)	
Degradation:	35 %	
Method:		
Year:		GLP:
Test substance:		
Remark:	Hydraulic retention time was 5.5 hours and activiated sludge retentio time was 6 days. Mass balance indicated the following distribution of DCB - 6% in effluent, 59% removed via stripping (due to volatility), 35% removed via biodegradatona d 0% adsorbed to biomass.	
Source:	NICNAS	
14-MAY-2003		(289)
Type:		
Inoculum:	other bacteria:simulated biological wasterwater treatment plant	
Concentration:	50 µg/l	
	150 µg/l	
Method:		
Year:		GLP:
Test substance:		
Remark:	Hydraulic retention time was 5.5 hours and activiated sludge retentio time was 6 days. Mass balance indicated the following distribution of DCB - 6% in effluent, 59% removed via stripping, 35% removed via biodegradatona d 0% adsorbed to biomass.	
Result:	A decrease in the elimination of DCB occurred when pulverised activated carbon was added to the activated sludge. When 25 mg/L of activated carbon was added there was 61% elimination,	

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with 50 mg/L there was 71%, with 100 mg/L there was 93%, and with 200 mg/L there was 94% elimination. Elimination includes biodegradation and adsorption. Without activated carbon there was no adsorption on biomass and there was 35% biodegradation.

Source: NICNAS
14-MAY-2003 (289)

Type:
Inoculum: other: Standard spiked soil
Concentration: 26.8 related to Test substance
Contact time: 259 day
Degradation: ca. 90 %
Method:
Year: GLP:
Test substance:
Remark: Units ug/kg. Loss process was a two-step first order process, with volatilisation the main means of loss.
Result: Concentration dropped to 2.82 after 259 days. Major loss occurred in first 32 days. Half-life in step one was 8.63 and in step two 191.

Source: NICNAS
03-JUL-2002 (285)

Type:
Inoculum: other: soil amended with sewage sludge
Concentration: 126 related to Test substance
Contact time: 259 day
Degradation: ca. 85 %
Method:
Year: GLP:
Test substance:
Remark: Units ug/kg. Loss process was a two-step first order process, with volatilisation the main means of loss.
Result: Concentration dropped to 19.9 after 259 days. Major loss occurred in first 32 days. Half-life in step one was 13.2 and in step two 892.

Source: NICNAS
03-SEP-2001 (285)

3.6 BOD5, COD or BOD5/COD Ratio

B O D 5

Method: other: complete mix continuous flow activated sludge systems
Concentration: 162 mg/l related to
BOD5: 2.6 mgO2/l

C O D

Method: other: complete mix continuous flow activated sludge systems
COD: 49 mg/g substance

Remark: retention time in system 6 days; influent BOD5=162; NOTE COD units are mg/l, influent COD=416; TOC in influent = 151 and in effluent = 17 mg/l.

Source: NICNAS
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B O D 5

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Method: other: complete mix continuous flow activated sludge systems
 Concentration: 159 mg/l related to
 BOD5: 3.2 mgO2/l

C O D

Method: other: complete mix continuous flow activated sludge systems
 COD: 40 mg/g substance

Remark: retention time in system 4 days; influent BOD5=159; NOTE COD units are mg/l, influent COD=428; TOC in influent = 154 and in effluent = 20 mg/l.

Source: NICNAS
 03-SEP-2001 (141)

B O D 5

Method: other: complete mix continuous flow activated sludge systems
 Concentration: 162 mg/l related to
 BOD5: 3.3 mgO2/l

C O D

Method: other: influent COD=416; complete mix continuous flow activated sludge systems
 COD: 35 mg/g substance

Remark: retention time in system 2 days; influent BOD5=162; influent COD=416.

Source: NICNAS
 03-SEP-2001 (141)

3.7 Bioaccumulation

Species: Cynoscion nebulosus (Fish, marine)

Exposure period:

Concentration: .009 µg/l

BCF: 6166

Elimination:

Method:

Year: GLP:

Test substance:

Country: Louisiana, USA

Remark: Results are given in paper as log BCF. Values presented here are BCF

Source: NICNAS

30-JUL-2002 (203)

Species: Cyprinus carpio (Fish, fresh water)

Exposure period: 56 day

Concentration: .01 mg/l

BCF: 90 - 260

Elimination:

Method: other: see remarks

Year: GLP:

Test substance:

Remark: Method:
 "Bioaccumulation test of chemical substance in fish and shellfish" stipulated in the Order Prescribing the Items of the Test Relating to the New Chemical Substance (1974, Order

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	of the Prime Minister, the Minister of Health and Welfare, the MITI No. 1). This guideline corresponds to "305C, Bioaccumulation: Degree of Bioconcentration in Fish" stipulated in the OECD Guidelines for Testing of Chemicals (May 12, 1981).	
Source:	Bayer AG Leverkusen	
24-AUG-2001		(31)
Species:	Cyprinus carpio (Fish, fresh water)	
Exposure period:	56 day	
Concentration:	.1 mg/l	
BCF:	150 - 230	
Elimination:		
Method:	other: see remarks	
Year:		GLP:
Test substance:		
Method:	"Bioaccumulation test of chemical substance in fish and shellfish" stipulated in the Order Prescribing the Items of the Test Relating to the New Chemical Substance (1974, Order of the Prime Minister, the Minister of Health and Welfare, the MITI No. 1). This guideline corresponds to "305C, Bioaccumulation: Degree of Bioconcentration in Fish" stipulated in the OECD Guidelines for Testing of Chemicals (May 12, 1981).	
Source:	Bayer AG Leverkusen	
24-AUG-2001		(31)
Species:	Ictalurus furcatus (Fish, fresh water)	
Exposure period:		
Concentration:	.009 µg/l	
BCF:	6607	
Elimination:		
Method:		
Year:		GLP:
Test substance:		
Country:	Louisiana, USA	
Remark:	Results are given in paper as log BCF. Values presented here are BCF	
Source:	NICNAS	
30-JUL-2002		(203)
Species:	Lepomis macrochirus (Fish, fresh water)	
Exposure period:	14 day at 16 degree C	
Concentration:	7.89 µg/l	
BCF:	89	
Elimination:		
Method:	other: closed system, intermittentflow-through	
Year:		GLP:
Test substance:	other TS: C14 labelled DCB	
Remark:	Half-life for elimination from tissue was less than 1 day	
Source:	NICNAS	
01-JUL-2003		(22) (276)
Species:	Micropogon undulatus (Fish, estuary, marine)	
Exposure period:		
Concentration:	.009 µg/l	
BCF:	8710	
Elimination:		
Method:		
Year:		GLP:

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Test substance:
Country: Louisiana, USA
Remark: Results are given in paper as log BCF. Values presented here are BCF
Source: NICNAS
30-JUL-2002 (203)

Species: Salmo gairdneri (Fish, estuary, fresh water)
Exposure period: 105 day at 15 degree C
Concentration: .94 µg/l
BCF: 560
Elimination:
Method:
Year: GLP:
Test substance:
Remark: This results is for whole fish.
Good correlation was found between the BCF and the octanol-water partition coefficient.
Standard deviation +/- 130.
Source: NICNAS
30-JUL-2002 (197)

Species: Salmo gairdneri (Fish, estuary, fresh water)
Exposure period: 119 day at 15 degree C
Concentration: .047 µg/l
BCF: 270
Elimination:
Method:
Year: GLP:
Test substance:
Remark: This result is for whole fish.
Good correlation was found between the BCF and the octanol-water partition coefficient.
Standard deviation +/- 21.
Source: NICNAS
30-JUL-2002 (197)

Species: other: Chironomus decorus (midge), larval stages
Exposure period: 48 hour(s)
Concentration:
BCF: .22
Elimination:
Method: other: flowthrough exposure system
Year: GLP:
Test substance:
Remark: BCF for midge larvae in high-organic-content sediment. 200 ml of 1 µg/L in 10 g of sediment = concentration in sediment, 0.02 µg/g.
Standard deviation - 0.04
Source: NICNAS
03-JUL-2002 (145)

Species: other: Chironomus decorus (midge), larval stages
Exposure period: 48 hour(s)
Concentration:
BCF: .23
Elimination:
Method: other: flowthrough exposure system
Year: GLP:
Test substance:
Remark: BCF for midge larvae in high-organic-content sediment, under

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	non-equilibrium exposure conditions. 200 ml of 1 ug/L in 10 g of sediment = concentration in sediment, 0.02 ug/g. Standard deviation - 0.07	
Source:	NICNAS	
03-JUL-2002		(145)
Species:	other: Chrinomus decorus (midge), larval stages	
Exposure period:	48 hour(s)	
Concentration:		
BCF:	1.08	
Elimination:		
Method:	other: flowthrough exposure system	
Year:	GLP:	
Test substance:		
Remark:	BCF for midge larvae in low-organic-content sediment, under non-equilibrium exposure conditions. 200 ml of 1 ug/L in 10 g of sediment = concentration in sediment, 0.02 ug/g. Standard deviation - 0.53	
Source:	NICNAS	
03-JUL-2002		(145)
Species:	other: Chrinomus decorus (midge), larval stages	
Exposure period:	48 hour(s)	
Concentration:		
BCF:	29	
Elimination:		
Method:	other: flowthrough exposure system	
Year:	GLP:	
Test substance:		
Remark:	BCF for midge larvae in interstitial water in high-organic-content sediment, under equilibrium exposure conditions. 200 ml of 1 ug/L in 10 g of sediment = concentration in sediment, 0.02 ug/g. Standard deviation - 5	
Source:	NICNAS	
03-JUL-2002		(145)
Species:	other: Chrinomus decorus (midge), larval stages	
Exposure period:	48 hour(s)	
Concentration:		
BCF:	29	
Elimination:		
Method:	other: flowthrough exposure system	
Year:	GLP:	
Test substance:		
Remark:	BCF for midge larvae in interstitial water in high-organic-content sediment, under non-equilibrium exposure conditions. 200 ml of 1 ug/L in 10 g of sediment = concentration in sediment, 0.02 ug/g. Standard deviation - 5	
Source:	NICNAS	
03-JUL-2002		(145)
Species:	other: Chrinomus decorus (midge), larval stages	
Exposure period:	48 hour(s)	
Concentration:		
BCF:	31	
Elimination:		
Method:	other: flowthrough exposure system	
Year:	GLP:	
Test substance:		
Remark:	BCF for midge larvae in overlying water above	

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	high-organic-content sediment, under equilibrium exposure conditions. 200 ml of 1 ug/L in 10 g of sediment = concentration in sediment, 0.02 ug/g. Standard deviation - 5	
Source:	NICNAS	
03-JUL-2002		(145)
Species:	other: Chrinomus decorus (midge), larval stages	
Exposure period:	48 hour(s)	
Concentration:		
BCF:	31	
Elimination:		
Method:	other: flowthrough exposure system	
Year:	GLP:	
Test substance:		
Remark:	BCF for midge larvae in interstitial water in low-organic-content sediment, under non-equilibrium exposure conditions. 200 ml of 1 ug/L in 10 g of sediment = concentration in sediment, 0.02 ug/g. Standard deviation - 18	
Source:	NICNAS	
03-JUL-2002		(145)
Species:	other: Chrinomus decorus (midge), larval stages	
Exposure period:	48 hour(s)	
Concentration:		
BCF:	49	
Elimination:		
Method:	other: flowthrough exposure system	
Year:	GLP:	
Test substance:		
Remark:	BCF for midge larvae in overlying water above high-organic-content sediment, under non-equilibrium exposure conditions. 200 ml of 1 ug/L in 10 g of sediment = concentration in sediment, 0.02 ug/g. Standard deviation - 10	
Source:	NICNAS	
03-JUL-2002		(145)
Species:	other: Chrinomus decorus (midge), larval stages	
Exposure period:	48 hour(s)	
Concentration:		
BCF:	1071	
Elimination:		
Method:		
Year:	GLP:	
Test substance:		
Remark:	BCF for midge larvae in overlying water above low-organic-content sediment, under non-equilibrium exposure conditions. 200 ml of 1 ug/L in 10 g of sediment = concentration in sediment, 0.02 ug/g. Standard deviation - 881	
Source:	NICNAS	
03-JUL-2002		(145)
Species:	other: Selenastrum capricornutum	
Exposure period:	24 hour(s)	
Concentration:	2 mg/l	
BCF:	10080	
Elimination:		
Method:	other: direct measurement of the compound in the algal	

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	concentrates and medium supernatants by gas-liquid chromatography	
Year:		GLP:
Test substance:		
Remark:	Compounds dosed simultaneously.	
Source:	NICNAS	
03-JUL-2002		(62)
Species:	other: Selenastrum capricornutum	
Exposure period:	24 hour(s)	
Concentration:		
BCF:	14900	
Elimination:		
Method:	other: direct measurement of the compound in the algal concentrates and medium supernatants by gas-liquid chromatography	
Year:		GLP:
Test substance:		
Remark:	This result is an average of the results presented in record 17 and 19.	
Source:	NICNAS	
03-JUL-2002		(62)
Species:	other: Selenastrum capricornutum	
Exposure period:	24 hour(s)	
Concentration:	10 mg/l	
BCF:	19700	
Elimination:		
Method:	other: direct measurement of the compound in the algal concentrates and medium supernatants by gas-liquid chromatography	
Year:		GLP:
Test substance:		
Remark:	compounds dosed singly	
Source:	NICNAS	
03-SEP-2001		(62)
Species:	other: oligochaete worms (mainly Tubifex tubifex and Limnodrilus hoffmeisteri)	
Exposure period:	79 day at 8 degree C	
Concentration:	.23 µg/l	
BCF:		
Elimination:		
Method:	other: Spiked Lake Ontario sediments	
Year:		GLP:
Test substance:		
Result:	Worms' uptake phase, 79 d CF=40. where CF= concentration on worm dry weight/concentration in sediment. Worms' depuration phase, 84 d not detected. Half-life in worms less than 5 days. Water concentration 0.0024 µg/l.	
Source:	NICNAS	
03-SEP-2001		(198)
Species:	other: Callinectes sapidus	
Exposure period:		
Concentration:	.009 µg/l	
BCF:	28840	
Elimination:		
Method:		
Year:		GLP:

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Test substance:
Country: Louisiana, USA
Remark: Results are given in paper as log BCF. Values presented here are BCF
Source: NICNAS
03-SEP-2001 (203)

Species: other:aquatic species
Exposure period:
Concentration:
BCF: 270
Elimination:
Method: other: estimated using the equation $BCF=0.76\log P-0.23$ (Ross and Welch 1979. EPA-560/11-80-010)
Year: GLP:
Test substance:
Remark: BCF is estimated
Source: NICNAS
03-SEP-2001 (60)

Species: other:centrtfged and decanted algal biomass
Exposure period: 12 day at 23 degree C
Concentration: 3 mg/l
BCF: 6212
Elimination:
Method:
Year: GLP:
Test substance:
Source: NICNAS
03-SEP-2001 (76)

Species:
Exposure period:
Concentration:
BCF: 66
Elimination:
Method:
Year: GLP:
Test substance:
Remark: The BCF is calculated using the equation $\log BCF = 0.85\log P-0.70$. The paper dealt with four organisms (2 fish, daphnia and algae).
Source: NICNAS
03-JUL-2002 (54)

3.8 Additional Remarks

Memo: Archived plough layer soil samples sewage sludge amended & control plot were examined (every 5 yr after sludge application for 30 yr). Levels in treated plot were slightly elevated.
Source: NICNAS
03-JUL-2002 (286)

Memo: Fate of 1,2-dcb in model waste stabilisation ponds: volatile loss 21.8%, degradation 71.1%, sedimentation 3.8%, water column residuals 0.9% a,d loss in effluent 2.4%.
Source: NICNAS
16-AUG-2001 (76)

- Memo: Removal from groundwater via various Summary results: initial concentration 5 ug/l, after steam stripping not detected, after activated carbon adsorption not detected, after biological treatment not detected, unchanged by metals treatment.
- Source: NICNAS
20-AUG-2001 (247)
- Memo: Steam-stripping using raw groundwater. Raw water 5 ug/l, dropped to < detection limit (ie not detected). Packed column steam stripping using lime treated water: initial concentration 260, dropped to <1 in run 1 and 3 in run 2.
- Source: NICNAS
20-AUG-2001 (247)
- Memo: Summaried environmental information and occurrence is given in this reference.
- Source: NICNAS
23-AUG-2001 (110)
- Memo: This book summaries data from a number of papers and reports on environmental fate and exposure in all media; including degradation, mobility and concentrations detected in the environment and organisms. It does't present any original data
- Source: NICNAS
20-MAY-2003 (130)
- Memo: removal in complete-mix activated sludge: influent conc=83 mg/l, effluent conc=<0.05 mg/l, removal >99.9%, means of removal 22% due to stripping and 78% due to biodegradation.
- Source: NICNAS
13-AUG-2001 (141)

AQUATIC ORGANISMS

4.1 Acute/Prolonged Toxicity to Fish

Type: flow through
 Species: Brachydanio rerio (Fish, fresh water)
 Exposure period: 96 hour(s)
 Unit: mg/l Analytical monitoring: yes
 LC50: 5.2
 Method: other: Fish, Acute Toxicity Test, OECD Guideline 203, 4.04.84
 Year: GLP: no
 Test substance:
 Remark: Analytical monitoring: GC-FID
 Source: Bayer AG Leverkusen
 24-AUG-2001 (219)

Type: flow through
 Species: Brachydanio rerio (Fish, fresh water)
 Exposure period: 14 day
 Unit: mg/l Analytical monitoring: yes
 NOEC: .37
 Method: other: OECD 204: Fish, Prolonged Toxicity Test: 14-day Study
 (4 April 1984)
 Year: GLP: no
 Test substance:
 Remark: Analytical monitoring: GC-FID
 Source: Bayer AG Leverkusen
 24-AUG-2001 (219)

Type: flow through
 Species: Salmo gairdneri (Fish, estuary, fresh water)
 Exposure period: 96 hour(s)
 Unit: mg/l Analytical monitoring: yes
 LC50: 1.61
 Method: other: flow through diluter
 Year: GLP:
 Test substance:
 Remark: Lake Superior water was used in test.
 Result: 96 h 50% effect concentration (abnormal swimming behaviour),
 EC50=1.55 mg/L
 Source: NICNAS
 03-SEP-2001 (6)

Type: flow through
 Species: Salmo gairdneri (Fish, estuary, fresh water)
 Exposure period: 22 hour(s)
 Unit: mg/l Analytical monitoring: yes
 LC50: 1.65
 Method: other: proportional diluter system (Mount and Brungs 1967)
 Year: GLP:
 Test substance:
 Remark: The exposure period was extended to 144 hours and the LC50
 was monitored: at 48h the LC50 reached 1.58 remaining
 constant throughout the 72h and 96h timepoints; LC50 was
 maximal at the 144 h timepoint
 Source: NICNAS
 03-SEP-2001 (56)

Type: flow through
 Species: Salmo gairdneri (Fish, estuary, fresh water)
 Exposure period: 96 hour(s)

Unit: mg/l Analytical monitoring:
 LC50: 1.58
 Method:
 Year: GLP:
 Test substance:
 Remark: measured concentration
 Source: NICNAS
 03-SEP-2001 (50)

Type: semistatic
 Species: *Oryzias latipes* (Fish, fresh water)
 Exposure period: 48 hour(s)
 Unit: Analytical monitoring:
 LC50: 67.6
 Method: OECD Guide-line 203 "Fish, Acute Toxicity Test"
 Year: 1982 GLP:
 Test substance:
 Remark: Results are given in paper as log LC50. Values presented here are LC50.
 Source: NICNAS
 03-SEP-2001 (296)

Type: static
 Species: *Cyprinodon variegatus* (Fish, estuary, marine)
 Exposure period: 48 hour(s)
 Unit: mg/l Analytical monitoring:
 LC50: 9.3
 Method: other: Methods for acute toxicity tests with fish, macroinvertebrates, and amphibians. US EPA 1975.
 Year: 1975 GLP:
 Test substance:
 Source: NICNAS
 03-SEP-2001 (118)

Type: static
 Species: *Cyprinodon variegatus* (Fish, estuary, marine)
 Exposure period: 96 hour(s)
 Unit: mg/l Analytical monitoring:
 NOEC: 9.7
 LC50: 9.7
 Method: other: Methods for acute toxicity tests with fish, macroinvertebrates, and amphibians. US EPA 1975.
 Year: 1975 GLP:
 Test substance:
 Remark: All dilution water was filtered, natural seawater of ambient salinity.
 LC50 results calculated statistically
 Source: NICNAS
 03-SEP-2001 (118)

Type: static
 Species: *Cyprinodon variegatus* (Fish, estuary, marine)
 Exposure period: 96 hour(s)
 Unit: mg/l Analytical monitoring:
 LC50: 9.7
 Method:
 Year: GLP:
 Test substance:
 Remark: without aeration
 Source: Bayer AG Leverkusen

24-AUG-2001 (50)

Type: static
 Species: Lepomis macrochirus (Fish, fresh water)
 Exposure period: 96 hour(s)
 Unit: mg/l Analytical monitoring:
 LC50: 5.6
 Method:
 Year: GLP:
 Test substance:
 Remark: 22 +/- 1 Grad C
 Source: Bayer AG Leverkusen
 24-AUG-2001 (50)

Type: static
 Species: Leuciscus idus (Fish, fresh water)
 Exposure period: 48 hour(s)
 Unit: mg/l Analytical monitoring: no
 LC50: 29
 Method: other: Bestimmung der Wirkung von Wasserinhaltsstoffen auf Fische. DEV, L 15
 Year: GLP: no
 Test substance:
 Source: Bayer AG Leverkusen
 24-AUG-2001 (50)

Type: static
 Species: Pimephales promelas (Fish, fresh water)
 Exposure period: 96 hour(s)
 Unit: mg/l Analytical monitoring:
 LC50: c 57
 Method: other
 Year: GLP:
 Test substance:
 Source: NICNAS
 03-SEP-2001 (71)

Type: static
 Species: Pimephales promelas (Fish, fresh water)
 Exposure period: 96 hour(s)
 Unit: mg/l Analytical monitoring:
 LC50: 57
 Method: other: methods proposed by The committee on Methods for Toxicity Tests
 Year: GLP:
 Test substance:
 Remark: visibly insoluble at the ranges tested - chemical administered in crystal form which sank o the bottom and remained undissolved. Deaths were observed throught the 96 h period.
 Source: NICNAS
 03-SEP-2001 (72)

Type: static
 Species: Pimephales promelas (Fish, fresh water)
 Exposure period: 96 hour(s)
 Unit: mg/l Analytical monitoring:
 LC50: 57
 Method:
 Year: GLP:
 Test substance:

Remark: 22 +/- 1 Grad C; nominal concentration
Source: NICNAS
03-SEP-2001 (50)

Type: static
Species: Salmo gairdneri (Fish, estuary, fresh water)
Exposure period: 48 hour(s)
Unit: mg/l Analytical monitoring:
LC50: 2.3
Method:
Year: GLP:

Test substance:
Remark: closed system, 15 degree C
Source: Bayer AG Leverkusen
24-AUG-2001 (50)

Type:
Species: Brachydanio rerio (Fish, fresh water)
Exposure period: 48 hour(s)
Unit: mg/l Analytical monitoring:
LC50: 6.8
Method: other:IRSA 1973
Year: GLP:

Test substance:
Source: NICNAS
03-SEP-2001 (54)

Type:
Species: Lepomis macrochirus (Fish, fresh water)
Exposure period: 24 hour(s)
Unit: mg/l Analytical monitoring:
LC50: c 6.3
Method: other:Methods for acute toxicity tests with fish,
macroinvertebrates, and amphibians. US EPA 1975
Year: 1975 GLP:

Test substance:
Source: NICNAS
03-SEP-2001 (51)

Type:
Species: Lepomis macrochirus (Fish, fresh water)
Exposure period: 96 hour(s)
Unit: mg/l Analytical monitoring:
LC50: c 27
Method:
Year: GLP:

Test substance:
Source: NICNAS
03-SEP-2001 (80)

Type:
Species: Menidia beryllina (Fish, estuary, marine)
Exposure period: 96 hour(s)
Unit: mg/l Analytical monitoring:
LC50: c 7.3
Method:
Year: GLP:

Test substance:
Source: NICNAS
03-SEP-2001 (80)

Type:
 Species: Oryzias latipes (Fish, fresh water)
 Exposure period: 48
 Unit: mg/l Analytical monitoring:
 LC50: 10
 Method: other: Japanese Industrial Standard (JIS K 0102-1986-71)
 "Testing methods for industrial waste water"
 Year: GLP:
 Test substance:
 Remark: water solubility < 10 mg/l
 Source: Bayer AG Leverkusen
 24-AUG-2001 (31)

Type:
 Species: Pimephales promelas (Fish, fresh water)
 Exposure period: 96 hour(s)
 Unit: mg/l Analytical monitoring:
 LC50: 5.8
 Method:
 Year: GLP:
 Test substance:
 Source: Bayer AG Leverkusen
 24-AUG-2001 (50)

Type:
 Species: Salmo gairdneri (Fish, estuary, fresh water)
 Exposure period: 48 hour(s)
 Unit: mg/l Analytical monitoring:
 LC50: 2.3
 Method: other: IRSA 1973
 Year: GLP:
 Test substance:
 Source: NICNAS
 03-SEP-2001 (54)

4.2 Acute Toxicity to Aquatic Invertebrates

Type:
 Species: Artemia sp. (Crustacea)
 Exposure period: 24 hour(s)
 Unit: mmol/l Analytical monitoring:
 EC50: 102
 Method:
 Year: GLP:
 Test substance:
 Source: NICNAS
 03-SEP-2001 (4)

Type: static
 Species: Ceriodaphnia sp. (Crustacea)
 Exposure period: 48 hour(s)
 Unit: µmol/l Analytical monitoring:
 EC50: 4.5
 Method: other: Standard Methods (Warne 1996) based on US EPA methods
 1993.
 Year: GLP:
 Test substance:
 Remark: Standard deviation range 3.0-6.7
 Source: NICNAS
 03-JUL-2002 (220)

Type:
Species: Daphnia magna (Crustacea)
Exposure period: 24 hour(s)
Unit: mg/l Analytical monitoring:
IC50 : .78
Method: other: AFNOR 1974
Year: GLP:
Test substance:
Remark: Endpoint was immobilization, reported as IC50.
Source: NICNAS
30-JUL-2002 (54)

Type:
Species: Daphnia magna (Crustacea)
Exposure period: 48 hour(s)
Unit: mg/l Analytical monitoring:
NOEC: .36
EC50: c 2.4
Method: other: Methods for acute toxicity tests with fish,
macroinvertebrates, and amphibians. US EPA 1975.
Year: 1975 GLP:
Test substance:
Remark: LC50 results calculated statistically
Source: NICNAS
03-SEP-2001 (155)

Type: semistatic
Species: Daphnia magna (Crustacea)
Exposure period: 24 hour(s)
Unit: mg/l Analytical monitoring:
EC0: 1
EC50: 1.7
Method: other: Provisional Procedure extended toxicology test with
Daphnia magna as of 1 January 1984 (Federal Environmental
Agency)
Year: GLP:
Test substance:
Source: NICNAS
03-SEP-2001 (149)

Type:
Species: Daphnia magna (Crustacea)
Exposure period: 48 hour(s)
Unit: Analytical monitoring:
EC50: 26
Method: other: Standard Methods (Warne 1996) based on US EPA methods
1993.
Year: GLP:
Test substance:
Source: NICNAS
03-SEP-2001 (220)

Type:
Species: Daphnia magna (Crustacea)
Exposure period: 21 day
Unit: mg/l Analytical monitoring:
NOEC: .63
Method: other: Verlaengerter Toxizitaetstest bei Daphnia magna
(Bestimmung der NOEC fuer Reproduktionsrate, Mortalitaet und
den Zeitpunkt des ersten Auftretens von Nachkommen, 21 d)
Stand: 01.01.1984

Year: GLP: no data
 Test substance:
 Remark: semi-static; closed vessels; nominal concentration
 Source: Bayer AG Leverkusen
 24-AUG-2001 (50)

Type:
 Species: Daphnia magna (Crustacea)
 Exposure period:
 Unit: mg/l Analytical monitoring:
 EC50: .74
 Method: other: analogy of OECD proposed (1979) short-term toxicity tests

Year: GLP:
 Test substance:
 Result: LC50 = 2.2
 Source: NICNAS
 03-SEP-2001 (60)

Type:
 Species: Daphnia magna (Crustacea)
 Exposure period: 24 hour(s)
 Unit: mg/l Analytical monitoring:
 EC50: c 2.4
 Method:

Year: GLP:
 Test substance:
 Source: NICNAS
 03-SEP-2001 (155)

Type:
 Species: Daphnia magna (Crustacea)
 Exposure period: 48 hour(s)
 Unit: mmol/l Analytical monitoring:
 EC50: 16
 Method:

Year: GLP:
 Test substance:
 Source: NICNAS
 03-SEP-2001 (4)

Type:
 Species: Daphnia magna (Crustacea)
 Exposure period: 48 hour(s)
 Unit: mg/l Analytical monitoring:
 EC50: 25.7
 Method:

Year: GLP:
 Test substance:
 Remark: In the paper the results are given as Log IC50 (ie log IC50=1.41). The values here are IC50
 Source: NICNAS
 03-SEP-2001 (121)

Type: other:QSAR
 Species: Daphnia magna (Crustacea)
 Exposure period: 48 hour(s)
 Unit: mg/l Analytical monitoring:
 EC50: c 32.3
 Method:
 Year: GLP:

Test substance:
Remark: The results are presented as log IC 50 in the paper (ie log IC50 = 1.51). They are reported here as IC50.
Source: NICNAS
03-SEP-2001 (121)

Type:
Species: Mysidopsis bahia (Crustacea)
Exposure period: 96 hour(s)
Unit: mg/l Analytical monitoring:
LC50 : 1.97
Method:
Year: GLP:
Test substance:
Source: NICNAS
09-JUL-2003 (262)

Type:
Species: Palaemonetes pugio (Crustacea)
Exposure period: 96 hour(s)
Unit: mg/l Analytical monitoring:
LC50 : 10
Method: other: static
Year: GLP:
Test substance:
Remark: 22 +/- 1 Grad C, nominal concentration
Source: NICNAS
03-SEP-2001 (50)

Type: static
Species: Palaemonetes pugio (Crustacea)
Exposure period: 96 hour(s)
Unit: mg/l Analytical monitoring:
EC50: 9.4
Method: other: methods proposed by The committee on Methods for Toxicity Tests
Year: GLP:
Test substance:
Remark: visibly insoluble at the ranges tested - chemical administered in crystal form which sank o the bottom and remained undissolved. Deaths were observed throught the 96 h period.
Source: NICNAS
03-SEP-2001 (72)

Type:
Species: other aquatic mollusc: Mercenaria mercenaria (hard clam) eggs
Exposure period: 48 hour(s)
Unit: mg/l Analytical monitoring:
EC50: > 100
Method:
Year: GLP:
Test substance:
Remark: Results in paper are Tlm in ppm. They are estimated by interpolation from experimental results.
Source: NICNAS
03-SEP-2001 (77)

Type:
Species: other aquatic mollusc: Mercenaria mercenaria (hard clam) larvae

Exposure period: 12 day
 Unit: mg/l Analytical monitoring:
 EC50: > 100
 Method:
 Year: GLP:
 Test substance:
 Remark: - Results in paper are TLm in ppm. They are estimated by interpolation from experimental results of exposure of larvae to concentrations for 10 days.
 Source: NICNAS
 03-SEP-2001 (77)

Type:
 Species: other:Tanytarsus dissimilis (Midge)
 Exposure period: 24 hour(s)
 Unit: mg/l Analytical monitoring: yes
 EC50: 19.9
 Method:
 Year: GLP:
 Test substance:
 Source: NICNAS
 03-SEP-2001 (56)

Type:
 Species: other:Tanytarsus dissimilis (Midge)
 Exposure period: 48 hour(s)
 Unit: mg/l Analytical monitoring: yes
 EC50: 12
 Method:
 Year: GLP:
 Test substance:
 Source: NICNAS
 03-SEP-2001 (56)

4.3 Toxicity to Aquatic Plants e.g. Algae

Species: Scenedesmus pannonicus (Algae)
 Endpoint: growth rate
 Exposure period:
 Unit: mg/l Analytical monitoring:
 EC50: 17
 Method: other: analogy of OECD proposed (1979) short-term toxicity tests
 Year: GLP:
 Test substance:
 Source: NICNAS
 03-SEP-2001 (60)

Species: Scenedesmus subspicatus (Algae)
 Endpoint: biomass
 Exposure period: 48 hour(s)
 Unit: mg/l Analytical monitoring:
 Method: other: Scenedesmus-Zellvermehrungs-Hemmtest, DIN 38412 Teil 9, modif. Bestimmung der Hemmwirkung von Wassernhaltsstoffen auf Gruenalgen
 Year: GLP:
 Test substance:
 Remark: EBC10: 3.0 mg/l EBC50: 14 mg/l
 Growth rate:
 EuC10: 7.8 mg/l EuC50: 13.5 mg/l

Source:	NICNAS	
03-SEP-2001		(50)
Species:	Scenedesmus subspicatus (Algae)	
Endpoint:	biomass	
Exposure period:	48 hour(s)	
Unit:	mg/l	Analytical monitoring:
EC10:	3	
EC50:	14	
Method:	other:DIN 38 412, part 9 (draft standard)	
Year:		GLP:
Test substance:		
Source:	NICNAS	
03-SEP-2001		(148)
Species:	Scenedesmus subspicatus (Algae)	
Endpoint:	growth rate	
Exposure period:	48 hour(s)	
Unit:	mg/l	Analytical monitoring:
EC10:	7.8	
EC50:	13.5	
Method:	other:DIN 38 412, part 9 (draft standard)	
Year:		GLP:
Test substance:		
Source:	NICNAS	
03-SEP-2001		(148)
Species:	Selenastrum capricornutum (Algae)	
Endpoint:	growth rate	
Exposure period:	96 hour(s)	
Unit:	mg/l	Analytical monitoring:
EC50:	2.2	
Method:	other: Galassi and Vighi (1981) modified version of US EPA Algal assay procedure - bottle test 1971	
Year:		GLP:
Test substance:		
Source:	NICNAS	
03-SEP-2001		(54)
Species:	Selenastrum capricornutum (Algae)	
Endpoint:	growth rate	
Exposure period:	96 hour(s)	
Unit:	mg/l	Analytical monitoring:
ErC50 :	98	
EC50 chlorophyll i	91.6rment :91.6	
Method:		
Year:		GLP:
Test substance:		
Source:	NICNAS	
09-JUL-2003		(263)
Species:	Selenastrum capricornutum (Algae)	
Endpoint:	other: photosynthesis inhibition	
Exposure period:	3 hour(s)	
Unit:	mg/l	Analytical monitoring:
EC50:	10	
Method:		
Year:		GLP:
Test substance:		
Source:	NICNAS	
03-SEP-2001		(54)

Species: Selenastrum capricornutum (Algae)
Endpoint:
Exposure period: 96 hour(s)
Unit: mg/l Analytical monitoring:
EC50: 91.6
Method:
Year: GLP:
Test substance:
Remark: Criterion: effect on Chlorophyll a content
Source: Bayer AG Leverkusen
24-AUG-2001 (50)

Species: Selenastrum capricornutum (Algae)
Endpoint:
Exposure period: 96 hour(s)
Unit: mg/l Analytical monitoring:
NOEC: < 10
EC50: 76.1
EC50 : 71.1
Method:
Year: GLP:
Test substance:
Source: NICNAS
09-JUL-2003 (263)

Species: Skeletonema costatum (Algae)
Endpoint:
Exposure period: 96 hour(s)
Unit: mg/l Analytical monitoring:
EC50: 44.2
Method:
Year: GLP:
Test substance:
Remark: Criterion: effect on Chlorophyll a content
Source: Bayer AG Leverkusen
24-AUG-2001 (50)

Species: Skeletonema costatum (Algae)
Endpoint:
Exposure period: 96 hour(s)
Unit: mg/l Analytical monitoring:
EC50 chlorophyll i 44.2
Method:
Year: GLP:
Test substance:
Source: NICNAS
09-JUL-2003 (263)

4.4 Toxicity to Microorganisms e.g. Bacteria

Type: aquatic
Species: Photobacterium phosphoreum (Bacteria)
Exposure period: 15 minute(s)
Unit: mg/l Analytical monitoring:
EC50: 3.1
5 min EC50 : 2.7
Method: other: Microtox test
Year: GLP:
Test substance:
Source: NICNAS

01-JUL-2003 (215)

Type: aquatic
 Species: Photobacterium phosphoreum (Bacteria)
 Exposure period: 30 minute(s)
 Unit: mg/l Analytical monitoring:
 EC50: 4
 Method: other: Microtox test
 Year: GLP:
 Test substance:
 Source: NICNAS
 01-JUL-2003 (137)

Type: aquatic
 Species: Pseudomonas fluorescens (Bacteria)
 Exposure period: 24 hour(s)
 Unit: mg/l Analytical monitoring: no
 EC0: 250
 Method: other: Determination of the biologically harmful effect of toxic waste water to bacteria. DEV, L 8 (German Standard Methods) (1968) modified
 Year: 1973 GLP: no
 Test substance:
 Remark: direct weight
 Source: Bayer AG Leverkusen
 24-AUG-2001 (24)

Type: aquatic
 Species: Pseudomonas putida (Bacteria)
 Exposure period: 16 hour(s)
 Unit: mg/l Analytical monitoring: no
 TT : 15
 Method: other: see remarks
 Year: GLP: no
 Test substance:
 Remark: Method: cell multiplication inhibition test
 Grenzwerte der Schadwirkung wassergefaehrdender Stoffe gegen Bakterien (Pseudomonas putida) und Gruenalgen (Scenedesmus quadricauda) im Zellvermehrungshemmtest. Bringmann, G., Kuehn, R.: Z. f. Wasser- und Abwasser-Forschung 10 (3/4), 87-98 (1977)
 TT = Toxicity Threshold
 Source: Bayer AG Leverkusen
 24-AUG-2001 (50)

Type: aquatic
 Species: other bacteria: Aerobic heterotrophic culture
 Exposure period: 15 hour(s)
 Unit: mg/l Analytical monitoring:
 IC50 : 910
 Method: other: s. Authors of this publication
 Year: GLP:
 Test substance:
 Remark: Inhibition of respiration, prolonged incubation compared to ISO 8192
 Source: Bayer AG Leverkusen
 24-AUG-2001 (32)

Type: other: Inhibition of N-oxidation
 Species: other bacteria: Nitrosomonas
 Exposure period: 24 hour(s)

Unit: mg/l Analytical monitoring:
 IC50 : 47
 Method: other: Inhibition of nitrification, similar to ISO/DIS 9509
 Year: GLP:
 Test substance:
 Source: Bayer AG Leverkusen
 24-AUG-2001 (32)

Type: other: Inhibition of bioluminescence
 Species: Photobacterium phosphoreum (Bacteria)
 Exposure period: 5 minute(s)
 Unit: mg/l Analytical monitoring:
 IC50 : 2.7
 Method: other: Microtox
 Year: GLP:
 Test substance:
 Source: Bayer AG Leverkusen
 24-AUG-2001 (32)

Type: other: Inhibition of gas production
 Species: other bacteria: Methanogenic bacteria
 Exposure period: 48 hour(s)
 Unit: mg/l Analytical monitoring:
 IC50 : 150
 Method: other: Owen, W.F., Bioassay for Monitoring Biochemical Methane
 Potential and Anaerobic Toxicity. Water Res. 13, 485 (1979)
 Year: GLP:
 Test substance:
 Source: Bayer AG Leverkusen
 24-AUG-2001 (32)

Type: other: Microtox system
 Species: other bacteria: lyophilised preparation of a luminous marine
 bacterium
 Exposure period: 5 minute(s)
 Unit: mg/l Analytical monitoring:
 EC50: 10.25
 Method: other: Microtox system
 Year: GLP:
 Test substance:
 Source: NICNAS
 03-SEP-2001 (166)

Type:
 Species: activated sludge
 Exposure period: 3 hour(s)
 Unit: mg/l Analytical monitoring:
 EC50: 100
 Method: other: OECD TG, Activated sludge, respiration inhibition test,
 draft 1.8.83, no 210.
 Year: GLP:
 Test substance:
 Source: NICNAS
 03-SEP-2001 (297)

Type:
 Species: Bacillus sp. (Bacteria)
 Exposure period: 30 minute(s)
 Unit: mg/l Analytical monitoring:
 EC50: 169
 Method:

Year: GLP:
Test substance:
Source: NICNAS
03-SEP-2001 (159)

Type:
Species: Tetrahymena pyriformis (Protozoa)
Exposure period: 24 hour(s)
Unit: mg/l Analytical monitoring:
EC50: 51
Method: other:new method developed by authors
Year: GLP:
Test substance:
Remark: This paper presents the results of the validation of a new
screening test method.
Source: NICNAS
03-JUL-2002 (298)

Type:
Species: Tetrahymena pyriformis (Protozoa)
Exposure period: 24 hour(s)
Unit: µmol/l Analytical monitoring:
EC50: 350
Method: other:new method developed by authors
Year: GLP:
Test substance:
Remark: This paper presents the results of the validation of a new
screening test method.
Source: NICNAS
03-JUL-2002 (298)

4.5 Chronic Toxicity to Aquatic Organisms

4.5.1 Chronic Toxicity to Fish

Species:
Endpoint:
Exposure period:
Unit: Analytical monitoring:
Method:
Year: GLP:
Test substance:
04-JUL-2001

4.5.2 Chronic Toxicity to Aquatic Invertebrates

Species: Daphnia magna (Crustacea)
Endpoint: mortality
Exposure period: 16 day
Unit: mg/l Analytical monitoring:
EC50: c 10.2
Method: other:QSAR
Year: GLP:
Test substance:
Remark: In the paper the results are given as Log IC50 (ie log
IC50=1.01). The values here are IC50
Source: NICNAS
03-SEP-2001 (121)

Species: Daphnia magna (Crustacea)
Endpoint: other: fertility
Exposure period: 14 day
Unit: mg/l Analytical monitoring:
EC50: .55
Method: other
Year: GLP:
Test substance:
Source: NICNAS
03-SEP-2001 (54)

Species: Daphnia magna (Crustacea)
Endpoint: other: reproduction and mortality
Exposure period: 21 day
Unit: mg/l Analytical monitoring:
NOEC: .63
EC50: 3.5
Method: other: Provisional Procedure extended toxicology test with
Daphnia magna as of 1 January 1984 (Federal Environmental
Agency)
Year: GLP:
Test substance:
Source: NICNAS
03-SEP-2001 (149)

Species: Daphnia magna (Crustacea)
Endpoint: reproduction rate
Exposure period: 16 day
Unit: mg/l Analytical monitoring:
EC50: c 3.2
Method: other: QSAR
Year: GLP:
Test substance:
Remark: In the paper the results are given as Log IC50 (ie log
IC50=0.51). The values here are IC50
Source: NICNAS
03-SEP-2001 (121)

TERRESTRIAL ORGANISMS

4.6.1 Toxicity to Soil Dwelling Organisms

Type: other: clay loam agricultural soil
Species: other soil dwelling microorganisms: bacteria and fungi
Endpoint: other:viabililty
Exposure period: 56 day
Unit:
Method: other: soil microcosms
Year: GLP:
Test substance:
Method:

Microcosms consisted of 70g (dw) of sieved, dried agricultural loam soil in 500 ml falsks. Moisture content was adjusted to 80% of field capacity, soil was mixed and then allowed to acclimatised for 7 days at room temperature. A single dose of 1,2-DCB was addedd to each microcosm. Concentrations used were 65,130, 325,1300 and 3250 ug/L. Three microcosms for each treatment were used.

Fungal hyphal length was determined by vital staining with fluorescein diacetate. This was determined at 7,14 and 49 days after the addition of 1,2-DCB.

Viable and nonviable bacteria counts were determined with a Baclight viability kit at 7, 14 and 49 days.

Result: Bactrial culture counts and identifiacion was done on day 56 after 1,2-DCB addition .
Fungal hyhal length declined i n response to all applied 1,2-DCB concentrations (65,130, 325,1300 and 3250 ug/L). Effect was rapid and recovery was insignificant.

With increasing 1,2-DCB concentration total bacterial counts declined, not significantly except for 3250 ug/L.

Anaylsis of bacterial culturability and identification indicated that with addition of increasing 1,2-DCB concentration had no impact on the total number or rate of colony development. Significantly greater counts of pseudomonads occurred with 1,2-DCB concentrations 65,130, and 325 ug/L (ie two orders of magnititude greater than control). Analysis of bacterial taxa composition indicated an increase in the percentage of pseudomonads and Bacillus and a decrease numbers of Arthrobacter and Micrococcus in in soil exposed to levels of 1,2-DCB of 325 ug/L and greater.

Source: NICNAS (254)
16-MAY-2003

Type: other: sieved agricultural soil
Species: soil dwelling microorganisms
Endpoint:
Exposure period:
Unit:
Method:
Year: GLP:
Test substance:
Method: Two experiments were under taken:
Experiment 1.
Examined the effect of 1,2-DCB and root addition on the size

and diversity of the soil microbial biomass. Microcosms in 500 ml screw cap conical flasks with Teflon lined lids, each contained 70 g (dry weight) of clay loam, agricultural soil and a moisture content of 80% were established. The soil was dosed with either 10 or 50 ug/g of 1,2-DCB. Controls without the addition of 1,2-DCB were also set-up. Six (6) grams of grass roots were added to half the microcosms. The microcosms were incubated at 20 C for 14 days. At 14 days soil samples were analysed for total fungal hyphal length by vital staining with fluorescein and the number of viable and non-viable bacterial numbers by the Baclight viability kit.

Experiment 2.

Determine the time course of microbial biomass response to 1,2-DCB and root addition. Microcosms in 500 ml screw cap conical flasks with Teflon lined lids with 100 g (dry weight) of clay loam, agricultural soil and moisture content of 80% were set-up. Six (6) grams of grass roots were added to half the microcosms. The dosage was 10 ug/g of 1,2-DCB. The experimental design was factorial giving four treatments: with and without roots and with and without 1,2-DCB. Two series of the experiment were set-up, with one using C14 labelled

1,2-DCB. Mineralisation of the label was determined by the use of a KOH trap.

The number and diversity of culturable bacteria in the soil under each treatment was determined in both experiments.

Result:

Experiment 1:

In the presence of roots and 1,2-DCB vital bacterial numbers increased slightly. Without roots but with 1,2-DCB there was a 50% decrease in vital bacterial numbers. The presence of roots appeared to buffer the inhibitory effects of 1,2-DCB. The presence of 1,2-DCB did not effect the fungal hyphal length in the absence of roots. However, the presence of roots greatly increased vital hyphal lengths (by three fold). Without roots the addition of 1,2-DCB at 10 ug/g increased the number of culturable bacteria by an order of magnitude; the addition of 50 ug/g of 1,2-DCB lead to a increase of more than two fold. The number of culturable bacteria in the soil with roots and 1,2-DCB dropped by up to 50%.

Experiment 2:

The presence of decaying root matter stimulated the decay of 1,2-DCB. The mineralisation rates with and without roots were similar initially but over time the difference grew until on day 28 the mineralisation in the presence of roots was 100% greater.

The presence of decaying root matter greatly increased bacterial and fungal biomass, leading to an enhanced ability to utilise diverse carbon sources by the soil community. The pseudomonads count, total and culturable bacterial counts increase in the presence of 1,2-DCB.

Source:
19-MAY-2003

NICNAS

(167)

Type: other: silt loam with 1.49% organic carbon
Species: soil dwelling microorganisms
Endpoint: other: soil microbial respiration (formation of carbon dioxide)
Exposure period: 6 day
Unit:

5.1 Acute Toxicity

5.1.1 Acute Oral Toxicity

Type: LD50
Species: rat
Strain:
Sex:
Number of
Animals:
Vehicle:
Value: = 1000 mg/kg bw
Method:
Year: GLP:
Test substance:
Source: NICNAS
24-AUG-2001 (171)

Type: LD50
Species: rat
Strain:
Sex:
Number of
Animals:
Vehicle:
Value: = 1516 mg/kg bw
Method:
Year: GLP:
Test substance:
Source: NICNAS
24-AUG-2001 (179)

Type: LD50
Species: rat
Strain:
Sex:
Number of
Animals:
Vehicle:
Value: = 5170 mg/kg bw
Method:
Year: GLP: no
Test substance:
Source: Bayer AG Leverkusen
24-AUG-2001 (304)

Type: LD50
Species: rat
Strain:
Sex:
Number of
Animals:
Vehicle:
Value: = 2138
Method:
Year: GLP: no data
Test substance:
Remark: Molecular connectivity indices provided a closer relationship to toxicity than physicochemical parameters; application of both physicochemical and molecular

connectivity indices however provided the best correlation

Source: NICNAS
10-SEP-2001 (92)

Type: LD50
Species: mouse
Strain:
Sex:
Number of
Animals:
Vehicle:
Value: = 2000 mg/kg bw
Method:
Year: GLP: no
Test substance:
Source: Bayer AG Leverkusen
24-AUG-2001 (271)

Type: LD50
Species: rabbit
Strain:
Sex:
Number of
Animals:
Vehicle:
Value: = 500 mg/kg bw
Method:
Year: GLP:
Test substance:
Remark: the route of application is not specified; probably the
test substance was orally administered
Source: Bayer AG Leverkusen
24-AUG-2001 (255)

Type: LD50
Species: rabbit
Strain:
Sex:
Number of
Animals:
Vehicle:
Value: = 1875 mg/kg bw
Method:
Year: GLP: no
Test substance:
Source: Bayer AG Leverkusen
24-AUG-2001 (271)

Type: LD50
Species: guinea pig
Strain:
Sex:
Number of
Animals:
Vehicle:
Value: = 3375 mg/kg bw
Method:
Year: GLP: no
Test substance:
Source: Bayer AG Leverkusen
24-AUG-2001 (271)

Type: LD0
Species: guinea pig
Strain:
Sex:
Number of Animals:
Vehicle:
Value: = 1000 mg/kg bw
Method:
Year: GLP: no
Test substance:
Source: Bayer AG Leverkusen
24-AUG-2001 (3)

Type: LD100
Species: guinea pig
Strain:
Sex: male/female
Number of Animals: 10
Vehicle: other: olive oil (by intubation as a 50% solution)
Value: <= 2000 mg/kg bw
Method:
Year: GLP: no
Test substance: other TS: purity: at least 99 %
Remark: All 800 mg/kg bw dosed animals survived; all 2000 mg/kg bw dosed animals died
Source: NICNAS
10-SEP-2001 (129)

Type: LD100
Species: guinea pig
Strain:
Sex:
Number of Animals:
Vehicle:
Value: = 2000 mg/kg bw
Method:
Year: GLP: no
Test substance:
Source: Bayer AG Leverkusen
24-AUG-2001 (3)

5.1.2 Acute Inhalation Toxicity

Type: LC100
Species: rat
Strain:
Sex:
Number of Animals:
Vehicle:
Exposure time: 4 hour(s)
Value: = 9.5 mg/l
Method:
Year: GLP:
Test substance:
Source: Bayer AG Leverkusen
24-AUG-2001 (274)

Type: LC50
Species: rat
Strain:
Sex:
Number of
Animals:
Vehicle:
Exposure time: 6 hour(s)
Value: = 1532 ppm
Method:
Year: GLP: no data
Test substance: other TS: purity: 99 %
Remark: LC50: ca. 9.38 mg/l
signs of toxicity: hypotension, somnolence, lacrimation;
retarded body weight gain up to day 14 of the observation
period; autopsy of the surviving animals on day 14 of the
observation period without observable findings in lung,
liver or kidney
Source: NICNAS
24-AUG-2001 (34)

Type: LC50
Species: rat
Strain:
Sex:
Number of
Animals:
Vehicle:
Exposure time: 4 hour(s)
Value: = 8.15 mg/l
Method:
Year: GLP:
Test substance:
Source: Bayer AG Leverkusen
24-AUG-2001 (273)

Type: LC50
Species: mouse
Strain:
Sex: female
Number of
Animals:
Vehicle:
Exposure time: 6 hour(s)
Value: = 1236 ppm
Method:
Year: GLP: no data
Test substance: other TS: purity: 99 %
Remark: LC50: ca. 7.43 mg/l
Source: NICNAS
24-AUG-2001 (34) (35)

Type: other: Acute airborne sensory irritation study in mice
Species: mouse
Strain: Swiss
Sex: male
Number of
Animals: 6
Vehicle: other: heat or bubbling air to vapourise the test substance
Exposure time: 5 minute(s)
Value: = 182 ppm

Method: other: Collecting on a solid adsorbant
Year: GLP: no data
Test substance: no data
Remark: 1,2-DCB at 182 ppm reduced the respiratory rate by 50%
(RD50)
Source: NICNAS
24-AUG-2001 (81)

5.1.3 Acute Dermal Toxicity

5.1.4 Acute Toxicity, other Routes

Type: LD50
Species: rat
Strain:
Sex:
Number of
Animals:
Vehicle:
Route of admin.: i.p.
Value: = 840 mg/kg bw
Method:
Year: GLP: no
Test substance:
Source: NICNAS
03-SEP-2001 (222) (304)

Type: LD50
Species: rat
Strain: other: F344 and Sprague-Dawley
Sex: male
Number of
Animals: 4
Vehicle: other: corn oil
Route of admin.: i.p.
Value: 1.66 - 1.76 ml/kg bw
Method:
Year: GLP: no
Test substance: no data
Source: NICNAS
03-SEP-2001 (151)

Type: LD50
Species: mouse
Strain: NMRI
Sex: male
Number of
Animals:
Vehicle: no data
Route of admin.: i.p.
Value: = 1228 mg/kg bw
Method:
Year: GLP: no data
Test substance: other TS: purity: 99 %
Source: NICNAS
24-AUG-2001 (174)

Type: other: Acute Toxicity

Species: rat
 Strain: Wistar
 Sex: male
 Number of Animals: 4
 Vehicle: other: arachidis oil
 Route of admin.: i.p.
 Value:
 Method:
 Year: GLP: no data
 Test substance:
 Remark: 1,2-DCB (all doses) resulted in significant body weight loss after 3 days; the relative liver weight was significantly increased and a rise in plasma ALT levels was observable at all doses; after 72 hours, distinct treatment-related histopathological changes in the liver were observable which were characterized by centrilobular hypertrophy and by hepatocellular degeneration and fibrosis (all doses); no change in the relative kidney weight or any treatment-related histopathological findings; 1 and 2 mmol/kg bw dosed animals at the same time point revealed a significant decrease in plasma total T4 and T3 levels, although alterations in hepatic thyroxine cannot be discounted as a mechanism for reduced levels of plasma thyroid hormone
 Source: NICNAS
 Test condition: Exposure Period: 24, 48, and 72h
 Frequency of Treatment: once
 Post Exposure Obs: Renal: Body and organ (kidney and liver) weight, liver histopathology, liver alanine asparagine aminotransferase (ALT), kidney glutathione (GSH), plasma blood urea nitrogen (BUN), and plasma thyroid hormone thyroxine (T4) and triiodothyronine (T3) levels
 10-SEP-2001 (88)

Type: LD50
 Species: rat
 Strain:
 Sex:
 Number of Animals:
 Vehicle:
 Route of admin.: s.c.
 Value: 5000 - 10000 mg/kg bw
 Method:
 Year: GLP: no data
 Test substance: other TS: purity: 98 % (technical substance)
 Remark: mortality: 0/3 at 5000 mg/kg bw and 3/3 at 10000 mg/kg bw
 Source: Bayer AG Leverkusen
 24-AUG-2001 (5)

5.2 Corrosiveness and Irritation

5.2.1 Skin Irritation

Species: rabbit
 Concentration: undiluted
 Exposure:
 Exposure Time: .5 minute(s)
 Number of

5. TOXICITY

DATE: 10-JUL-2003

ID: 95-50-1

Animals: 2
 PDII:
 Result: slightly irritating
 EC classificat.:
 Method: other: after about 30 seconds one eye was flushed for 2 minutes with flowing water; the eyes were examined after 2, 24, 48 or 168 hours
 Year: GLP: no
 Test substance: other TS: purity: at least 99%
 Remark: undiluted 1,2-DCB caused slight to moderate pain and slight conjunctival irritation clearing completely within 7 days; irrigation reduced pain and conjunctival irritation
 Source: NICNAS
 10-SEP-2001 (129)

Species: rabbit
 Concentration:

Exposure:
 Exposure Time:
 Number of
 Animals:

PDII:
 Result: slightly irritating
 EC classificat.:
 Method: other: exposure time: 24 hours, intact skin, observation period: 7 days (the experiment was performed according to the recommended guideline of ETAD)
 Year: GLP:
 Test substance: other TS: o-dichlorobenzene, chemically pure (no further data)
 Source: Bayer AG Leverkusen
 03-SEP-2001 (25)

Species: rabbit
 Concentration:

Exposure:
 Exposure Time:
 Number of

Animals:

PDII:
 Result: moderately irritating
 EC classificat.:
 Method: other: exposure time: 72 hours, site of application: intact or abraded back skin, dose: 0.5 ml/animal, semi-occlusive; observations were made after 24 and 72 hours
 Year: GLP: no
 Test substance:
 Source: Bayer AG Leverkusen
 03-SEP-2001 (1)

Species: rabbit
 Concentration: .5 undiluted

Exposure: Semioclusive
 Exposure Time: 4 hour(s)
 Number of
 Animals: 6
 PDII:
 Result:

5. TOXICITY

DATE: 10-JUL-2003

ID: 95-50-1

EC classificat.:
 Method: other: scored according to Draize Test
 Year: GLP:
 Test substance:
 Remark: The study provided no individual animal data and Draize scores were not provided
 Result: Slight to moderate erythema and oedema were noted up to 72 h post exposure to 1,2-DCB; the effects lessened by 120 h and disappeared altogether by 168 h post exposure.
 Source: NICNAS
 Test condition: Concentration of 1,2-DCB was 0.5 mL of undiluted sample; 6 rabbits were tested (3 of each sex)
 19-SEP-2001 (299)

5.2.2 Eye Irritation

Species: rabbit
 Concentration:
 Dose:
 Exposure Time:
 Comment:
 Number of Animals:
 Result: slightly irritating
 EC classificat.:
 Method: other: eyes not rinsed, observation period: 7 days (the experiment was performed according to the guideline of ETAD)
 Year: GLP:
 Test substance: other TS: o-dichlorobenzene, chemically pure (no further data)
 Remark: slight conjunctival effects were observable up to 2 days after application
 Source: Bayer AG Leverkusen
 24-AUG-2001 (25)

Species: rabbit
 Concentration:
 Dose:
 Exposure Time:
 Comment:
 Number of Animals:
 Result: slightly irritating
 EC classificat.:
 Method: other: eyes not rinsed, observation period: 7 days
 Year: GLP: no
 Test substance:
 Remark: conjunctival effects persisted throughout the 7-day observation period
 Source: Bayer AG Leverkusen
 24-AUG-2001 (2)

5.3 Sensitization

Type: other
 Species: rabbit
 Number of Animals:
 Vehicle:

Result:
Classification:
Method: other: rabbits were exposed via inhalation to o-dichlorobenzene at a concentration of 0.05 mg/l for 7 months (5 days a week, 4 hours daily)
Year: GLP:
Test substance:
Remark: sensitization became obvious at early stages of poisoning in the absence of any pointers to systemic toxic action; as the signs of intoxication developed, allergic tests became negative but again took on a positive value closer to the cessation of experiment; o-dichlorobenzene triggered the production of antibodies to erythrocyte lysate and of antitissue antibodies to autoantigenes from the renal tissue (no further data)
Source: Bayer AG Leverkusen
24-AUG-2001 (236)

5.4 Repeated Dose Toxicity

Species: rat Sex: male
Strain: Sprague-Dawley
Route of admin.: inhalation
Exposure period: 2d or 4d
Frequency of treatment: 6 h/d
Post. obs. period: no
Doses: 309 ppm (= ca. 1.86 mg/l)
Control Group: other: clean filtered air
LOAEL: =
Method:
Year: GLP: no data
Test substance: other TS: purity: >99.0 %
Remark: liver damage was investigated in the rats using serum enzyme activities measurements
Result: significant increase in the serum activities of glutamate dehydrogenase (4d) and sorbitol dehydrogenase (2d and 4d); serum activities of glutamic oxaloacetic transaminase and glutamic pyruvic transaminase not significantly changed
Source: NICNAS
24-AUG-2001 (45)

Species: rat Sex: male/female
Strain: no data
Route of admin.: inhalation
Exposure period: 6 to 7 months
Frequency of treatment: 7 h/d, 5 d/w
Post. obs. period: no
Doses: 49 ppm (=ca. 0.3 mg/l) and 93 ppm (= ca. 0.57 mg/l)
Control Group: other: air exposed control (for 93 ppm only)
Method:
Year: GLP: no
Test substance: other TS: purity: at least 99 %
Result: Exposure to 1,2-DCB at 49 ppm revealed no adverse effects as determined by average body and organ weight, gross appearance, behaviour, growth, mortality, and gross and microscopic examination of tissues; at the highest dose

studied (93 ppm) average body weight and spleen weight
decreased decreased

Source: NICNAS (129)
05-SEP-2001

Species: rat Sex: no data
Strain: no data
Route of admin.: inhalation
Exposure period: 4 months
Frequency of treatment: 4 h/d, 6 d/w
Post. obs. period: no data
Doses: 0.2 mg/l
Control Group: no data specified
Method:
Year: GLP:
Test substance:
Result: changes of neurodynamics in the cerebral cortex were observable, as the relationships among principal neural processes were impaired, inhibition was enhanced and stimulation weakened

Source: Bayer AG Leverkusen (272)
24-AUG-2001

Species: rat Sex: no data
Strain: no data
Route of admin.: inhalation
Exposure period: 9 months
Frequency of treatment: no data
Post. obs. period: no data
Doses: 0.001 mg/l
Control Group: no data specified
Method:
Year: GLP:
Test substance:
Result: the treatment modified conditioned activity of the rats by lowering the induction of conditioned reflexes, lengthening their latent period, making reflex eliminations more frequent and, in broad, upsetting the balance of stimulation and inhibition processes in the brain cortex

Source: Bayer AG Leverkusen (269)
24-AUG-2001

Species: rat Sex: male
Strain: Wistar
Route of admin.: gavage
Exposure period: 7 d
Frequency of treatment: daily
Post. obs. period: no data
Doses: 500 mg/kg bw/d
Control Group: no data specified
Method:
Year: GLP: no data
Test substance:
Result: an induction of hyaline droplet accumulation in the renal cortex of the treated rats was not detectable

Source: Bayer AG Leverkusen (33)
24-AUG-2001

Species: rat Sex: male
Strain: Fischer 344
Route of admin.: gavage
Exposure period: 6 or 7 d
Frequency of treatment: daily
Post. obs. period: no
Doses: 0.8 or 2.0 mmol/kg bw/d (= 118 or 294 mg/kg bw/d)
Control Group: yes, concurrent vehicle
Method:

Year: GLP: no data
Test substance: other TS: purity: 99.0 %
Result: no significant increase in renal protein droplet formation was observed; incorporation of 3H-thymidine into renal DNA, a biochemical measurement of cell proliferation, was not significantly increased compared to control values

Source: NICNAS (63) (64)
24-AUG-2001

Species: rat Sex: female
Strain: Wistar
Route of admin.: gavage
Exposure period: 1, 3 or 5 d
Frequency of treatment: daily
Post. obs. period: no
Doses: 500 mg/kg bw/d
Control Group: yes, concurrent vehicle
Method:

Year: GLP: no
Test substance:
Result: the porphyrin content in the Harderian gland increased considerably at 1 day after administration, but returned to control values at 5 days post administration; there was no effect on the activity of Harderian gland delta-aminolevulinic acid-synthetase, while hepatic delta-aminolevulinic acid-synthetase activity was increased 2-3 times the normal level; no changes in the delta-aminolevulinic acid-dehydratase activity in the liver or in the Harderian gland were observable up to 5 days after administration; the relative liver weight increased during duration of treatment, whereas the relative weight of the Harderian gland remained unaffected

Source: NICNAS (93)
24-AUG-2001

Species: rat Sex: male
Strain: Wistar
Route of admin.: gavage
Exposure period: 7 d
Frequency of treatment: daily
Post. obs. period: no
Doses: 500 mg/kg bw/d
Control Group: yes, concurrent no treatment

Method:
Year: GLP: no data
Test substance:
Remark: the urine was collected on day 7 and tested for presence of rat urinary kidney-derived antigens ("RUA") and of LDH
Result: in untreated rats antigen excretion was within the normal range; slightly to moderately enhanced urinary excretion of most of the antigens was seen after application of o-dichlorobenzene; urinary level of LDH was in the normal range after application of o-dichlorobenzene
Source: Bayer AG Leverkusen (96)
24-AUG-2001

Species: rat Sex: female
Strain: no data
Route of admin.: gavage
Exposure period: 192 d
Frequency of treatment: daily, 5 d/w
Post. obs. period: no
Doses: 18.8, 188 or 376 mg/kg bw/d
Control Group: yes, concurrent vehicle
Method:
Year: GLP: no
Test substance: other TS: purity: at least 99 %
Remark: the animals received a total of 138 doses in 192 days
Result: all dose groups: no adverse effect on growth or mortality at all dose levels: at 188 mg/kg and 376 mg/kg, significant increase in the average weight of liver and kidneys: at 376 mg/kg a significant decrease in splenic weight; microscopical findings: slight to moderate cloudy swelling of the liver
Source: NICNAS (129)
05-SEP-2001

Species: rat Sex: male
Strain: other: Albino
Route of admin.: gavage
Exposure period: 15 d
Frequency of treatment: daily
Post. obs. period: no data
Doses: 450 mg/kg bw/d
Control Group: yes
Method:
Year: GLP: no
Test substance:
Remark: 1,2-DCB increased hepatic levels of coproporphyrin, protoporphyrin and uroporphyrin; decreased hepatic activity of catalase; histologic examination revealing severe liver damage with intense necrosis and fatty change over large areas
Source: NICNAS (217)
24-AUG-2001

Species: rat Sex: male/female
Strain: Sprague-Dawley
Route of admin.: gavage
Exposure period: 10 d
Frequency of

treatment: daily
 Post. obs. period: no
 Doses: 37.5, 75, 150 or 300 mg/kg bw/d
 Control Group: yes, concurrent vehicle
 NOAEL: = 75 mg/kg bw
 LOAEL: = 150 mg/kg bw
 Method:
 Year: GLP: yes

Test substance: other TS: purity: 99 %
 Remark: At 300 mg/kg bw/day a decrease in male total body weight gain and absolute organ weight (heart, kidneys, spleen, testes and thymus) were observed; significant increase (p < 0.05) in absolute and relative liver weights and the development of hepatocellular necrosis was evident; plasma ALT levels were significantly elevated after treatment with 300 mg/kg bw for both sexes while for females, cholesterol levels were elevated at all doses compared with controls; leukocytosis was present in males at 150 and 300 mg/kg bw while the absolute and relative weights of female livers increased at these doses; spleen weights decreased only at 300 mg/kg bw; histopathological findings showed presence of slight hepatocellular lesions (40% of males treated with 300mg/kg bw)

Source: NICNAS
 05-SEP-2001 (218)

Species: rat Sex: male/female
 Strain: Sprague-Dawley
 Route of admin.: gavage
 Exposure period: 90 d
 Frequency of treatment: daily
 Post. obs. period: no
 Doses: 25, 100 or 400 mg/kg bw/d
 Control Group: yes, concurrent vehicle
 NOAEL: = 25 mg/kg bw
 LOAEL: = 100 mg/kg bw
 Method:
 Year: GLP: yes

Test substance: other TS: purity: 99 %
 Remark: At 400 mg/kg bw per day a significant decrease (p < 0.05) in total body weight gain was observed for males but not females; significant increases (p < 0.05) in absolute and relative liver weights occurred for both sexes at 100 and 400 mg/kg bw and absolute and relative kidney weights were increased at 400 mg/kg bw for both sexes and absolute kidney weights increased for females at 100 mg/kg bw; plasma ALT levels were elevated at 100 and 400 mg/kg bw in the male but the female levels did not reach significance; In both sexes: an increase in bilirubin occurred at the highest dose; no evidence of leukocytosis or other haematological change; histopathological findings included centrilobular degeneration, centrilobular hypertrophy and evidence of apoptosis at 400 mg/kg bw
 Statistical Methods:
 ANOVA (body weights, organ weights, organ weight ratios, food and water consumption, haematology, and clinical chemistry); treatment related effects measured by the Dunnett's t-test (control v. treatment); non-normally

distributed data by the Kruskal-Wallis test (between dose-groups); Fisher's Trend Test and Logrank Test (histopathology)

Result:

- Body weight
At 400 mg/kg bw per day a significant decrease ($p \leq 0.05$) in total body weight gain was observed for males but not females compared to controls.
- Serum clinical chemistry
Plasma ALT levels were significantly elevated ($p \leq 0.05$) at 100 and 400 mg/kg bw in males compared to controls however levels in females did not reach significance; increased bilirubin ($p \leq 0.05$) occurred at the highest dose in both sexes. BUN was significantly increased ($p \leq 0.05$) in 400 mg/kg dosed males compared to controls.
- Haematology
No evidence of leukocytosis or other haematological changes for either sex.
- Mortality and time to death
all animals survived treatment period
- Organ weight changes
Significant increases in absolute and relative liver weights occurred for both sexes at 100 mg/kg bw and 400 mg/kg bw compared to controls and absolute and relative kidney weights were increased at 400 mg/kg bw for both sexes compared to controls. Absolute kidney weights increased for females at 100 mg/kg bw.
- Histopathology
Treatment-related hepatocellular changes in 400 mg/kg d treated males and females consisted of statistically significant ($p \leq 0.05$) increases in centrilobular degeneration, centrilobular hypertrophy and evidence of single cell necrosis at 400 mg/kg bw for both sex

Source: NICNAS

Test condition: The oral toxicity of 1,2-DCB for male and female Sprague-Dawley rats were assessed following exposure to 0, 25, 100 or 400 mg/kg bw per day for 90 days by gavage;

Test Subjects:

- Age at study initiation: 80 d (OECD guideline specifies less than 56 d for a 90 d subchronic study.)
- No. of animals: 80 animals divided into 4 treatment groups (10/sex/dose)
- Clinical observations performed: Both sexes: body weight and food consumption; ophthalmoscopic examination prior to and during last week. Haematological parameters consisting of hemoglobin (Hgb), hematocrit (Hct), red blood cell (RBC) count, white blood cell (WBC) count, mean cell volume, platelet count, differential leukocyte count and cell morphology.
- Serum clinical chemistry performed:
Serum clinical chemistry consisting of alanine aminotransferase (ALT), aspartate aminotransferase (AST),

lactate dehydrogenase (LDH), serum cholesterol (Chol), phosphorus (P), calcium (Ca), glucose (Glu), blood urea nitrogen (BUN), and creatinine (Creat), sodium (Na), potassium (K), total protein (TP), albumin (ALB), total bilirubin (TB), and alkaline phosphatase (ALKP).

• Organs grossly examined at necropsy:
Weighed and examined brain, liver spleen, lungs, thymus kidneys, adrenal glands, heart, and testes/ovaries; examined gross lesions, skin mammary glands, clitoral or preputial glands, mandibular and mesenteric lymph nodes, thigh muscle, sciatic nerve, sternbrae, femur, duodenum, ileum, jejunum, salivary gland, colon, cecum, rectum, pancreas, urinary bladder, seminal vesicles, prostate, nasal cavity (with turbinates), pituitary, and Zymbal's gland of each animal.

Conclusion: In the SD rat the critical endpoints following 90 day exposure to 1,2-DCB at subchronic oral doses are hepatic and renal effects and related clinical chemistry changes. The NOAEL was 25 mg/kg bw per day and the LOAEL 100 mg/kg bw (based upon increased absolute and relative liver weight in males and females; increased plasma ALT levels in males) (218)

07-SEP-2001

Species: rat Sex: male/female
Strain: other: F344/N
Route of admin.: gavage
Exposure period: 14 d
Frequency of treatment: daily
Post. obs. period: 6 d
Doses: 60, 125, 250, 500 or 1000 mg/kg bw/d
Control Group: yes, concurrent vehicle
Method:
Year: GLP: no data
Test substance: other TS: purity: >99 %
Remark: At the highest dose studied (1000 mg/kg bw) 100% mortality was observed by day 5 while 500 mg/kg bw resulted in reduced body weight gain (-12%)

Source: NICNAS (190)
10-SEP-2001

Species: rat Sex: male/female
Strain: other: F344/N
Route of admin.: gavage
Exposure period: 13 w
Frequency of treatment: 5 d/w
Post. obs. period: no
Doses: 30, 60, 125, 250 or 500 mg/kg bw/d
Control Group: yes, concurrent vehicle
NOAEL: = 60 mg/kg bw
LOAEL: = 125 mg/kg bw

Method:
Year: GLP: no data
Test substance: other TS: purity: >99 %
Result: all dose groups: dose-related increase in liver weights with significant increases in liver weight/body weight ratios at 125 mg/kg and above; slight and generally dose-related

increases in serum cholesterol, triglycerides and total proteins may be indicative of hepatic effects; minimal changes in haematology and clinical chemistry parameters; 24 h urine volume increased 57% over controls in males; 3-5 times the urinary concentration of uroporphyrin and coproporphyrin in males and females than in controls; microscopy findings: at 500 mg/kg bw moderate centrolobular hepatocellular necrosis, centrolobular hepatic degeneration or necrosis of individual hepatocytes found in 7/8 of surviving females and 8/10 males; renal tubular degeneration in 6/10 males and thymic lymphoid depletion in 4/10 males

Source:
10-SEP-2001

NICNAS

(190)

Species: rat Sex: male/female
Strain: other: F344/N
Route of admin.: gavage
Exposure period: 103 w
Frequency of treatment: 5 d/w
Post. obs. period: no
Doses: 60 or 120 mg/kg bw/d
Control Group: yes, concurrent vehicle
NOAEL: = 120 mg/kg bw
Method:
Year: GLP: no data
Test substance: other TS: purity: >99 %
Remark:

-Body weight
High-dosed male rats showed an immediate slight decrease in body weight gain at week-1 (-3%) which persisted at weeks 22 and 60 (-5%) recovering at week 99 (-1%), while females experienced an increase in weight gain (+3 to +11%) for the same period. These changes were not statistically significant.

-Mortality and time to death
In males 8/50 controls, 14/50 low dose and 31/50 high dosed animals died. At the highest dose, male rats exhibited a significant decrease ($p < 0.001$) in survival, however, five of these deaths were accidental and twelve others were attributed to handling/gavage errors. The survival of female rats was similar to control animals (19/50 controls, 17/50 low dose and 18/50 high dose females died.)

-Histopathology
Histological examination in both sexes revealed no increase in non-neoplastic lesions in the liver, kidney, bone marrow, spleen, thymus or other organs.
Although the incidence of pheochromocytoma in males was increased in the low-dose group (16/50) the high-dose incidence (6/49) was lower than the control animals (9/50) with no significant dose-response trend being evident

Source: NICNAS

Test condition: Test Subjects:
• Age at study initiation: 7 wks.
• No. of animals per sex per dose: 50 per dose group.

Dose: Hepatic necrosis in 250 mg/kg dosed males in a thirteen-week study was considered potentially

life-shortening and therefore precluded from inclusion in the two-year study.

Study Design:

- Satellite group: 15 sentinel animals/sex
- Clinical observations performed: body weight; clinical pathology

- Organs examined at necropsy:

macroscopic: all major tissues or organs including eyes, thigh muscle, and spinal chord.

microscopic: tissue masses, abnormal lymph nodes, mammary gland, salivary gland, bone marrow, sternbrae, femur or vertebrae, thymus, trachea, lungs and bronchi, heart, thyroid, parathyroid, esophageus, stomach, small intestine, colon, liver, pancreas, spleen, kidneys, adrenals, urinary bladder, prostate/testes or ovaries/uterus, brain, and pituitary, eyes, thigh muscle, and spinal chord (only if grossly abnormal).

Conclusion:

Non-neoplastic Effects:

NOAEL (male & female): 120 mg/kg bw/day

LOAEL (male & female) no treatment-related pathologies observed at any dose

Under the conditions of the study, 1,2-DCB was not considered to be carcinogenic in rats;

05-SEP-2001

(190)

Species: rat Sex: male
Strain: no data
Route of admin.: gavage
Exposure period: 9 months
Frequency of treatment: daily
Post. obs. period: no data
Doses: 0.001, 0.01 or 0.1 mg/kg bw/d
Control Group: other: yes, concurrent vehicle (sunflower oil)
Method:
Year: GLP: no

Test substance:

Result: 0.001 mg/kg bw/d: no toxic effects; 0.01 mg/kg bw/d: similar but less pronounced effects as seen in the 0.1 mg/kg bw/d-group (no further data) 0.1 mg/kg bw/d: inhibition of higher nervous activity; statistically significant inhibition of erythropoiesis; thrombocytosis; inhibition of mitotic activity in the bone marrow; neutropenia; marked increase of 17-ketosteroids in the urine; increase in the weight coefficient of the adrenals; reduced vitamin C concentration in the adrenals; increase in the blood serum activity of alkaline phosphatase and transaminase; decrease in the SH groups in whole blood; markedly reduced levels of alkaline phosphatase and moderately increased levels of acid phosphatase in the liver and kidneys; decrease in the hepatic and renal concentrations of

di-triphosphopyridinenucleotides (DPN and TPN), succinic dehydrogenase, glucose-6-phosphatase and alpha-glycerophosphate in the liver and kidneys; increase in gamma globulin (no data provided)

Source: NICNAS

05-SEP-2001

(270)

Species: rat Sex: female
Strain: Wistar
Route of admin.: oral unspecified
Exposure period: 3 d
Frequency of treatment: daily
Post. obs. period: no
Doses: 250 mg/kg bw/d
Control Group: other: yes, concurrent vehicle (2% tragacanth gum solution)
Method:
Year: GLP: no
Test substance:
Result: Significant increase in the relative liver weight; hepatic glycogen and triglyceride contents not significantly affected; significant increase in hepatic microsomal protein content; no significant change of the hepatic cytochrome P-450 or cytochrome b5 content; effects on hepatic drug-metabolizing enzymes: activity of aminopyrine demethylase and of delta-aminolevulinic acid synthetase was significantly enhanced, activity of aniline hydroxylase not significantly changed

Source: NICNAS

05-SEP-2001

(11) (12)

Species: rat Sex: no data
Strain: no data
Route of admin.: oral unspecified
Exposure period: 60 d or 120 d
Frequency of treatment: no data
Post. obs. period: no data
Doses: no data
Control Group: yes, concurrent vehicle
Method:
Year: GLP: no data
Test substance:
Result: slightly increased liver weights; increased triglyceride levels; decrease in the level of ATP in the liver; decrease in the respiratory control of liver mitochondria in state 3 respiration, increase in the respiratory control of liver mitochondria in state 4 respiration

Source: Bayer AG Leverkusen

24-AUG-2001

(175)

Species: rat Sex: male
Strain: other: COBS-CD (SD) Br
Route of admin.: s.c.
Exposure period: 16 d
Frequency of treatment: daily
Post. obs. period: no
Doses: 40, 200 or 1000 mg/kg bw/d
Control Group: yes
NOAEL: = 40 mg/kg bw
Method:
Year: GLP: yes

5. TOXICITY

DATE: 10-JUL-2003

ID: 95-50-1

Test substance: other TS: purity: 98 %
 Result: all dose levels: no myelotoxic or cytogenetic effects
 (no significant chromosomal damage to bone marrow cells
 observable)
 200 and 1000 mg/kg bw/d: significant increases in relative
 liver weights
 1000 mg/kg bw/d: increased mortality and decreased body
 weight gain
 Source: Bayer AG Leverkusen
 24-AUG-2001 (214)

Species: mouse Sex: male
 Strain: Swiss
 Route of admin.: inhalation
 Exposure period: 4 d, 9 d or 14 d
 Frequency of
 treatment: 6 h/d, 5 d/w
 Post. obs.
 period: no
 Doses: 64 and 163 ppm (385 and 980 mg/m³ respectively)
 Control Group: other: air-exposed control
 Method:
 Year: GLP:

Test substance: other TS: purity: 99%
 Result: Olfactory epithelium in the dorsal meatus affected by
 lesions at all doses; complete loss of olfactory epithelium,
 leaving only the partly denuded basement membrane; lesion
 severity graded as very severe at 4 d exposure, severe at 9
 d exposure, moderate at 14 day exposure; respiratory
 epithelium remained unaffected as did the trachea & lungs
 Source: NICNAS
 24-AUG-2001 (303)

Species: mouse Sex: male/female
 Strain: B6C3F1
 Route of admin.: gavage
 Exposure period: 14 d
 Frequency of
 treatment: daily
 Post. obs.
 period: 2 d
 Doses: 250, 500, 1000, 2000 or 4000 mg/kg bw/d
 Control Group: yes, concurrent vehicle
 LOAEL: = 250 mg/kg bw
 Method:
 Year: GLP: no data

Test substance: other TS: purity >99 %
 Remark: groups of five male and five female mice were used
 Result: Most of the treated animals died; 250 mg/kg bw/d: hepatic
 necrosis in 1/3 females examined; hepatocellular
 degeneration in 1/3 males examined; 500 mg/kg bw/d: hepatic
 necrosis in 3/3 males examined
 Source: NICNAS
 10-SEP-2001 (190)

Species: mouse Sex: male/female
 Strain: B6C3F1
 Route of admin.: gavage
 Exposure period: 14 d
 Frequency of
 treatment: daily

Post. obs.
 period: 2 d
Doses: 30, 60, 125, 250 or 500 mg/kg bw/d
Control Group: yes, concurrent vehicle
NOAEL: = 60 mg/kg bw
LOAEL: = 125 mg/kg bw
Method:
 Year: GLP: no data
Test substance: other TS: purity: >99 %
Remark: groups of five male and five female mice were used; tissues of 4 high dose male and females were examined histologically
Result: all dose groups: mean body weights comparable among groups
125 mg/kg bw/d: death of one female animal
500 mg/kg bw/d: death of one male animal; results of histological examination: mild hepatocellular necrosis in 2/4 males, moderate focal hepatic necrosis in 1/4 females, mild multifocal hepatitis in 1/4 females, mild cytomegaly and karyomegaly in 2/4 females, hepatocellular degeneration in 1/4 females
Source: NICNAS
10-SEP-2001 (190)

Species: mouse Sex: male/female
Strain: B6C3F1
Route of admin.: gavage
Exposure period: 13 w
Frequency of treatment: 5 d/w
Post. obs.
 period: no
Doses: 30, 60, 125, 250 or 500 mg/kg bw/d
Control Group: yes, concurrent vehicle
Method:
 Year: GLP: no data
Test substance: other TS: purity: >99 %
Remark: groups of ten male and ten female mice were used
LOAEL: 30 mg/kg bw in females and 250 mg/kg bw in males
Result: NOAEL: not identified in females and 125 mg/kg bw in males
all dose groups: decrease in relative spleen weights in female mice; only minor changes in haematology values; no consistent gross lesions observable at necropsy
125 mg/kg bw/d: no compound-related lesions in livers or other organs 250 mg/kg bw/d: death of one male animal; compound-related hepatic lesions in males: necrosis of individual hepatocytes observed in 2/10 males, hepatocellular degeneration observed in 1/10 males, pigment deposition observed in 1/10 males 500 mg/kg bw/d: death of four males and three females; weight gains and final body weights depressed relative to controls; significant increase in relative liver weights; urinary concentration of coproporphyrin three times higher in female mice than in controls; twofold increase in the hepatic concentration of porphyrins in females; microscopy findings: centrolobular hepatic necrosis, necrosis of individual hepatocytes or hepatocellular degeneration observed in 9/10 males and 9/10 females; multiple foci of mineralization of myocardial fibers in the hearts of 3/10 males and 8/10 females; some necrosis, myositis and mineralization in skeletal muscle; lymphoid depletion observable in the thymus of 2/10 males

and 2/10 females; lymphoid depletion observable in the spleen of 4/10 males and 2/10 females; necrosis of lymphocytes in the spleen in 1/10 females; deposits of hemosiderin in the livers of 4/10 males and 2/10 females

Source: NICNAS (190)
10-SEP-2001

Species: mouse Sex: male/female
Strain: B6C3F1
Route of admin.: gavage
Exposure period: 103 w
Frequency of treatment: 5 d/w
Post. obs. period: no
Doses: 60 or 120 mg/kg bw/d
Control Group: yes, concurrent vehicle
NOAEL: = 60 mg/kg bw
LOAEL: = 120 mg/kg bw
Method:
Year: GLP: no data
Test substance: other TS: purity: >99 %
Result: -Body weight
Mean body weights of dosed and control male and female mice were comparable throughout the study duration.

-Mortality and time to death
The survival of male and female mice was similar to control animals.

-Histopathology
There appeared to be a dose-related trend in tubular regeneration of the kidney in male mice (control, 17%; low dose, 24%; high dose, 35%) however, statistical significance was not reported. The incidence of malignant histiocytic lymphoma in male (control, 0/50; low-dose, 1/50; high-dose, 4/50) and female (control, 0/49; low-dose, 0/50; high-dose, 3/49) mice was significantly increased (p < 0.05). However, these findings were dismissed, as the numbers of animals with all types of lymphomas (combined), which is considered to be a better indicator, had not increased.

Source: NICNAS
Test condition: Test Subjects:
· Age at study initiation: 7 wks.
· No. of animals per sex per dose: 50 per strain per sex per dose group.
Dose: Hepatic necrosis in 250 mg/kg dosed males in a thirteen-week study was considered potentially life-shortening and therefore precluded from inclusion in the two-year study.

- Study Design:
· Satellite group: 15 sentinel animals/sex
· Clinical observations performed: body weight; clinical pathology
· Organs examined at necropsy:
macroscopic: all major tissues or organs including eyes, thigh muscle, and spinal chord.
microscopic: tissue masses, abnormal lymph nodes, mammary gland, salivary gland, bone marrow, sternbrae, femur or vertebrae, thymus, trachea, lungs and bronchi, heart,

thyroid, parathyroid, esophageus, stomach, small intestine, colon, liver, gallbladder, pancreas, spleen, kidneys, adrenals, urinary bladder, prostate/testes or ovaries/uterus, brain, and pituitary, eyes, thigh muscle, and spinal chord (only if grossly abnormal).
 Conclusion: NOAEL: Non-neoplastic effects at 60 mg/kg bw/day in males; 120 mg/kg bw/day in females
 LOAEL: 120 mg/kg bw/day (increased tubular regeneration) in males; no treatment-related pathologies observed at any dose in females

Under the conditions of the study, 1,2-DCB was not considered to be carcinogenic in mice.

10-SEP-2001

(190)

Species: rabbit Sex: male/female
 Strain: no data
 Route of admin.: inhalation
 Exposure period: ranging from 6 to 7 months
 Frequency of treatment: 7 h/d, 5 d/w
 Post. obs. period: no
 Doses: 93 ppm (= ca. 0.569 mg/l)
 Control Group: other: air-exposed control
 Method:
 Year: GLP: no
 Test substance: other TS: purity: at least 99 %
 Remark: two rabbits of each sex were used
 Result: no adverse effects as judged by the criteria which follow: gross appearance, behaviour, growth, mortality, organ-weight studies, qualitative urine tests on females for blood, sugar, albumin and sediment, terminal blood urea nitrogen values for females, haematological data, and gross and microscopic examination of the tissues

Source:
05-SEP-2001

(129)

Species: rabbit Sex: no data
 Strain: no data
 Route of admin.: inhalation
 Exposure period: 7 months
 Frequency of treatment: 4 h/d, 5 d/w
 Post. obs. period: no data
 Doses: 0.05 mg/l
 Control Group: no data specified
 Method:
 Year: GLP:

Test substance:
 Result: a sensitizing potential of o-dichlorobenzene was discovered; sensitization became obvious at early stages of poisoning in the absence of any pointers to systemic toxic action; as the signs of intoxication developed, allergic tests became negative but again took on a positive value closer to the cessation of experiment; o-dichlorobenzene triggered the production of antibodies to erythrocyte lysate and of antitissue antibodies to autoantigenes from the renal tissue (no further data)

Source: Bayer AG Leverkusen

24-AUG-2001

(236)

Species: rabbit Sex: no data
Strain: no data
Route of admin.: inhalation
Exposure period: 7-8 months
Frequency of treatment: 4 h/d, 5 d/w
Post. obs. period: no data
Doses: 0.05 mg/l
Control Group: yes
Method:
Year: GLP:
Test substance:
Result: effects on adrenal cortex function: short increase in the blood plasma level of 11-oxycorticosteroids at 3 and 5 months of exposure
Source: Bayer AG Leverkusen

24-AUG-2001

(53)

Species: rabbit Sex: female
Strain: other: New Zealand (no further data)
Route of admin.: dermal
Exposure period: 5 d
Frequency of treatment: daily
Post. obs. period: 12 d
Doses: 0.1 ml/animal/d
Control Group: yes
Method:
Year: GLP: no
Test substance: other TS: undiluted o-dichlorobenzene (no further data)
Remark: the inner aspect of the ear of two rabbits was painted daily with 0.1 ml of 1,2-DCB
Result: 1,2-DCB had no chloracnegenic properties; no systemic toxic effects were noted in the rabbits; the microscopic examination of the rabbit livers showed no abnormalities (no further data)

Source: NICNAS
05-SEP-2001

(178)

Species: rabbit Sex: no data
Strain: no data
Route of admin.: s.c.
Exposure period: unspecified
Frequency of treatment: repeated administration (no further data)
Post. obs. period: no data
Doses: unspecified
Control Group: no data specified
Method:
Year: GLP: no data
Test substance:

Result: blood dyscrasias characterized by agranulocytosis, with little or no effect on red blood cells
Source: Bayer AG Leverkusen

24-AUG-2001

(287)

Species: dog Sex: male
Strain:
Route of admin.: inhalation
Exposure period: 14 d
Frequency of treatment: daily, 2 h/d
Post. obs. period: no data
Doses: 2 ml per cubic metre (= ca. 2.64 mg/l)
Control Group: no
Method:
Year: GLP: no
Test substance:
Remark: one animal was used in the study
Result: no signs of toxicity were observable
Source: Bayer AG Leverkusen
24-AUG-2001 (216)

Species: guinea pig Sex: male/female
Strain: no data
Route of admin.: inhalation
Exposure period: ranging from 6 to 7 months
Frequency of treatment: 7 h/d, 5 d/w
Post. obs. period: no
Doses: 49 ppm (= ca. 0.3 mg/l) and 93 ppm (=ca. 0.569 mg/l)
Control Group: other: air-exposed control
Method:
Year: GLP: no
Test substance: other TS: purity: at least 99 %
Remark: Numbers of animals: 8 per sex
Result: At 93 ppm there was a decrease in the average male splenic weight with no change in morphology; no adverse effects for both sexes as determined by gross appearance, gross and microscopic examination of (unspecified) tissues, growth, behaviour, mortality, organ weight; females: in addition, qualitative urine tests in females for blood, sugar, albumin, sediment, and terminal blood urea nitrogen values were normal; no adverse effects were seen at 49 ppm
Source: NICNAS
07-SEP-2001 (129)

Species: monkey Sex: female
Strain: no data
Route of admin.: inhalation
Exposure period: ranging from 6 to 7 months
Frequency of treatment: 7 h/d, 5 d/w
Post. obs. period: no
Doses: 93 ppm (= ca. 0.569 mg/l)
Control Group: other: air-exposed control
Method:
Year: GLP: no
Test substance: other TS: purity: at least 99 %
Remark: two monkeys were used
Result: no adverse effects as judged by the criteria which follow: gross appearance, behaviour, growth, mortality, organ-weight studies, haematological data, qualitative

urine tests for blood, sugar, albumin and sediment, gross and microscopic examination of the tissues
Source: NICNAS
24-AUG-2001 (129)

5.5 Genetic Toxicity 'in Vitro'

Type: Ames test
System of testing: Eight strains of Salmonella typhimurium
Concentration: approximately 1 to 5 ul/plate
Cytotoxic Conc.: no data
Metabolic activation: without
Result: negative
Method:
Year: GLP: no
Test substance: no data
Source: NICNAS
24-AUG-2001 (10)

Type: Ames test
System of testing: Salmonella typhimurium TA 98, TA 100, UTH 8414, UTH 8413
Concentration: 50-2000 ug/plate
Cytotoxic Conc.:
Metabolic activation: with and without
Result: negative
Method:
Year: GLP: no data
Test substance:
Source: NICNAS
24-AUG-2001 (69)

Type: Ames test
System of testing: Salmonella typhimurium TA 98, TA 100, TA 1535, TA 1537
Concentration: 1-100 ug/plate
Cytotoxic Conc.:
Metabolic activation: with and without
Result: negative
Method:
Year: GLP: no data
Test substance: other TS: purity: 95 %
Source: Bayer AG Leverkusen
24-AUG-2001 (116)

Type: Ames test
System of testing: Salmonella typhimurium TA 97, TA 98, TA 100, TA 102, TA 1535, TA 1537, TA 1538
Concentration: no data
Cytotoxic Conc.:
Metabolic activation: with and without
Result: negative
Method:
Year: GLP: no data

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Test substance:
Source: NICNAS
24-AUG-2001 (146)

Type: Ames test
System of testing: Salmonella typhimurium TA 98, TA 100, TA 1535, TA 1537, TA 1538
Concentration: the compound was tested at five doses (no further data)
Cytotoxic Conc.:
Metabolic activation: with and without
Result: negative
Method:
Year: GLP: no data

Test substance:
Source: NICNAS
24-AUG-2001 (154)

Type: Ames test
System of testing: Salmonella typhimurium TA 98, TA 100, TA 2637
Concentration: 0.005-0.5 mg/plate
Cytotoxic Conc.:
Metabolic activation: with and without
Result: negative
Method:
Year: GLP: no data

Test substance:
Source: Bayer AG Leverkusen
24-AUG-2001 (188)

Type: Ames test
System of testing: Salmonella typhimurium TA 98, TA 100, TA 1535, TA 1537, TA 1538
Concentration: 0.02, 0.04, 0.08, 0.16, 0.32, 0.64, 1.28 or 2.56 ul/plate
Cytotoxic Conc.: 2.56 ul/plate
Metabolic activation: with and without
Result: negative
Method:
Year: GLP: no data

Test substance: other TS: purity: 98 %
Source: NICNAS
24-AUG-2001 (235)

Type: Ames test
System of testing: Salmonella typhimurium TA 98, TA 100, TA 1535, TA 1537
Concentration: 3.3, 10.0, 33.0, 100 or 333.0 ug/plate (exception: strain TA 100, no activation: 100.0, 1000.0, 10000.0 or 13000.0 ug/plate)
Cytotoxic Conc.:
Metabolic activation: with and without
Result: negative
Method:
Year: GLP:
Test substance: other TS: purity: 95 %

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DATE: 10-JUL-2003

ID: 95-50-1

Source:	NICNAS	
10-SEP-2001		(190) (251) (252)
Type:	Ames test	
System of testing:	Salmonella typhimurium TA 98, TA 100, TA 1535, TA 1537, TA 1538	
Concentration:	in this assay each chemical was usually tested at a minimum of six concentrations, with the highest non-toxic concentration tested being 10 mg/plate (no further data)	
Cytotoxic Conc.:		
Metabolic activation:	with and without	
Result:	negative	
Method:		
Year:	GLP: no data	
Test substance:	other TS: "technical grade" product or equivalent (no further data)	
Source:	NICNAS	
24-AUG-2001		(288)
Type:	Ames test	
System of testing:	Salmonella typhimurium TA 100	
Concentration:	0.001-5.0 ul/plate	
Cytotoxic Conc.:		
Metabolic activation:	with and without	
Result:	negative	
Method:		
Year:	GLP: no data	
Test substance:		
Source:	Bayer AG Leverkusen	
24-AUG-2001		(191)
Type:	Ames test	
System of testing:	Salmonella typhimurium TA 98, TA 100, TA 1535, TA 1537, TA 1538	
Concentration:	0.1, 1, 50 or 100 ul/plate	
Cytotoxic Conc.:		
Metabolic activation:	with and without	
Result:	negative	
Method:		
Year:	GLP: no data	
Test substance:		
Source:	Bayer AG Leverkusen	
24-AUG-2001		(157)
Type:	Bacillus subtilis recombination assay	
System of testing:	Bacillus subtilis strain H 17 (arg-, trp-, recE+) and Bacillus subtilis strain M 45 (arg-, trp-, recE-)	
Concentration:	0.6 ml	
Cytotoxic Conc.:		
Metabolic activation:	with and without	
Result:		
Method:		
Year:	GLP: no data	

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DATE: 10-JUL-2003

ID: 95-50-1

Test substance:
 Remark: result: 1,2-DCB showed DNA damaging potential
 without S9 activation but showed no damaging potential with
 S9 activation
 Source: NICNAS
 24-AUG-2001 (165)

Type: Bacillus subtilis recombination assay
 System of testing: Bacillus subtilis M45 (recA-) and H17 (recA+)
 Concentration:
 Cytotoxic Conc.:
 Metabolic activation: without
 Result: negative
 Method:
 Year: GLP: no data
 Test substance: other TS: "technical grade" product or equivalent (no further
 data)
 Source: NICNAS
 24-AUG-2001 (288)

Type: Bacterial reverse mutation assay
 System of testing: Aspergillus nidulans
 Concentration: 200 ug/ml
 Cytotoxic Conc.:
 Metabolic activation: without
 Result: negative
 Method:
 Year: GLP: no
 Test substance: other TS: o-dichlorobenzene was |relatively pure| (no further
 data)
 Source: NICNAS
 24-AUG-2001 (207) (208)

Type: Cytogenetic assay
 System of testing: Chinese hamster ovary cells
 Concentration: 20.2, 60.5 or 202 ug/ml (without metabolic activation) and
 20.2, 60, 152, or 202 ug/ml (with metabolic activation)
 Cytotoxic Conc.:
 Metabolic activation: with and without
 Result: negative
 Method:
 Year: GLP: no data
 Test substance: other TS: purity: 99.4 %
 Remark: type: chromosomal aberration assay
 Source: NICNAS
 24-AUG-2001 (158) (251)

Type: Cytogenetic assay
 System of testing: Chinese hamster ovary cells
 Concentration: 75, 100 or 143 ug/ml
 Cytotoxic Conc.:
 Metabolic activation: with and without
 Result: negative

Method:
Year: GLP: no data
Test substance: other TS: purity: 99.7 %
Remark: type: chromosomal aberration assay
Source: Bayer AG Leverkusen
24-AUG-2001 (29)

Type: DNA damage and repair assay
System of testing: primary rat hepatocytes
Concentration: up to 0.089 mM (= 13 mg/l) (highest nontoxic concentration)
Cytotoxic Conc.:
Metabolic activation: no data
Result: negative
Method:
Year: GLP: no data
Test substance:
Remark: method: autoradiographic hepatocyte/DNA-repair test
Source: NICNAS
24-AUG-2001 (234) (291)

Type: Escherichia coli reverse mutation assay
System of testing: Escherichia coli WP2 uvrA
Concentration: in this assay, each test chemical was assayed at a minimum of six concentrations, with the highest non-toxic concentration tested being 10 mg/plate (no further data)
Cytotoxic Conc.:
Metabolic activation: with and without
Result: negative
Method:
Year: GLP: no data
Test substance: other TS: "technical grade" product or equivalent (no further data)
Source: NICNAS
24-AUG-2001 (288)

Type: Gene mutation in Saccharomyces cerevisiae
System of testing: Saccharomyces cerevisiae D4
Concentration: 0.1, 1, 50 or 100 ul/plate
Cytotoxic Conc.:
Metabolic activation: with and without
Result: negative
Method:
Year: GLP: no data
Test substance:
Source: Bayer AG Leverkusen
24-AUG-2001 (157)

Type: HGPRT assay
System of testing: Chinese hamster ovary cells
Concentration: 88-220 ug/ml (with and without metabolic activation) and 16-180 ug/ml (with metabolic activation)
Cytotoxic Conc.:
Metabolic activation: with and without

Result: negative
Method:
Year: GLP: no data
Test substance: other TS: purity: 99.7 %
Source: Bayer AG Leverkusen (30)
24-AUG-2001

Type: Mitotic recombination in *Saccharomyces cerevisiae*
System of testing: *Saccharomyces cerevisiae* D3
Concentration: five concentrations of the test chemical were tested (no further data)
Cytotoxic Conc.:
Metabolic activation: with and without
Result: negative
Method:
Year: GLP: no data
Test substance: other TS: "technical grade" product or equivalent (no further data)
Source: NICNAS (288)
24-AUG-2001

Type: Mouse lymphoma assay
System of testing: L5178Y mouse lymphoma cells
Concentration: 3.25, 6.5, 13, 26, 39, 52, 65, 78, 104 or 130 ug/ml (without metabolic activation) and 6.5, 13, 26, 39, 52 or 78 ug/ml (with metabolic activation)
Cytotoxic Conc.:
Metabolic activation: with and without
Result:
Method:
Year: GLP: no data
Test substance:
Result: result: without S9 activation, 1,2-DCB was evaluated as nonmutagenic; with metabolic activation, 1,2-DCB was found to be mutagenic
Source: NICNAS (182) (251)
24-AUG-2001

Type: Sister chromatid exchange assay
System of testing: Chinese hamster ovary cells
Concentration: 5.9, 19.7 or 59 ug/ml (without metabolic activation) and 19.7, 59 or 197 ug/ml (with metabolic activation) or 300, 400 or 500 ug/ml (with metabolic activation)
Cytotoxic Conc.:
Metabolic activation: with and without
Result:
Method:
Year: GLP: no data
Test substance: other TS: purity: 99.4 %
Remark: result: a negative response was observed without metabolic activation, a positive response was observed with metabolic activation
Source: NICNAS (158) (251)
24-AUG-2001

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Type: other: DNA damage and repair
System of testing: Prophage-induction in Escherichia coli
Concentration: 431.78 - 221073.40 uM
Cytotoxic Conc.: 442146.79 uM
Metabolic activation: with and without
Result: negative
Method:
Year: GLP: no data
Test substance:
Remark: type: Microscreen prophage-induction assay;
Source: NICNAS
24-AUG-2001 (85)

Type: other: Differential toxicity assay
System of testing: Escherichia coli p3478 (polA-) and W3110 (polA+)
Concentration: at least two concentration levels of the test compound were used (no further data)
Cytotoxic Conc.:
Metabolic activation: without
Result: positive
Method:
Year: GLP: no data
Test substance: other TS: "technical grade" product or equivalent (no further data)
Source: NICNAS
24-AUG-2001 (288)

Type: other: bacterial bioluminescence assay
System of testing: one strain of Photobacterium phosphoreum
Concentration: no data
Cytotoxic Conc.:
Metabolic activation: no data
Result: negative
Method:
Year: GLP: no data
Test substance:
Source: NICNAS
24-AUG-2001 (95)

Type: other: in vivo-in vitro replicative DNA synthesis assay
System of testing: [methyl-3H]-thymidine-incorporation in mouse hepatocytes
Concentration: 1000 mg/kg bw and 2000 mg/kg bw
Cytotoxic Conc.:
Metabolic activation: no data
Result: negative
Method:
Year: GLP: no data
Test substance:
Remark: Results were negative for both doses at all time points
Source: NICNAS
Test condition: The role of 1,2-DCB as an inducer of DNA synthesis was assessed using an in vivo-in vitro replicative DNA synthesis assay with hepatocytes derived from male B6C3F1 mice;

animals were administered 1,2-DCB (1000 or 2000 mg/kg bw) by gavage and hepatocytes prepared 24, 39 or 48 hours later; replicative DNA synthesis was assessed after the addition of [methyl-3H]-thymidine followed by autoradiography

05-SEP-2001 (173)

Type: other: inhibition of the DNA synthesis
System of testing: human lymphocytes
Concentration: 1.47, 14.7 or 147 ug/ml
Cytotoxic Conc.:
Metabolic activation: with and without
Result:
Method:
Year: GLP: no data
Test substance: other TS: purity: 99 %
Remark: In the absence of metabolic activation, 1,2-DCB markedly reduced thymidine uptake at a dose studied and viability was 15 % of controls; thymidine uptake in the presence of metabolic activation remained unchanged at all doses studied; at 1 mM, cell viability decreased to 50 % of controls in the presence of metabolic activation

Source: NICNAS
05-SEP-2001 (204)

Type: other: umu test (DNA damage assay)
System of testing: Salmonella typhimurium TA1535/pSK1002
Concentration: highest concentration of o-dichlorobenzene examined in this study: 435 ug/ml
Cytotoxic Conc.:
Metabolic activation: with and without
Result: negative
Method:
Year: GLP: no data
Test substance:
Source: NICNAS

24-AUG-2001 (185)

Type: other: umu test (DNA damage assay)
System of testing: Salmonella typhimurium TA1535/pSK1002
Concentration: 100 ug/ml
Cytotoxic Conc.:
Metabolic activation: with and without
Result: negative
Method:
Year: GLP: no data
Test substance:
Source: NICNAS

24-AUG-2001 (200)

Type: other
System of testing: HeLa cells
Concentration: 350 ug/ml
Cytotoxic Conc.:
Metabolic

activation:
Result:
Method:
Year: GLP: no
Test substance: other TS: purity: >99 %
Remark: 1,2-DCB markedly inhibited the amino acid and uridine incorporation in unexposed HeLa cells; HeLa cells were exposed for 30 minutes to 350 ug/ml dosages of 1,2-DCB and the effects on [3H]uridine and 14C-labeled amino acids incorporation into RNA and protein were determined
Source: NICNAS
05-SEP-2001 (183)

5.6 Genetic Toxicity 'in Vivo'

Type: Cytogenetic assay
Species: rat Sex: male
Strain: other: COBS-CD (SD) Br
Route of admin.: s.c.
Exposure period: 16 d
Doses: 40, 200 or 1000 mg/kg bw/d
Result:
Method:
Year: GLP: yes
Test substance: other TS: purity: 98 %
Remark: type: chromosomal aberration assay
Result: o-dichlorobenzene did not induce a statistically significant increase in the number of chromosomal aberrations in bone marrow cells relative to the control at any dose
Source: Bayer AG Leverkusen
24-AUG-2001 (214)

Type: Cytogenetic assay
Species: rat Sex: male/female
Strain: Sprague-Dawley
Route of admin.: i.p.
Exposure period: the animals received a single i.p. injection and were sacrificed 6, 12 or 24 h later
Doses: 150, 300 or 600 mg/kg bw (6 h assay) and 135, 270 or 540 mg/kg bw (12 h assay and 24 h assay)
Result:
Method:
Year: GLP: no data
Test substance: other TS: purity: 99.7 %
Remark: the objective of this study was to assess the ability of o-dichlorobenzene to induce chromosomal aberrations in rat bone marrow cells
Result: type: chromosomal aberration assay
o-dichlorobenzene did not cause an increase in the frequency of chromosomal breaks or aberrations in the bone marrow cells
Source: Bayer AG Leverkusen
24-AUG-2001 (28)

Type: Drosophila SLRL test
Species: Drosophila melanogaster Sex: male
Strain:
Route of admin.: inhalation
Exposure period: single exposure for 4 h (concentrations: 2800, 4000 or 4300 ppm) or for 6 h (concentration: 2300 ppm)

Doses: 2300, 2800, 4000 or 4300 ppm (= 14.03, 17.08, 24.4 or 26.23 mg/l)

Result:
Method:
Year: GLP: no data

Test substance:
Result: o-dichlorobenzene did not induce sex-linked recessive lethal mutations

Source: Bayer AG Leverkusen
24-AUG-2001 (27)

Type: Drosophila SLRL test
Species: Drosophila melanogaster Sex: no data
Strain:
Route of admin.:
Exposure period:
Doses:
Result: negative
Method:
Year: GLP: no data

Test substance:
Source: Bayer AG Leverkusen
05-SEP-2001

Type: Micronucleus assay
Species: mouse Sex: male
Strain: NMRI
Route of admin.: i.p.
Exposure period: see remarks
Doses: 93.5, 187.5, 281 or 375 mg/kg bw
Result:
Method:
Year: GLP: no data

Test substance: other TS: purity: 99 %
Remark: 1,2-DCB was administered in two equal doses of 93.5, 187.5, 281 or 375 mg/kg bw, 24 hours apart; the animals were killed 30 hours after the first injection of 1,2-DCB

Result: 1,2-DCB induced a dose-related increase in the formation of micronucleated polychromatic erythrocytes, observed in femoral bone marrow

Source: NICNAS
24-AUG-2001 (174)

Type: Micronucleus assay
Species: mouse Sex: male
Strain: B6C3F1
Route of admin.: i.p.
Exposure period: 3 d
Doses: 50, 100, 150, 200 or 250 mg/kg bw/d
Result: negative
Method:
Year: GLP: no data

Test substance:
Remark: this assay employed three daily exposures; bone marrow samples were obtained 24 hours following the final exposure

Source: NICNAS
24-AUG-2001 (231)

Type: other: (white/white+) eye mosaic assay

Species: Drosophila melanogaster Sex: female
Strain:
Route of admin.: inhalation
Exposure period: 17 hours
Doses: 500, 1000 or 2000 ppm (ca. 3, 6 or 12 mg/l)
Result: negative
Method:
Year: GLP: no data
Test substance:
Remark: 2000 ppm = lethal dose
the (w/w+) eye mosaic assay is an in vivo short-term test
measuring genetic damage in somatic cells of Drosophila
after treatment of larvae
Source: NICNAS
24-AUG-2001 (277)

Type: other: (white/white+) eye mosaic assay
Species: Drosophila melanogaster Sex: female
Strain:
Route of admin.: oral feed
Exposure period: chronic exposure (no further data)
Doses: 5 or 10 mM
Result:
Method:
Year: GLP: no data
Test substance:
Remark: 10 mM = lethal dose
the (w/w+) eye mosaic assay is an in vivo short-term test
measuring genetic damage in somatic cells of Drosophila
after treatment of larvae
Result: marginally positive response associated with cytotoxicity
Source: NICNAS
24-AUG-2001 (277)

Type: other: DNA damage assay
Species: rat Sex: female
Strain: Sprague-Dawley
Route of admin.: gavage
Exposure period: see remarks
Doses: 100 or 300 mg/kg bw
Result:
Method:
Year: GLP: no data
Test substance:
Remark: experimental design: hepatic DNA damage by alkaline elution;
female rats received two doses of 300 mg/kg bw of 1,2-DCB;
the first and second dose 21 and 4 h before
sacrifice, respectively; no indications of hepatic DNA damage
were evident
Source: Bayer AG Leverkusen
10-SEP-2001 (144)

5.7 Carcinogenicity

Species: rat Sex: male/female
Strain: other: F344/N
Route of admin.: gavage
Exposure period: 103 w
Frequency of

treatment: 5 d/w
 Post. obs. period: no
 Doses: 60, 120 mg/kg body weight (dose volume: 5 ml/kg bw)
 Result: negative
 Control Group: yes, concurrent vehicle
 Method:
 Year: GLP: no data
 Test substance: other TS: purity: >99 %
 Remark: Histological examination in both sexes revealed no increase in non-neoplastic lesions in the liver, kidney, bone marrow, spleen, thymus or other organs; although the incidence of pheochromocytoma in males was increased in the low-dose group (16/50) the high-dose incidence (6/49) was lower than the control animals (9/50) with no significant dose-response trend being evident; under the conditions of the study, 1,2-DCB was not considered to be carcinogenic in rats
 Source: NICNAS
 10-SEP-2001 (190)

Species: rat Sex: male
 Strain: no data
 Route of admin.: gavage
 Exposure period: 9 months
 Frequency of treatment: daily
 Post. obs. period: no data
 Doses: 0.001, 0.01 or 0.1 mg/kg bw/d
 Result:
 Control Group: yes, concurrent vehicle
 Method:
 Year: GLP: no
 Test substance:
 Result: the macroscopic, histological and histochemical data did not reveal evidence of carcinogenic activity with the concentrations investigated (no further data)
 Source: NICNAS
 24-AUG-2001 (270)

Species: mouse Sex: male/female
 Strain: B6C3F1
 Route of admin.: gavage
 Exposure period: 103 w
 Frequency of treatment: 5 d/w
 Post. obs. period: no
 Doses: 60, 120 mg/kg body weight (dose volume: 5 ml/kg bw)
 Result:
 Control Group: yes, concurrent vehicle
 Method:
 Year: GLP: no data
 Test substance: other TS: purity: >99 %
 Remark: There appeared to be a dose-related trend in tubular regeneration of the kidney in male mice (control, 17%; low dose, 24%; high dose, 35%) however, statistical significance was not reported; incidence of malignant histiocytic lymphoma in male (control, 0/50; low-dose, 1/50; high-dose 4/50) and female (control, 0/49; low-dose, 0/50; high-dose, 3/49) mice was significantly increased (p < 0.05) however,

these findings were dismissed, as the numbers of animals with all types of lymphomas (combined), which is considered to be a better indicator, had not increased; under the conditions of this study, there was no evidence of carcinogenicity of 1,2-DCB for male or female B6C3F1 mice

Source: NICNAS (190)
10-SEP-2001

Species: rat Sex: male/female
Strain: Sprague-Dawley
Route of admin.: i.p.
Exposure period: see remarks
Frequency of treatment: see remarks
Post. obs. period: see remarks
Doses: 1.0 mmol/kg bw (= 147 mg/kg bw)
Result: negative
Control Group: yes
Method: other: see remarks
Year: GLP: no data
Test substance: no data
Remark: in an initiation-promotion bioassay (rat liver foci bio-assay), 1,2-DCB was tested for its ability to enhance the incidence of diethylnitrosamine-initiated GGT foci (focal hepatic areas with increased gamma-glutamyltranspeptidase activity): the animals received a 2/3 partial hepatectomy followed 1 day later by oral (gavage) administration of 0.5 mmol/kg bw (= 51 mg/kg bw) of diethylnitrosamine (initiator); the rats were then administered 1,2-DCB by i.p. injection at 1 and 5 weeks; 2 weeks after the final dose of 1,2-DCB was administered, the rats were sacrificed; the prepared liver sections were analyzed for the incidence of GGT foci and other lesions

Result: 1,2-DCB did not initiate or promote tumour formation using the g-glutamyltranspeptidase-positive foci (compared with controls)

Source: NICNAS (123)
24-AUG-2001

5.8 Toxicity to Reproduction

Type: Two generation study
Species: rat Sex: male/female
Strain: no data
Route of admin.: inhalation
Exposure Period: see remarks
Frequency of treatment: daily exposure time unspecified
Premating Exposure Period
male: see remarks
female: see remarks
Duration of test: see remarks
Doses: 50, 150 or 400 ppm (= ca. 0.305, 0.915 or 2.44 mg/l)
Control Group: yes
Method:
Year: GLP: no data
Test substance:
Remark: study design: groups of male and female rats (designated

as the F0 generation) were exposed to vapour of o-dichlorobenzene at concentrations of 50, 150 and 400 ppm for 10 weeks prior to mating, during mating, gestation and lactation; groups of male and female rats were selected from the progeny of the F0 generation and this constituted the F1 generation; the F1 generation was similarly exposed to o-dichlorobenzene for 11 weeks postweaning, mating, gestation and lactation; all F2 pups were observed through weaning only

Result: no compound-related mortality was observed; no treatment related effects were observed on reproductive performance or fertility indices in either generation in this study; body weights of F0 and F1 adults in the high dose group were significantly depressed during the growth period and continued to be lower until terminal sacrifice; pup weights were significantly lower in the high dose group and minimally lower in the mid dose group; liver weights were increased in the mid and high dose group males and females while kidney weights were increased in mid and high level males; these organ weight changes were accompanied by histopathological changes in the liver and kidney; only a slight increase in liver weight was observed in the low dose males

Source: Bayer AG Leverkusen (184)
24-AUG-2001

Type: Two generation study
Species: rat Sex: male/female
Strain: Crj: CD(SD)
Route of admin.: inhalation
Exposure Period: 281 d
Frequency of treatment: see TC freetext field
Premating Exposure Period

male: see TC freetext field
female: see TC freetext field
Duration of test: 281 d
Doses: Target exposure levels: F0 and F1: 0, 50, 150 and 400 ppm
Control Group: yes
Method:
Year: GLP:
Test substance:
Remark: Study Design: Eight additional females (F0 and F1) were sorted into each treatment group (satellite group); Clinical observations performed (Parental generation Data)
Adult Body weight: F0 and F1 adult males recorded weekly throughout study duration; F0 and F1 adult females recorded weekly, during pre-mating treatment periods, on Days 0, 7, 14 and 20 of gestation and on Days 0, 4, 14 and 21 of lactation; Additionally, body weights on Day 28 of lactation were recorded for the F0 generation females; Body weights were not recorded for F0 and F1 satellite females;
Pup Body Weight: F1 litter weights were recorded on Days 0, 4 (pre- and post-cull), 14, 21 and 28 of lactation; F2 litter weights were recorded on Days 0, 4 (pre- and post-cull), 7, 14 and 21 of lactation; Post-mortem Data: Terminal Body weight and Organ Weight Data F0 and F1 (Adult); Gross Post-mortem evaluations (Adult Generations); Gross Post-mortem evaluations - F1 and F2 Pups; Histopathological Evaluations - Adult Generations: Litter observations: Litters examined twice daily for general

appearance of pups and presence of dead pups; Dead or Stillborn: Weighed and given gross internal and external examination including internal sex determination. Pups found dead were not eviscerated; Organs examined at necropsy (macroscopic): F0 and F1 Adults: liver, kidneys, testes and brain weights were recorded; microscopic: F0 and F1 Adults, control and high dose: liver, kidneys, pituitary gland, testes, epididymides, seminal vesicles, prostate, vagina, uterus, ovaries; Livers of all F0 and F1 adults in low & mid-dose groups; Kidneys of F0 and F1 males from all dosed groups were evaluated for eosinophilic granules and granular casts

Result: Mortality:
Some mortality was seen among the control and treated adult animals in each generation however no adverse effect of treatment was indicated

Body weight:
(F0): High-dosed males had significantly lower body weight throughout the exposure period and a significantly lower terminal body weight (-10%) compared to controls; high-dosed females had significantly lower body weight during pre-mating and at termination (-5%); (F1): High-dosed males had significantly lower body weight throughout the exposure period and significantly lower terminal body weight (-19%) compared to controls; high-dosed females had significantly lower body weight during pre-mating, gestation and lactation periods and at termination (-9%)

Food consumption data (Pre-mating treatment Interval):
F0 and F1: Statistically significant increases in food consumption amongst mid- and high-dosed groups

Physical Observation Data- F0: Anogenital (A-G) staining at weeks 8 and 12 in mid-dosed males increased slightly above control groups; high-dosed groups showed excessive salivation at weeks 2-4, 8 and 12 (males) and weeks 3 and 4 (females)

F1: High-dosed groups showed excessive salivation with increased incidence early in the pre-mating treatment period at weeks 21, 22, 24 and 28 (males) and weeks 21-24 (females); three control males at week 37-38 (post-mating period) presented with ocular lesions, chromodacryorrhea, swollen jaw area, squinted eyes and dry eyes; all symptoms suggestive of SDAV infection; SDAV antibodies were detected from serum collected from all 3 animals; females were reported as free of symptoms of SDAV infection

Mating Indices, Pregnancy Rates and Male Fertility Indices:
F0 & F1: Mating indices, pregnancy rates and male fertility indices were comparable between treatment groups & controls; of the males that failed to mate with females, very few failed to mate with females in a satellite group; at necropsy, one F0 female had three uterine implantation scars however the status of implantation in the absence of parturition is unclear; consequently, the animal was not included in pregnancy rate calculations

Gestation Length and Parturition Data: F1 and F2 litters:
Gestation: A small, statistically significant decrease in

gestation length was observed in low-dosed animals; mean gestation length for F2 litters was comparable to control for each of the treated groups

Parturition: Mean number of live and total pups per F1 litter at birth was statistically higher in the low- and mid-dosed animals when compared to controls; the mean number of dead pups in each treated group of the F1 and F2 litters was not significantly different from controls; F1 pup viability indices (ratio of live/total at birth) were similar to controls; a statistically significant increase in pup viability for low-dosed F2 litters was noted

Litter Size Data: F1 litters: Mean litter size was statistically higher in the low- and mid-dosed animals
F2 litters: Mean litter size was comparable between control and treated groups

Litter Survival Indices:

F1 litter Interval: The litter survival index was comparable between control and treated groups

F2 litter Interval: The litter survival index was comparable between control and treated groups

Unselected F1 High-dose Pups: Male and female F1 high dose pups left untreated and maintained on basal diets showed no significant change in food consumption or weight gain from F1 control group data (for the 10-week growth period coincident with the pre-mating treatment period of the F1 adult generation)

Pup Weight Data - Lactation Interval

F1 Pups: A statistically significant decrease in mean pup weight was seen at Day 0 in mid- and Days 0, 14, 21 and 28 in high-dosed groups; at Day 28, mean pup weight in the high-dosed group was 11% lower than controls

F2 Pups: A statistically significant decrease in mean pup weight was seen at Days 14 and 21 in high-dosed groups only; at Day 21, mean pup weight was 21% lower than controls

Pup Survival Indices:

F1 Litters: A statistically significant increase in the pup survival index for mid-dosed animals was noted during Days 4-21 of the lactation

F2 Litters: A statistically significant decrease in the pup survival index (94.3%) for high-dosed animals compared to controls (98.1%) was noted during Days 0-4 of the lactation interval largely attributed to the loss of all pups within a single litter; pup survival for the high-dose group over Days 4-21 lactation was comparable to controls

Dead Pup Observations:

F1 Litters: The numbers of dead pups recovered at birth or during the 28-day lactation period were 29 controls, 23-low dosed, 11 mid-dosed and 19 high-dosed animals did not present with external or internal malformations

F2 Litters: The numbers of dead pups recovered at birth or

during the 21-day lactation period were 25 controls, 13-low dosed, 12 mid-dosed and 19 high-dosed animals did not present with external or internal malformations

Post-mortem Data- Organ Weight Data (F0 and F1 Adults):
F0: High-dose: Mean brain weight (males) were statistically significantly lower; mean relative brain weight was statistically significantly higher in females

Mid- and high-dose: relative kidney weights were statistically slightly higher in females absolute and relative kidney weights in males were statistically significantly higher

Absolute and relative liver weights (both sexes) were statistically higher in mid and high-dosed groups; absolute liver weights were significantly higher in low-dosed males

Relative testes weight in high-dosed animals was statistically significantly higher than controls; absolute testes weights and mean/brain weight ratios were comparable to controls

F1: High-dose: Absolute brain weight (both sexes) were statistically significantly lower than controls, relative brain weight was statistically significantly higher for males

Mid- and high-dose: Relative kidney weights (males) were statistically significantly higher; Absolute and relative liver weights (both sexes) were statistically higher than control groups

Relative testes weight in high-dosed animals was statistically significantly higher than controls; absolute testes weights and testes/brain weight ratios were comparable to controls

Gross Post-mortem Evaluations - Adult Generations F0 and F1 Adults: No adverse effects noted; F1 and F2 Pups: A small number of unilateral occurrences of dilated renal pelves predominantly in females of both generations in treated and control groups

Histopathological Evaluations
Liver (F0 and F1 Adults): Hypertrophy of central lobular hepatocytes was evident in most high-dose adults (both sexes) exposed to 400 ppm dichlorobenzene; Similar effects were noted in mid-dosed males and to a lesser extent in mid-dosed females; no effects were noted in low-dosed animals

Kidney (F0 and F1 Adults):
High dosed (and to a lesser extent mid-dosed) males developed dilated tubular lumens with intraluminal granular casts, predominantly at the cortico-medullary junctions; dose-dependent increase in intracytoplasmic granules/droplets in the proximal convoluted tubular epithelium; no effects were reported in females

Source: NCINAS
Test condition: Frequency of Treatment

Adults:F0 Males and females: daily 7 d/wk, 6 h/d from 10-week pre-mating period and during mating; males continued to be exposed until sacrifice (3-4 weeks post-mating); females were exposed daily during the Day 0-19 gestation interval; F0 Females were not exposed from Day 20 of gestation to Day 4 of lactation; daily exposure resumed on Day 5 of lactation until scheduled sacrifice after weaning of F1 litters; F1 and F2 Pups:Two randomly selected F1 pups from each sex and litter were exposed from Day 29 postpartum; these represented the F1 adult generation; F1 animals were then exposed 7 d/wk, 6 h/d for an 11-week pre-mating period and then as for F0 animals; resultant F2 pups were exposed and sacrificed on Day 21 of lactation; exposure period F0: 104-106 d (males); 142 d (females) F1: 148 or 149 d (males); 157 or 158 d (females)

Statistical Methods

All interval data were tested for equal variance by Bartlett's test. Significance amongst treated groups were determined by standard one-way ANOVA and their significance from controls using the Dunnett's test. Unequal variances were determined by the Kruskal-Wallis test and their significance from controls using the summed rank (Dunn) test. Incidence rate data (mortality, mating, pregnancy and fertility) including pup and litter survival data were tested for significance using contingency tables. Differences between groups were determined using a standard chi-square analysis and significance compared to controls were determined using a 2x2 Fisher Exact test.

Conclusion: Under the conditions of the study, no treatment related effects on fertility were observed; Mid- and high (400 ppm) exposure revealed kidney effects in males and liver effects in males and females; The only effect on pups was reduced body weight during lactation at 400 ppm; The NOAEL for

adult toxicity is 50 ppm and LOAEL is 100 ppm

05-OCT-2001

(26)

Type: other
Species: rat Sex: male
Strain: Sprague-Dawley
Route of admin.: i.p.
Exposure Period: single administration
Frequency of treatment:
Duration of test:
Doses: 50, 100, 250, 300 or 800 mg/kg bw
Control Group: yes
Method:
Year: GLP: no data

Test substance:
Remark: in this assay the induction of sperm abnormalities was investigated in rats treated with 1,2-DCB

Result: the animals were sacrificed 10 days post-exposure light microscopic observation of sperm suspensions revealed morphological abnormalities in sperm such as banana heads, acrosomal defects, and tail curlings and twisting; both sperm head and tail abnormalities seem to show a dose response relationship between concentration of 1,2-DCB and percent abnormality

Source: NICNAS

24-AUG-2001

(181)

5.9 Developmental Toxicity/Teratogenicity

Species: rat Sex: female
 Strain: Fischer 344
 Route of admin.: inhalation
 Exposure period: days 6 through 15 of gestation
 Frequency of treatment: 6 h/d
 Duration of test: the dams were sacrificed on day 16 of gestation
 Doses: 1.2, 2.4 or 3 mg/l
 Control Group: yes
 Method:
 Year: GLP: yes
 Test substance: other TS: purity: 98.81 %
 Remark: the objective of this study was to establish maximum tolerated exposure levels of o-dichlorobenzene via inhalation for pregnant rats for use in the definitive teratology study
 Result: all exposure levels: no statistically significant effects on reproductive parameters
 2.4 mg/l: decreased food consumption and increased relative liver and kidney weights in the pregnant rats
 3 mg/l: severe maternal toxicity, evidenced by significant decreases in body weight, body weight gain and food consumption, increases in relative liver and kidney weights, and signs of systemic toxicity at gross necropsy observable in pregnant rats; embryoletality observable among the rats exhibiting the most severe signs of maternal toxicity
 Source: Bayer AG Leverkusen (115)
 24-AUG-2001

Species: other: rat and rabbit Sex: male/female
 Strain: other: Fischer-344 and New Zealand White
 Route of admin.: inhalation
 Exposure period: rats: 6 h/day on days 6 through 15 of gestation; rabbits: days 6 through 18 gestation
 Frequency of treatment: 6 h/d
 Duration of test: the rats were sacrificed on day 21 of gestation and rabbits on day 29 gestation
 Doses: 0.6, 1.2 or 2.4 mg/l (100, 200 or 400 ppm)
 Control Group: other: the control group of rats and rabbits were exposed to filtered room
 Method:
 Year: GLP: no data
 Test substance: other TS: purity: 98.81 %
 Result: Rabbits: decrease in body weight gain in dams during the first three days of exposure at all dose levels; at doses up to 400 ppm 1,2-DCB did not prove to be embryotoxic, fetotoxic or teratogenic in the rabbit based on observations of the number of pregnancies, litter size, resorption rate, foetal body measurements or foetal malformations.

Rats: significant decrease in body weight gain from gestation days 6 through to 20 at all dose levels; a significant increase in maternal liver weights occurred with rats exposed to 400 ppm; the only developmental treatment-related effect was a significant increase in the occurrence of delayed ossification of cervical vertebral

centra in the highest dose group, however, these effects occurred at maternally toxic doses

Source: NICNAS (117) (136)
07-SEP-2001

Species: rat Sex: female
Strain: Sprague-Dawley
Route of admin.: gavage
Exposure period: days 6 through 15 of gestation
Frequency of treatment: daily
Duration of test: no data
Doses: 50, 100 or 200 mg/kg bw/d
Control Group: no data specified
Method:
Year: GLP: no data
Test substance:
Remark: 1,2-DCB did not have any teratological effect (no further data)

Source: NICNAS
Test condition: maternal weight gain, changes in microscopic examination
24-AUG-2001 (223)

5.10 Other Relevant Information

Type: Biochemical or cellular interactions
Remark: twenty-two hours after a single i.p. injection of 14C-o-dichlorobenzene (dose: 127 uCi/kg bw) into male rats and mice, the test substance was covalently bound to DNA of liver, kidney, lung and stomach; in all assayed organs, the specific activity of DNA from mouse organs was higher than that measured in rat organs: this difference was particularly remarkable in the case of lung DNA; no particular organ-specific difference was observed as regards labelling of mouse DNA, whereas labelling of rat liver DNA was higher than that of DNA from other rat organs; the extent of binding to RNA of various organs was higher than that of DNA, with mouse RNA labelling again higher than rat RNA labelling; no difference between rat and mouse organs was observed as regards the extent of protein binding, which was higher than DNA labelling

Source: Bayer AG Leverkusen (67)
24-AUG-2001

Type: Biochemical or cellular interactions
Remark: in vitro assay: the enzyme-mediated interaction of 14C-o-dichlorobenzene with calf thymus DNA or synthetic polyribonucleotides was carried out by a microsomal mixed-function oxidase system and microsomal glutathione-transferases: the binding of 14C-o-dichlorobenzene to calf thymus DNA mediated by liver microsomes increased linearly with incubation time up to 90 minutes, then it reached a plateau; microsomal enzymes from liver and lung bioactivated o-dichlorobenzene to intermediate(s) capable of interacting with exogenous DNA; rat liver microsomes were more efficient than mouse liver microsomes, but the opposite situation was observed for lung microsomes; the activity of cytosolic enzymes was very low or negligible; the copresence of microsomal and cytosolic fractions from rodent lung in the incubation mixture gave rise to a synergistic effect,

<p>Source: 06-AUG-1993</p>	<p>which did not occur when the liver fractions were used; the pattern of ¹⁴C-o-dichlorobenzene interaction with microsomal RNA and proteins resembled that of the interaction with DNA; however, microsomal protein labelling was higher than microsomal RNA or calf thymus DNA labellings</p>	<p>(67)</p>
<p>Type: Remark:</p>	<p>Biochemical or cellular interactions the c-mitotic activity of some benzene derivatives, including o-dichlorobenzene, was studied in <i>Allium cepa</i> (onion); full c-mitosis was observed at a concentration of 300 uM; partial disturbances in mitosis were observable at a concentration of 100 uM and normal mitosis was seen at a concentration of 30 uM</p>	
<p>Source: 24-JUL-2001</p>	<p>Bayer AG Leverkusen</p>	<p>(201)</p>
<p>Type: Remark:</p>	<p>Biochemical or cellular interactions 1,2-DCB binding in the rat lung increased after 6 h and was less marked after 24 h exposure; 1,2-DCB binding preceded necrosis of bronchiolar epithelium by 24 h; phenobarbital pretreatment slightly decreased binding</p>	
<p>Source: Test condition:</p>	<p>NICNAS Species: rat Strain: Sprague-Dawley No. of animals: 6 Sex: Male Route of Administration: intraperitoneal injection Dose: 0.5 mM/kg 1,2-DCB-[¹⁴C] Frequency of Treatment: once</p>	
<p>Test substance: 10-AUG-2001</p>	<p>GLP: no data Purity not stated</p>	<p>(213)</p>
<p>Type: Remark:</p>	<p>Chemobiokinetics general studies The study investigate the affinity of 1,2-DCB for the Thyroxin (T4) binding site of transthyretin (TTR) in human serum using an in vitro standard T4 competition assay; 1,2-DCB was an inefficient competitor for the T4 binding site of human TTR</p>	
<p>Source: Test condition:</p>	<p>NICNAS Species: human serum Route of Administration: ex vivo Dose: 100 uM Frequency of Treatment: T4 competition assay GLP: no data</p>	
<p>10-AUG-2001</p>		<p>(268)</p>
<p>Type: Remark:</p>	<p>Chemobiokinetics general studies 1,2-DCB increased peak latencies and significantly decreased peak N160 amplitude (ED50 151.6 mg/kg) at 0.5, 1, 2 and 4 hours after dosing; colonic temperature decreased in parallel; other peak amplitudes were not significantly altered</p>	
<p>Source: Test condition:</p>	<p>NICNAS Species: rat Strain: Long-Evans Sample size: 15-19 per treatment group Sex: Male</p>	

	Route of Administration: intraperitoneal Dose: 53, 105, 210 or 420 mg/kg Testing Period: 0.5, 1, 2, 4 and 24 h Frequency of testing: once GLP: no data	
15-AUG-2001		(122)
Type:	Cytotoxicity	
Remark:	No evidence of toxicity (as evaluated by intracellular K+ content, lactate dehydrogenase leakage and protein synthesis) in Sprague-Dawley rat liver slices maintained in dynamic organ culture for up to 5 hours with 1mM (= ca. 147 mg/l) 1,2-DCB compared to untreated controls; phenobarbital treated rats revealed toxicity in all parameters whether following 3 h or 6 h incubated with 1.0 mM 1,2-DCB	
Source:	NICNAS	
Test condition:	Species: rat Strain: Sprague Dawley No. of animals: liver slices Sex: M Route of Administration: ex vivo Dose (mM): 1.0 mM Exposure (h): 3h and 6h continuous incubation Frequency of Treatment: once GLP: no data	
10-AUG-2001		(41)
Type:	Cytotoxicity	
Remark:	A majority of treated animals presented with liver necrosis at all dose/exposure times studied and renal damage; frequent eye and nose irritation	
Source:	NICNAS	
Test condition:	Species: rat; mouse; guinea pig Strain: not stated No. of animals: 2-10 per group Sex: M Route of Administration: inhalation Dose (%): 0.005-0.080 rats; 0.005 mouse; 0.080 guinea pig Exposure: 0.5 h - 50 h Frequency of Treatment: once GLP: no data	
Test substance:	Both commercial and pure 1,2-DCB were tested, however no values were stated	
24-AUG-2001		(58)
Type:	Cytotoxicity	
Remark:	1,2-DCB caused hepatic cytotoxicity as measured by increased intracellular K+ and decreased protein synthesis; potentiation of toxicity was observed with liver slices prepared from phenobarbital-induced rats; liver slices prepared from Fischer-344 rats were substantially more affected by 1,2-DCB than from Sprague-Dawley	
Source:	NICNAS	
Test condition:	Species: rat Strain: Sprague Dawley and Fisher 344 No. of animals: 4 animals per dose Sex: M Route of Administration: ex vivo Dose: 1, 2 and 5 mM Exposure (h): liver slices were incubated for up to 6 h Frequency of Treatment: once	

	GLP: no data	
Test substance: 29-AUG-2001	1,2-DCB dissolved in 1% DMSO	(100)
Type: Remark:	Cytotoxicity primary cultures of rat hepatocytes were treated with o-dichlorobenzene at a concentration of 0.5 mM (= 73.5 mg/l) for 20 hours; the acute cytotoxicity was assessed by the following cellular markers: leakage of intracellular lactate dehydrogenase, glycogenolytic activity as a specific function of hepatocytes and observations of cytopathic effects: in this assay o-dichlorobenzene did not reveal significant cytotoxic effects	
Source: 24-AUG-2001	Bayer AG Leverkusen	(180)
Type: Remark:	Cytotoxicity in vitro assay: the effects of o-, m-, and p-dichlorobenzene on isolated rat liver and kidney cells were examined; isomers of dichlorobenzene (o-, m-, p-) did not have any effects at 0.5 mM (= ca. 73 mg/l) on the glutathione contents and the viabilities of hepatocytes but decreased them at 1 mM (= ca. 147 mg/l); the potencies were: o-isomer>= m-isomer>= p-isomer; those of hepatocytes obtained from phenobarbital pretreated rats were decreased by dichlorobenzenes at 0.5 mM; the potencies were: o-isomer>= m-isomer> p-isomer; amounts of glutathione conjugates of o- and m-dichlorobenzene outside of the cells were increased; the amounts of oxidized glutathione were not different from control experiments; in the case of renal cells, decreases in glutathione contents and viabilities by dichlorobenzenes (1 mM) appeared without phenobarbital pretreatment; the potencies were: o-isomer> m-isomer>= p-isomer	
Source: 24-AUG-2001	Bayer AG Leverkusen	(194)
Type: Remark:	Cytotoxicity in vitro assay: the effects of o-dichlorobenzene on rat hepatocyte functions were studied; the viability of hepatocytes as well as glutathione concentrations were decreased; o-dichlorobenzene diminished the content of cytochrome P 450 and decreased lipid peroxidase and xanthine oxidase activities	
Source: 24-AUG-2001	Bayer AG Leverkusen	(206)
Type: Remark:	Cytotoxicity cancer promotion activity test with HL-60 cells established from human leukaemia HL-60 cells incubated in vitro with 1,2-DCB for 20 hours; the morphological change of the cells was examined using phorbol-myristate-acetate (PMA) as differentiating agent; cell viability in HL60 cells following 20 h exposure to 200 mM 1,2-DCB was entirely eliminated; morphological change of HL-60 cells to macrophages was not observed following exposure to 1,2-DCB, suggesting that 1,2-DCB is not a cancer promotor	
Source: Test condition:	NICNAS Cell Type: HL60 Dose: 200 mM	

Exposure 20 h continuous incubation (log phase)
 Frequency of Treatment: once
 GLP: no data
 Post Exposure Obs: Cytotoxicity measured by trypan blue exclusion

Test substance: 1,2-DCB was dissolved in 0.05% DMSO to a final concn of 200 mM

05-SEP-2001 (264)

Type: Cytotoxicity
 Remark: No alteration in serum IL-6 at any dose; non-statistically significant increases in TNF-alpha levels post 6 h exposure to 500 and 600 mg/kg with effects being undetectable at other dose/time points; statistically significant decrease in serum-borne-induced immunosuppression of AFC and NK cell activity

Source: NICNAS
 Test condition: Species: mice
 Strain: Swiss OF1
 No. of animals: 8 mice per group. One control group and five treated groups exposed for various time periods per dose tested
 Sex: M
 Route of Administration: gavage
 Dose: 300; 500 and 600 mg/kg bw (controls recieved corn oil)
 Exposure Period: treated groups of 6 h 16, 24, 48 and 72 h
 Frequency of Treatment: once
 GLP: no data
 Post Exposure Obs: Humoral immune response of antibody forming cell (AFC) and natural killer cell (NK) cytotoxicity activity. Immunosuppressive effect on serologic tumour necrosis factor-alpha (TNF-a) and interleukin-6 (IL-6).

Test substance: purity: 99%

29-AUG-2001 (17)

Type: Distribution
 Remark: 1 week after termination of the administration the animals were killed and the contents of 1,2-DCB in the fatty tissue of the kidneys and of the inner genitals were determined; after administration of 2 or 4 mg/kg bw/d of 1,2-DCB for 4 weeks, the content of the substance in the fatty tissue was determined to be 30 or 60 mg/kg of fat tissue, respectively; after administration for 3 months at 4 mg/kg bw/d, the content of 1,2-DCB in fat tissue amounted to 100 mg/kg of fat tissue; in the animals dosed with 4 mg/kg bw/d for 4 w, the 1,2-DCB concentrations in fat tissue were nearly unchanged 1 week after termination of the application, however, 1,2-DCB was not detected 3 weeks after the end of the administration

Source: NICNAS
 Test condition: Species: rat
 Strain: albino
 Number of animals:
 Sex: Male
 Route of Administration: gavage
 Dose: 2, 4 mg/kg/bw
 Testing Period: 4, 8 or 12 wks
 Frequency of testing: once
 GLP: no data
 Post Exposure Obs: contents of 1,2-DCB in the fatty tissue of the kidneys and of the inner genitals were determined

24-JUL-2001

(131)

Type: Distribution
Remark: the translobular uptake pattern of ¹⁴C-labeled-1,2-DCB in the rat liver examined by the recirculating autologous blood liver perfusion procedure showed 1,2-DCB was completely absorbed during the first passage through the liver; subsequent perfusion indicated rapid reversible hepatic uptake and release were observable, with an average hepatic transit time of 1.3 min

Source: NICNAS

Test condition: Species: rat
Strain: Sprague-Dawley
Number of animals: 12 (2 per treatment group; excluding controls)
Sex: Male
Route of Administration: hood perfusion
Dose: 0.65 uM
Testing Period:
Frequency of testing: once
GLP: no data
Post Exposure Obs: elution of 1,2-DCB in situ at the "void volume" was monitored as an indicator of hepatic uptake efficiency

Test substance: 1,2-DCB 99% pure

10-AUG-2001

(260)

Type: Excretion
Remark: Catechols were excreted during a period of 3-4 days following administration of 0.5 g/kg; the peak excretion occurred on the second day; the average catechol excretion amounted to 7.8 % of the administered dose of 1,2-DCB. In a second experiment, three rabbits were each fed with 1500 mg of 1,2-DCB and their urines collected for 24 h: in the hydrolysed urine 4,5-dichlorocatechol was identifiable

Source: NICNAS

Test condition: Species: rabbit
Strain: Chinchilla
No. of animals: 3
Sex: Female
Route of Administration: gavage
Dose: 0.5 g/kg and 1500 mg
Frequency of Treatment: once
GLP: no data
Post Exposure Obs: Urinalysis over 5 day period post treatment for excretion of catechols

24-AUG-2001

(15)

Type: Excretion
Remark: after oral administration of o-dichlorobenzene to mammals (probably to dogs) small amounts of mercapturic acid were detectable in the urine (no further data)

Source: Bayer AG Leverkusen

24-JUL-2001

(23)

Type: Excretion
Method: Species: human Strain:
Sample size: 8
Sex: M
Route of Administration: not applicable
Dose: 0
Testing Period: 60 minutes

Frequency of testing: once
GLP: no data
Post Exposure Obs: Incidental trace amounts of 1,2-DCB was identified in subjects during cryogenic sampling in respired air.

Remark: 1,2-DCB was identified in expired air in 7 out of 8 subjects at concentrations between 0.001 and 26.0 ug/hr. Previous exposure to o-DCB (cake form) used as a deodorant in the wash room, was thought to contribute to the trace composition in subjects during the cryogenic sampling

Source: NICNAS
24-AUG-2001 (68)

Type: Immunotoxicity
Remark: 4 h exposure to vapourised 1,2-DCB induced adrenal dependent leucopenic effect without any change in red blood cell (RBC) and leucocyte differential (LD) counts compared to untreated controls; leukopenia was dose-dependent and significant at 10 ppm and above

Source: NICNAS
Test condition: Species: rat
Strain: Sprague-Dawley
No. of animals: 10 (per group)
Sex: Male
Route of Administration: Inhalation
Dose: 5-29 ppm
Exposure Period: 4 h
Frequency of Treatment: once
GLP: no data
Post Exposure Obs: Haematological effects

30-AUG-2001 (46)

Type: Immunotoxicity
Remark: 1,2-DCB reduced peritoneal macrophage phagocytic activity in mice by 78% of control; the data parallel the cytotoxicity by 1,2-DCB

Source: NICNAS
Test condition: Species: mice
Strain: ddy
No. of animals: 3
Sex: Female
Route of Administration: ex vivo
Dose: 200 mM
Exposure (h): 15-20
Frequency of Treatment: once
GLP: no data
Post Exposure Obs: Phagocytic activity of peritoneal macrophages

Test substance: 1,2-DCB was dissolved in 0.05% DMSO to a final concentration of 200 mM

30-AUG-2001 (264)

Type: Metabolism
Remark: The primary oxidation metabolite of 1,2-DCB is 3:4-dichlorophenol (which is excreted as the glucuronic and sulphate conjugates) whilst 3:4-dichlorophenylmercapturic acid is a minor metabolite (5% of the dose); conjugates of 2:3-dichlorophenol, 4:5-dichlorocatechol & 3:4-catechol are also excreted as minor metabolites; excretion of 1,2-DCB metabolites is slow, being completed within 5-6 days after dosing

Source:	NICNAS	
Test condition:	Species: rabbits Strain: Chinchilla Number of animals: 3 Sex: not stated Route of Administration: gavage Dose: 500 mg/kg bw Exposure Period: 48 hr Frequency of Treatment: once Control Group: GLP: no data Post Exposure Obs.: 6-day period; daily urinalysis of glucuronic acid, ethereal sulphate, total catechols and mercapturic acid	
14-AUG-2001		(16)
Type:	Metabolism	
Remark:	A time-dependent increase in the metabolism of 1,2-DCB to aqueous soluble metabolites excreted into the incubation medium; metabolites retained by the liver slices remained low	
Source:	NICNAS	
Test condition:	Species: rat Strain: Fischer-344 Number of animals: 3 Sex: Male Route of Administration: dynamic organ culture Dose: 0.5 mM Exposure Period: 2h, 4h and 6h Frequency of Treatment: once Control Group: GLP: no data Post Exposure Obs.: determine 1,2-DCB metabolites excreted by the rat liver slice system following exposure to 1,2-DCB	
24-AUG-2001		(20)
Type:	Metabolism	
Remark:	A time-dependent increase in the concentration of aqueous soluble metabolites into the incubation medium and not the liver slices; the variability between metabolism amongst individual human livers was marked	
Source:	NICNAS	
Test condition:	Species: human Number of samples: 3 Sex: Male Route of Administration: dynamic organ culture Dose: 0.5 mM Exposure Period: 2h, 4h and 6h Frequency of Treatment: once Control Group: GLP: no data Post Exposure Obs.: determine 1,2-DCB metabolites excreted by human liver slice system following exposure to 1,2-DCB	
30-AUG-2001		(21)
Type:	Metabolism	
Remark:	whole-body exposure to 1,2-DCB vapours for 4 hours; the MAL (median active level of exposure) required for eliciting a 50 % decrease in hepatic glucose-6-phosphatase staining intensity was 598 ppm (= ca.3.66 mg/l); the MAL responsible for a 50 % decrease in the respiratory rate of mice (RD50)	

was 181 ppm (= ca. 1.11 mg/l), following a 15 minute exposure to 1,2-DCB

Source: NICNAS
Test condition: Species: mice
Strain: Swiss OF1
Number of animals: 6 per exposure level
Sex: Male
Route of Administration: inhalation
Dose: 116, 153, 196 and 273 ppm (15 min); 392-976 ppm (4 h)
Exposure Period: 15 minutes and 4-h
Frequency of Treatment: once
Control Group:
GLP: no data
Post Exposure Obs.: upper respiratory tract irritation (15 min exposure); hepatic glucose-6-phosphatase staining intensity (4-h exposure)

Test substance: 1,2-DCB > 99% purity
24-AUG-2001 (82)

Type: Metabolism
Remark: 1,2-DCB (all doses) resulted in significant body weight loss after 3 days; the relative liver weight was significantly increased and a rise in plasma ALT levels was observable at all doses; after 72 hours, distinct treatment-related histopathological changes in the liver were observable which were characterized by centrilobular hypertrophy and by hepatocellular degeneration and fibrosis (all doses); no change in the relative kidney weight or any treatment-related histopathological findings; 1 and 2 mmol/kg bw dosed animals at the same time point revealed a significant decrease in plasma total T4 and T3 levels, although alterations in hepatic thyroxine cannot be

discounted as a mechanism for reduced levels of plasma thyroid hormone

Source: NICNAS
Test condition: Species: rats
Strain: Wistar
No. of animals: 4 animals per dose
Sex: Male
Route of Administration: intraperitoneal
Dose: 1, 2, and 4 mmol/kg (= 147, 294 or 588 mg/kg bw) in arachidis oil (controls received arachidis oil)
Exposure Period: 24, 48, and 72h

Frequency of Treatment: once
GLP: no data
Post Exposure Obs: Renal: Body and organ (kidney and liver) weight, liver histopathology, liver alanine asparagine aminotransferase (ALT), kidney glutathione (GSH), plasma blood urea nitrogen (BUN), and plasma thyroid hormones thyroxine (T4) and triiodothyronine (T3) levels

Test substance: >98% purity
10-SEP-2001 (88)

Type: Metabolism
Remark: 1,2-DCB metabolism was greatest in human adult than fetal samples; levels of 1,2-DCB metabolites (glucuronides, sulfates and glutathione and cysteine conjugates) and covalent binding were compared to levels for 1,3-DCB and 1,4-DCB

Source: NICNAS

Test condition:	Species: rat and human adult and fetal liver slices Strain: Sprague Dawley Number of animals: 3 rats Sex: Route of Administration: organ culture Dose: 0.1 mM Testing Period: Frequency of testing: once GLP: no data Post Exposure Obs: covalent binding; metabolite formation: glucuronide, glutathione-cysteine, and sulfate	
14-AUG-2001		(98)
Type: Remark:	Metabolism 1,2-DCB significantly increased hepatic UDP-glucuronyltransferase activity toward chloramphenicol and p-nitrophenol; no significant increase in the enzyme activity of hepatic microsomal NADPH-cytochrome c reductase was noted; a moderate decrease in hepatic cytochrome P-450 content and a reduction in the hepatic activity of NADH-cytochrome b5 reductase was observed	
Source: Test condition:	NICNAS Species: rat Strain: Wistar Number of animals: 4-8 Sex: Male Route of Administration: intraperitoneal (i.p.) Dose: 1.36 mmol/kg Testing Period: Frequency of testing: once GLP: no data Post Exposure Obs: effect of 1,2-DCB on microsomal drug-metabolising enzymes: reduced nicotinamide adenine dinucleotide phosphate (NADPH)-cytochrome c reductase; NADH-cytochrome b5 reductase; cytochrome-P450 content; and uridine diphosphate (UDP)-glucuronyltransferase (UDPGT)	
14-AUG-2001		(138)
Type: Remark:	Metabolism 24 hours after administration there was no significant increase in the activity of benzo(a) pyrene hydroxylase in either the intestine or liver when compared to controls	
Source: Test condition:	NICNAS Species: rat Strain: Sprague-Dawley Number of animals: 5 Sex: Male Route of Administration: intraperitoneal (i.p.) Dose: 500 mg/kg Testing Period: Frequency of testing: once GLP: no data Post Exposure Obs: effect of 1,2-DCB on liver and intestinal benzo(a)pyrene hydroxylase activity (AHH)	
25-JUL-2001		(162)
Type: Remark:	Metabolism rabbits received single oral doses of 500 mg/kg bw of o-dichlorobenzene: the following metabolites were excreted with the urine within 5 days (values given as % of dose excreted): mercapturic acid (5 %), monophenols (40 %), catechols	

	(4 %), total O-conjugates = conjugated glucuronic acid + ethereal sulphate (69 %)	
Source: 24-AUG-2001	Bayer AG Leverkusen	(292)
Type:	Metabolism	
Remark:	The paper examines the relative contribution of various human cytochrome P450 enzymes in the formation of phenolic metabolites from 1,2-DCB with microsomes derived from various cell lines. Incubation of 1,2-DCB with microsomes containing specific human P450 enzymes and human liver microsomes revealed similar effects. Essentially, CYP2E1 induced the formation of phenolic metabolites 23TCP and 34TCP (349 and 1210 pmol.min ⁻¹ .nmol P450 ⁻¹ , respectively) from 1,2-DCB. These activities were inhibited in the presence of acetone in both systems. Caution should be taken in interpreting the data since only one substrate concentration was investigated (100 uM), differences in Km, therefore, are not taken into account, in particular in respect to in vivo extrapolation. Moreover, the degree of phenolic metabolites is also dependant upon the enzymatic activity and concentration of candidate CYP enzyme involved.	
Source:	NICNAS	
Test condition:	Species: Human liver microsomes and various cell lines Route of Administration: ex vitro Substrate concentration: 100 uM (final) Incubation Period: 10-30 minutes (HPLC determination) Frequency of Incubation: once GLP: no data Post Incubation Obs: see Remark Freetext	
Test substance:	not stated	
19-JUL-2001		(132)
Type:	Metabolism	
Remark:	Human liver slices metabolised 1,2-DCB to a greater extent than those from rats; total metabolism and covalent binding did not correlate with cytotoxicity; glutathione-cysteine conjugate was the major metabolite for 1,2-DCB in rat and human liver slices	
Source:	NICNAS	
Test condition:	Species: rat and humans Strain: Sprague-Dawley and Fischer-344 rats No. of animals: 4 per strain and 7 humans Sex: M Route of Administration: in vitro Dose: 1 mM Frequency of Treatment: 2 and 6 h incubations in culture medium GLP: no data Post Exposure Obs: comparative metabolism and covalent binding of reactive metabolites of 1,2-[14C]-DCB in liver slices	
Test substance:	1,2-DCB 99% pure dissolved in 1% DMSO	
05-SEP-2001		(102)
Type:	Metabolism	
Remark:	Water-soluble metabolites after the addition of 1,2-[14C]-DCB to microsomal preparations showed substantial species and sex differences. Microsomes from female rats metabolised o-DCB faster than their male equivalents; microsomes from male mice were more efficient	

	with respect to 1,2-DCB metabolism than microsomes from female mice; Microsomal metabolism of 1,2-DCB was 7-fold faster by mice compared to rats; covalent binding of metabolites was higher in mice of both sexes compared to rats; induction of CYP2E1 by benzene inhalation resulted in increased metabolism of 1,2-DCB in rats but induction of CYP3A by pregnenolone 16-alpha-carbonitrile did not increase metabolism except in female rats where a 6-fold increase was recorded.	
Source:	NICNAS	
Test condition:	Species: rat and mouse hepatic microsomes Strain: SPF (Wistar strain) and B6C3F1 No. of animals: not stated Sex: both sexes Route of Administration: in vitro Dose: 0.1 mM Frequency of Treatment: once GLP: no data Post Exposure Obs: 1,2-DCB metabolites with or without induction of CYP3A or CYP2E1	
14-AUG-2001		(186)
Type:	Toxicokinetics	
Remark:	BDPF flow was significantly increased and BDPF protein concentration significantly reduced compared to controls; SGPT activity remained affected	
Source:	NICNAS	
Test condition:	Species: rat Strain: Holtzman No. of animals: 4 or more Sex: Male Route of Administration: intraperitoneal injection (1 ml/kg) Dose: 5 mmol/kg Frequency of Treatment: once GLP: no data Post Exposure Obs: Rat bile duct-pancreatic fluid (BDPF) flow, protein concentration and serum glutamic pyruvic transaminase (SGPT) activity were monitored 24 h after 1,2-DCB exposure	
10-SEP-2001		(295)
Type:	other	
Remark:	increased state 4 respiration and a decreased state 3 respiration	
Source:	NICNAS	
Test condition:	Species: rat (hepatocytes) Strain: Donryu No. of animals: 2 Sex: Male Route of Administration: ex vivo Dose: 0.24 mM Frequency of Treatment: once GLP: no data Post Exposure Obs: Inhibitory effects of 1,2-DCB on mitochondrial respiration based upon oxygen consumption and the degree of inhibition in State 3 and 4 respiration	
14-AUG-2001		(192)
Type:	other	
Remark:	rats received twice daily dermal applications of o-di-	

Source: 24-AUG-2001	chlorobenzene (skin painting on the shaved ventral side; size of site of application: ca. 10 square centimetres); the treatment was tolerated very badly by the animals; one rat died after 5 applications showing signs of severe general damage; another rat died after 9 administrations and gross examination showed a light-spotted liver and renal changes; no dermal changes were observable at the site of application Bayer AG Leverkusen	(216)
Type: Remark: Source: Test condition: 19-JUL-2001	other: 1,2-DCB effects on Staes 3 and 4 oxidative respiration 1,2-DCB induced a decrease in respiratory control index via inhibition of Stae 3 respiration and /or acceleration of State 4 respiration in parallel with significant K+ efflux NICNAS Species: rat (hepatocytes) Strain: Donryu No. of animals: 2 Sex: Male Route of Administration: ex vivo Dose: 0.24 mM Frequency of Treatment: once GLP: no data Post Exposure Obs: Inhibitory effects of 1,2-DCB on mitochondrial respiration based upon oxygen consumption and the degree of inhibition in State 3 and 4	(193)
Type: Remark: Source: Test condition: 11-APR-2001	other: 1,2-DCB effects on rat pancreas and liver 1,2-DCB induced a statistically significant change in BDPF parameters: BDPF flow increased by greater than 900% whilst BDPF protein concentration decreased by at least 75% compared to vehicle controls; chloride, bile flow and SGPT activity were all unchanged compared to vehicle control treated animals NICNAS Species: rat Strain: Holtzman Number of animals: 4 (minimum) Sex: M Route of Administration: intraperitoneal (ip) Dose: 5 mmol/kg (50% solution in sesame oil) Testing Period: 24 h Frequency of testing: once GLP: no data Post Exposure Obs: Pancreatic-hepatobiliary function: bile duct-pancreatic fluid (BDPF; mg/min/kg bw) flow; PDPF protein and electrolyte concentration; SGPT activity	(294)
Type: Remark: Source: Test condition: 24-AUG-2001	other: 1,2-DCB in milk fat Gas chromatographic and mass spectral identification of 1,2-DCB was confirmed in cow milk fat; its origin may be from pesticides NICNAS The authors identify volatiles (including 1,2-DCB) in irradiated milk fat; processes used: ethyl ether extraction and gas-liquid chromatographic separation; rapid scan-mass spectrometry	(140)

Type: other: 1,2-DCB partition coefficient(s)
 Remark: Blood/air partition coefficient for 1,2-DCB was 423 (at 37 degrees centigrade)
 Source: NICNAS
 Test condition: the partition coefficient of blood/air for 1,2-DCB was determined by means of a vial-equilibration method
 14-AUG-2001 (229)

Type: other: 1,2-DCB residues in Human Fat & Milk
 Remark: Arithmetic means for 1,2-DCB levels detected were: 13 ug/kg (adipose tissue) and 9 ug/kg (breast milk)
 Source: NICNAS
 Test condition: Species: Human
 Number of samples: 15 (adipose tissue) and 12 (breast milk)
 Sex: Male and Female (adipose tissue); Female (breast milk)
 Route of Administration: ex vivo samples derived from adipose tissue and breast milk
 Post Exposure Obs: Capillary GL chromatographic analysis of 1,2-DCB in adipose tissue and breast milk
 14-AUG-2001 (133)

Type: other: 1,2-DCB residues in Market Milk & Fat
 Remark: Arithmetic means for 1,2-DCB levels detected were: 2.6 ng/g (cows milk) and 1 ng/g (fresh meat)
 Source: NICNAS
 Test condition: Species: Cow
 Number of samples: 9 (raw milk) and 3 (fresh beef)
 Route of Administration: biological monitoring in ex vivo samples derived from cows milk and beef samples
 Post Exposure Obs: Gas chromatographic analysis of 1,2-DCB in cows milk and beef samples
 14-AUG-2001 (134)

Type: other: Excretion and Metabolism of 1,2,4-TCB
 Remark: Small amounts of 1,2-DCB were excreted in the expired air; reductive dechlorination of TCB to 1,2-DCB in vivo; approximately 66% and 17% excreted in urine and feces respectively as within 168 h however 1,2-DCB metabolites were not detected
 Source: NICNAS
 Test condition: Species: rat
 Strain: Wistar
 Sex: Male
 Number of animals: 3-5 per group
 Route of Administration: perorally
 Dose: 50 mg/kg [14C]-1,2,4-TCB
 Exposure Period: 12, 24,48 and 168 h
 Frequency of Treatment: once
 Control Group:
 GLP: no data
 Post Exposure Obs.: Excretion and metabolism of 1,2,4-TCB
 30-AUG-2001 (250)

Type: other: Metabolism
 Remark: experimental design: the rats received two doses of 100 or 300 mg/kg bw of 1,2-DCB; the first dose was given 21 hours before sacrifice of the rats; the second dose was given 4 hours before sacrifice

Result: the hepatic ornithine decarboxylase activity was increased at 300 mg/kg; the other biochemical assays showed no significant changes; no deaths occurred (mortality: 0/8); an increase in only hepatic ornithine decarboxylase activity but not in hepatic cytochrome P-450 content is considered a negative result for cell proliferation

Source: NICNAS
Test condition: Species: rat
Strain: Sprague-Dawley
Number of animals:
Sex: Female
Route of Administration: gavage
Dose: 100 or 300 mg/kg bw
Testing Period:
Frequency of testing: once
GLP: no data
Post Exposure Obs: the effects of 1,2-DCB on four biochemical assays: hepatic DNA damage by alkaline elution; hepatic ornithine decarboxylase activity; serum alanine aminotransferase activity and hepatic cytochrome P-450 content were determined

05-SEP-2001 (144)

Type: other: Oxidative Stress related Hepatotoxicity
Remark: Liver and serum levels of lipid peroxidation products increased in a time-dependent manner and were detected at 3 hours in the liver and at 12 hours in serum; serum ALT activity increased in a time-dependent manner; extensive staining of lipid peroxidation-protein adducts in

centrilobular regions at 24 hours; 1,2-DCB-induced a marked decrease in serum ALT activity in the absence of necrosis; Kupffer cells from rats at 24 hours showed a 3-fold increase in basal superoxide production from treated animals; PMA (Phorbol Myristate Acetate) stimulation in Kupffer cells of 1,2-DCB-treated animals resulted in 72% more superoxide compared to untreated controls

Source: NICNAS
Test condition: Species: rat
Strain: Fischer 344
Number of animals: 3
Sex: Male
Route of Administration: intraperitoneal (ip)
Dose: 3.6 mmol/kg
Testing Period: 48 h
Frequency of testing: 3, 12, 16, 24 and 48 h
GLP: no data
Post Exposure Obs: liver and serum lipid peroxidation products (through the formation of 4-HNE protein adducts); serum ALT activity and changes in liver histopathology

Test substance: 1,2-DCB in corn oil: purity not stated
14-AUG-2001 (128)

Type: other: Toxicokinetics and Metabolism
Remark: Highest concentrations of 1,2-[14C]-DCB were found at 6 hours in the kidney, urinary bladder, perirenal fat, liver, small intestine, and skin (including subcutaneous fat); urinary metabolites included 2,3-dichlorophenol, 3,4-dichlorophenol and their sulfate and mercapturic acid derivatives; no significant differences were observed in metabolic profiles for different doses of 1,2-DCB and no hydroquinone or quinone metabolites were detected; recovery

	of urinary (75-85%) and faecal (19% low dose and 7% high dose) radioactivity indicated excretion was essentially complete within 24 hours at the lower doses and by 48 hours for the high dose	
Source:	NICNAS	
Test condition:	Species: rat Strain: Wistar (Cr1:(WI)WUBR) Number of animals: 3 per/dose time-point Sex: Male Route of Administration: gavage Dose: 5, 50, or 250 mg/kg bw Testing Period: 1-96 h Frequency of testing: once GLP: no data Post Exposure Obs: tissue distribution, elimination, and urinary metabolites of 1,2-DCB were investigated	
Test substance:	1,2-DCB purity at least 98%	(126)
20-AUG-2001		
Type:	other: Toxicokinetics and Metabolism	
Remark:	Major metabolites of 1,2-[14C]DCB by rat hepatic microsomes: 2,3-dichlorophenol, 3,4-dichlorophenol and dihydrodiol and glutathione-epoxide conjugates; sprague-Dawley microsomes the least active however highest covalent binding (31%); F344 rats possessed lowest level of epoxide hydrolase activity; microsomes produced mainly one glutathione epoxide conjugate and amount increased by phenobarbital induction, indicating CYP2B1/2 enzymes are primarily involved in the metabolism of 1,2-DCB	
Source:	NICNAS	
Test condition:	Species: rat Strain: Wistar (Cr1:(WI)WUBR); Fischer-344 (F344); Sprague-Dawley Number of animals: 3 Sex: Male Route of Administration: gavage Dose: 80 uM Testing Period: 15 minutes (ex vivo) Frequency of testing: once GLP: no data Post Exposure Obs: Metabolism and covalent binding of 1,2-[14C]DCB by rat hepatic microsomes; epoxide hydrolase activity; glutathione-epoxide conjugates; phenobarbital induction to determine species of microsomes	
Test substance:	1,2-D[14C]B radiochemical purity > 98%	(124)
20-AUG-2001		
Type:	other: Toxicokinetics and Metabolism	
Remark:	Using hepatic microsomes determined in vitro Vmax and Km: 0.14 nmol/mg protein/min and 4.8 uM (rat) and 0.27 nmol/mg/min and 7.5 uM (humans); data used in physiologically based pharmacokinetic model	
Source:	NICNAS	
Test condition:	Species: Strain: Number of animals: Sex: Route of Administration: Dose: Testing Period: Frequency of testing:	

	GLP: no data Post Exposure Obs: Using a 'fitted' Michaelis-Menten constant for Vmax and Km, GSH-depletion and covalent binding was monitored as a mechanism of 1,2-DCB oxidation in rat liver microsomes; physiologic and biochemical parameters, partition coefficients and adsorption rate constants are also determined	
05-SEP-2001		(125)
Type:	other: Toxicokinetics and Metabolism (role of P450 enzymes in the biotransformation of 1,2-DCB to epoxide metabolites in man)	
Remark:	Metabolites produced included 2,3-dichlorophenol, 3,4-dichlorophenol and dihydrodiol and glutathione-epoxide conjugates; glutathione conjugation was catalysed by glutathione-S-transferases; the rate of conversion of 1,2-DCB was 0.14 nmol/min/mg protein; covalent binding amounted to 4.6% of total metabolites; addition of glutathione to the microsomal preparations resulted in increased formation of glutathione-epoxide conjugates and a decrease in dihydrodiol formation; inhibition of epoxide hydrolase resulted in a decrease in dihydrodiols and increased covalent binding; the presence of ascorbic acid did not affect covalent binding to human microsomes; CYP2E1 is the major human cytochrome involved the metabolism of 1,2-DCB	
Source:	NICNAS	
Test condition:	Species: human Strain: Number of samples: liver microsomes (pooled from 5 individuals) Sex: Route of Administration: ex vivo Dose: 0.85 kBq [1,2-14C]DCB Testing Period: 15 minutes Frequency of testing: once GLP: no data Post Exposure Obs: Metabolism and covalent binding of [1,2-14C]DCB by human hepatic microsomes; epoxide hydrolase activity; glutathione-epoxide conjugation; phenobarbital induction to determine species of microsomes	
05-SEP-2001		(124)
Type:	other: acute toxicity	
Remark:	a dog was exposed via inhalation to o-dichlorobenzene at a concentration of 2 ml per cubic metre (= ca. 2.64 mg/l) for 1 hour; no signs of toxicity were observable; in a further experiment the dog was exposed to 4 ml per cubic metre (= ca. 5.29 mg/l) of o-dichlorobenzene: transient drowsiness occurred	
Source:	Bayer AG Leverkusen	
11-APR-2001		(216)
Type:	other: acute toxicity	
Remark:	mice, rats and guinea pigs were exposed via inhalation for 1 hour to an atmosphere saturated with o-dichlorobenzene; the mice showed transient central stimulation lasting ca. 20 minutes; afterwards depression of the central nervous system, muscle twitching, irregular respiration and cyanosis occurred and the animals died within 24 hours; the rats and guinea pigs also showed central stimulation,	

- but they recovered within a few hours and no deaths occurred
- Source: Bayer AG Leverkusen (216)
11-OCT-1993
- Type: other: acute toxicity
Remark: rats were exposed to atmospheres saturated with o-dichlorobenzene at various temperatures (20, 30 or 95 degrees Centigrade) by dynamic vaporisation (whole-body exposure; exposure time: 0.5, 1, 3 or 7 hours; observation period: 14 days); deaths occurred in male and female rats exposed for 7 hours at 20 degrees Centigrade, in male rats exposed for 7 hours at 30 degrees Centigrade, in male and female rats exposed for 1 or 3 hours at 95 degrees Centigrade and in female rats exposed for 7 hours at 95 degrees Centigrade; signs of toxicity: behaviour disorder, difficulty of breathing, sedation, irritation of the visible mucous membranes of eyes and noses, state of agitation
- Source: Bayer AG Leverkusen (25)
18-OCT-1993
- Type: other: acute toxicity
Remark: male rats were injected (i.p.) with 2 or 3 mmol/kg bw (= 294 or 441 mg/kg bw) of o-dichlorobenzene; hepatic and renal toxicity was quantitated 24 hours after injection of o-dichlorobenzene; plasma transaminase activity was increased by o-dichlorobenzene as a function of dose administered; hepatic degeneration (centrilobular necrosis) was evident in the treated animals within 24 hours after injection of o-dichlorobenzene; the kidneys of animals treated with 2 mmol/kg bw of o-dichlorobenzene were of relatively normal integrity; blood urea nitrogen levels were not altered within 24 hours after treatment; renal cortical slice accumulation of p-aminohippurate or tetraethylammonium was decreased at 3 or 2 mmol/kg bw, respectively
- Source: Bayer AG Leverkusen (266)
03-NOV-1993
- Type: other: acute toxicity
Remark: male rats received a single i.p. injection of 4 mmol/kg bw (= 588 mg/kg bw): increased urine output and decreased food consumption were observable; hepatic toxicity was characterized by increased liver weight and a marked elevation in plasma transaminase activity; renal alterations were characterized by increased kidney weight at 48 hours, increased proteinuria and alterations in organic ion accumulation; renal cortical slice uptake of p-aminohippurate and tetraethylammonium were decreased within 24 hours after treatment while only basal p-aminohippurate uptake was decreased at 48 hours
- Source: Bayer AG Leverkusen (266)
03-NOV-1993
- Type: other: acute toxicity
Remark: 1,2-DCB (2 or 3 mmol/kg) induced a significant increase in plasma ALT and BUN levels associated with increases in CYP2E1 and CYP2B activity; plasma ALT activity markedly increased in pyridine treated animals for both dose levels the effect being less marked following phenobarbital or b-naphthoflavone pretreatment; liver weights increased in all three treatment groups for both dose levels; liver

histopathology revealed centrilobular damage at 2 mmol/kg being most marked at 3 mmol/kg; urinary output increased approximately 3-fold in 3 mmol/kg treated animals; phenobarbital and pyridine pretreatment resulted in renal toxicity (as increased BUN); kidney weights were also increased following 1,2-DCB exposure for each of the three inducing agents

Source: NICNAS
Test condition: Species: rat
Strain: Fischer 344
No. of animals: 4 animals per group
Sex: Male
Route of Administration: intraperitoneal (ip)
Dose: 2 or 3 mmol/kg bw; 294 or 441 mg/kg bw, respectively
Exposure Period:
Frequency of Treatment: once
GLP: no data
Post Exposure Obs: Plasma alanine aminotransferase (ALT) and blood urea nitrogen (BUN) levels and urinary output as determinants of acute hepatic and renal toxicity of 1,2-DCB were assessed following ip pretreatment with phenobarbital (to induce CYP2A1, CYP2A2 and CYP 2B), betanaphthoflavone (to induce CYP1A1), pyridine (to induce CYP2E1) or piperonyl butoxide (to inhibit mixed function oxidase)

24-AUG-2001 (267)

Type: other: cell transformation assay
Remark: cell transformation assay: adult rat liver cell lines (established from the liver of F344 rats) were incubated with 1,2-DCB at a concentration of 131 mg/l; 1,2-DCB induced weak cell transformation in adult rat liver epithelial cells

Source: Bayer AG Leverkusen
Test condition: Species: Rat (hepatocyte cell lines)
Strain: F344
No. of animals:
Sex:
Route of Administration: in vitro
Dose: 131 mg/l
Exposure (h):
Frequency of Treatment: once
GLP: no data
Post Exposure Obs: cell transformation

Test substance: other TS: purity = 98.8 %
10-SEP-2001 (233)

Type: other: effect of 1,2-DCB on sulphur metabolism in dogs
Remark: urinary output of sulphur was increased in 1,2-DCB dosed animals compared to controls

Source: NICNAS
Test condition: Species: dog
Number of animals: 5
Sex: not stated
Route of Administration: gavage
Dose: 50 mg/kg/bw or 250 mg/kg/bw
Testing Period:
Frequency of testing: 4
GLP: no data
Post Exposure Obs: effect of 1,2-DCB on sulphur metabolism as measured in the urine

24-AUG-2001 (57) (119)

Type: other: hepatotoxic effects
 Remark: 1,2-DCB dosed animals revealed hepatic glycogen loss and minimal necrosis of centrilobular parenchymal cells; phenobarbital pretreated animals followed by exposure to 1,2-DCB revealed a marked increase in centrilobular hepatotoxicity via glycogen loss and massive hepatic necrosis

Source: NICNAS
 Test condition: Species: rat
 Strain: Sprague-Dawley (NIH)
 Number of animals: 4
 Sex: M
 Route of Administration: intraperitoneal (i.p.)
 Doses: not stated (in 0.03 ml sesame oil)
 Exposure Period: 24 hr
 Frequency of Treatment: once
 Control Group: sesame oil
 GLP: no data
 Post Exposure Obs: hepatocellular morphology in 1,2-DCB and phenobarbital (80 mg/kg bw, i.p.) pretreated animals

05-SEP-2001 (43)

Type: other: hepatotoxic effects
 Remark: Following single 4 h exposure 1,2-DCB increased GPT, GLDH and SDH activity at concentrations of 305 ppm or more, GOT activity was increased at concentrations greater than or equal to 609 ppm; only minor enzyme activity changes following repeated exposure

Source: NICNAS
 Test condition: Species: rat
 Strain: Sprague-Dawley
 No. of animals: 8 per treatment/control group
 Sex: Male
 Route of Administration: inhalation
 Dose: 204-774 ppm
 Exposure Period: single treatment of 4 h or 6 h daily for 2-4 days
 Frequency of Treatment:
 GLP: no data
 Post Exposure Obs: Hepatotoxic responses: Serum glutamate dehydrogenase (GLDH); glutamic oxaloacetic transaminase (GOT); glutamic pyruvic transaminase (GPT) and sorbitol dehydrogenase (SDH) activities

Test substance: 1,2-DCB purity >99.0%
 10-SEP-2001 (44)

Type: other: hepatotoxic effects
 Remark: Significant dose-dependent increase in GLDH and SDH above 369 ppm; linear concentration-dependent decrease in centrilobular G6-Pase staining intensity

Source: NICNAS
 Test condition: Species: rat
 Strain: Sprague-Dawley
 No. of animals: 10 per treatment/control group
 Sex: Male
 Route of Administration: inhalation
 Dose: 246-739 ppm
 Exposure Period: Controls and one treated group at 4 h
 Frequency of Treatment: once
 GLP: no data

Post Exposure Obs: Serum glutamate dehydrogenase (GLDH) and sorbitol dehydrogenase (SDH) activities; centrilobular liver-cell injury determined by glucose-6-phosphatase (G-6-Pase) staining intensity
 Test substance: 99% pure
 20-AUG-2001 (47)

Type: other: hepatotoxic effects
 Remark: Pre-exposure to ketones (except acetone) enhanced 1,2-DCB-induced increase in serum GLDH activity, while increases in cytochrome P-450 content and GST activity were similar to levels seen in ketone only exposures

Source: NICNAS
 Test condition: Species: rat
 Strain: Sprague-Dawley
 No. of animals: 5 per treatment/control group
 Sex: Male
 Route of Administration: inhalation
 Dose: 374-392 ppm
 Exposure Period: 4 h 1,2-DCB with and without pretreatment with ketones
 Frequency of Treatment: once
 GLP: no data
 Post Exposure Obs: Liver function tests were conducted by monitoring serum glutamate dehydrogenase (GLDH)

activity; hepatic cytochrome P-450 content; hepatic glutathione-S-transferase (GST) activity; 1,2-DCB effects were also examined in Ketone pretreated animals
 20-AUG-2001 (48)

Type: other: hepatotoxic effects
 Remark: a time-dependent statistically significant decrease in intracellular K+, increase in LDH leakage, and inhibition of protein synthesis was observed up to 6 h in 2 mM dosed animals; the effect was time-dependent with statistically significant results occurring at 6 h for protein synthesis and 4 h for LDH release

Source: NICNAS
 Test condition: Species: human
 No. of animals: 10 human donor/biopsy liver tissue
 Route of Administration: ex vivo incubation
 Dose: 0.1 mM; 1 mM and 2 mM
 Exposure Period: 2 h, 4 h and 6 h
 Frequency of Treatment: once
 GLP: no data
 Post Exposure Obs: three viability parameters were used to assess toxicity were; membrane integrity: potassium (K+) content; Lactate Dehydrogenase (LDH); and protein synthesis
 Test substance: purity 99%
 05-SEP-2001 (99)

Type: other: hepatotoxic effects
 Remark: o-dichlorobenzene was administered i.p. at a dose of 5.4 mmol/kg bw (= 794 mg/kg bw) to two different strains of rats, i.e. Fischer-344 and Sprague Dawley rats; Fischer-344 rats administered o-dichlorobenzene had 75 fold greater plasma alanine aminotransferase activities than the Sprague Dawley rats; morphological examination of liver obtained from Fischer-344 and Sprague Dawley rats confirmed the great difference in hepatotoxicity induced by o-dichlorobenzene; pretreat-

Source: 23-JUL-2001
 Remark: ment (i.p.) of animals with phenobarbital potentiated the hepatotoxicity of o-dichlorobenzene in both strains of rats administered a non hepatotoxic dose of 0.9 mmol/kg bw (= 132 mg/kg bw) of o-dichlorobenzene
 Bayer AG Leverkusen (112)

Type: other: hepatotoxic effects
 Remark: the hepatotoxicity of o-dichlorobenzene, as determined by plasma alanine aminotransferase activity and histopathology in male Fischer-344 and Sprague Dawley rats, was compared at doses of 0.9, 1.8, 4.5 or 5.4 mmol/kg bw (= 132, 265, 662 or 794 mg/kg bw); within this dose range Fischer-344 rats demonstrated a dose dependent increase in alanine aminotransferase activity, whereas, Sprague Dawley rats were resistant to o-dichlorobenzene induced elevation in alanine aminotransferase activity; histopathology studies of animals dosed with o-dichlorobenzene (5.4 mmol/kg bw) exhibited centrilobular necrosis in Fischer-344 rats but not in Sprague Dawley rats (route of administration unspecified, probably i.p.)
 Source: 01-SEP-1993 Bayer AG Leverkusen (113)

Type: other: hepatotoxic effects
 Remark: Plasma ALT levels were significantly elevated over control values in animals receiving 1,2-DCB alone while pretreatment with methyl palmitate resulted in an 80% decrease in plasma ALT activity; a significant decrease of 70% in serum ALT activity was also noted in animals pretreated with SOD, prior to 1,2-DCB administration; the protective effect of methyl palmitate and superoxide dismutase was confirmed by histopathology; neither methyl palmitate nor superoxide dismutase conferred protection in phenobarbital treated animals
 Source: NICNAS
 Test condition: Species: Rat
 Strain: Fischer-344
 No. of animals: not stated
 Sex: Male
 Route of Administration: intraperitoneal (i.p.)
 Dose: 3.6 mmol/kg bw (= 529 mg/kg bw)
 Exposure Period:
 Frequency of Treatment: once
 GLP: no data
 Post Exposure Obs: Serum ALT levels and liver histopathology with and without pre-treatment with methyl palmitate (an inhibitor of Kupffer cell activity); with and without pretreated with the superoxide scavenger, superoxide dismutase (SOD; as the polyethylene glycol conjugate)
 20-AUG-2001 (111)

Type: other: hepatotoxic effects
 Remark: Covalent binding within necrotic centrolobular hepatocytes was detectable 6 and 24 hours following i.p. administration of 14C-labeled 1,2-DCB (1.33 mmole/kg bw); phenobarbital induction potentiated the appearance of necrotic centrolobular hepatocytes, hepatic glycogen loss and massive necrosis
 Source: NICNAS
 Test condition: Species: rat
 Strain: Sprague-Dawley

	No. of animals: 3 to 6 Sex: M Route of Administration: Intraperitoneal (i.p.) Dose: 0.1 - 1.33 mmol/kg bw Exposure Period: 6 and 24 h Frequency of Treatment: once GLP: no data Post Exposure Obs: hepatic morphology; effect of phenobarbital pretreatment on hepatic 1,2-DCB concentration and protein binding	
24-AUG-2001		(211) (212)
Type:	other: hepatotoxic effects	
Remark:	in vitro assay: rat liver slices were incubated with o-dichlorobenzene; at 1.0 mM (= 147 mg/l), o-dichlorobenzene resulted in an inhibition of protein synthesis, in a loss of intracellular K ⁺ content and in release of lactate dehydrogenase	
Source:	Bayer AG Leverkusen	
15-OCT-1993		(239)
Type:	other: hepatotoxic effects	
Remark:	1,2-DCB treated animals exhibited an significant increase in plasma GPT activity 24 hours post treatment; concomitant CCl ₄ treatment resulted in: a marginal elevation in GPT activity; 50% reduction in urinary and faecal elimination of 1,2-DCB metabolites, significantly reduced aqueous soluble 1,2-DCB metabolites in the liver and 3-fold increase in expired umetabolised 1,2-DCB	
Source:	NICNAS	
Test condition:	Species: rat Strain: F-344 No. of animals: 3 to 6 per strain Sex: Male Route of Administration: Intraperitoneal (i.p.) Dose: 2.7 mmol/kg bw (= 397 mg/kg bw) + concomitant i.p. injection of carbon tetrachloride (CCl ₄) at a single dose of 1.0 mmol/kg bw (= 154 mg/kg bw) Exposure Period: Frequency of Treatment: once GLP: no data Post Exposure Obs: plasma glutamate-pyruvate transaminase (GPT) activity and excretion of 1,2-DCB metabolites with and without CCl ₄ treatment	
20-AUG-2001		(244) (245)
Type:	other: hepatotoxic effects	
Remark:	the three isomers of dichlorobenzene exhibited marked differences in hepatotoxicity following i.p. administration in male F344 rats; plasma glutamate-pyruvate transaminase activity, measured 24 hours post exposure, was markedly elevated following a 1.8 mmol/kg bw (= 265 mg/kg bw) dose of o-dichlorobenzene; m-dichlorobenzene produced only a moderate elevation following a 4.5 mmol/kg bw (= 662 mg/kg bw) dose, while p-dichlorobenzene produced no elevation in glutamate-pyruvate transaminase activity at this dose; ultra-structurally, o- and m-dichlorobenzene induced elevations in glutamate-pyruvate transaminase activity were associated with a centrolobular pattern of hepatic necrosis; the role of cytochrome P-450 mediated bioactivation in dichlorobenzene-induced hepato-	

toxicity was demonstrated by elevated glutamate-pyruvate transaminase activities following an otherwise nontoxic 0.9 mmol/kg bw (= 132 mg/kg bw) dose of either o- or m-dichlorobenzene in phenobarbital-pretreated animals; the p-isomer of dichlorobenzene showed no induction of toxicity with phenobarbital-pretreatment; hepatic glutathione concentrations were reduced 0.5, 3 and 5 hours after a 1.8 mmol/kg bw dose of either o- or m-dichlorobenzene
 Source: Bayer AG Leverkusen (243)
 24-JUL-2001

Type: other: hepatotoxic effects
 Remark: Soluble metabolites of 1,2-DCB correlated with the covalent binding of radiolabel to hepatic proteins over a 12 to 24 hour period;
 1,2-DCB treatment resulted in a substantial loss in hepatic glutathione content at 1.5 hours; highly significant increase in ALT levels was observed for 1,2-DCB doses of 265 mg/kg bw or greater; histological examination revealed severe centrilobular hepatic damage; prior phenobarbital treatment associated hepatotoxicity with hepatic cytochrome P450; depletion of hepatic glutathione by phorone

pre-treatment resulted in a significant increase in plasma ALT levels 24 hours after administration with 1,2-DCB demonstrating a role for glutathione in mediating the hepatotoxicity of 1,2-DCB; F344 strain are more sensitive to 1,2-DCB hepatotoxicity determined by large increase in plasma ALT levels at 24 hours compared with no increase in S-D rats.

Source: NICNAS
 Test condition: Species: rat
 Strain: Fischer-344 and Sprague-Dawley
 No. of animals: 3-8 per dose
 Sex: M
 Route of Administration: Intraperitoneal (i.p.)
 Dose: 0.9-5.4 mmol/kg bw (132 -794 mg/kg bw)
 Exposure Period:
 Frequency of Treatment: once
 GLP: no data
 Post Exposure Obs: Plasma alanine aminotransferase (ALT) activity and in vivo covalent binding of 1,2-[14C]-DCB (0.9 mmol/kg bw; 132 mg/kg bw) equivalents to hepatic proteins with and without hepatic glutathione depletion; liver histology

Test substance: 1,2-DCB purity > 99% (246)
 20-AUG-2001

Type: other: hepatotoxic effects
 Remark: successive exposure to Ketones and 1,2-DCB provoked a significant decrease in G-6-Pase staining intensity in the centrolobular area (29-42%) relative to 1,2-DCB controls

Source: NICNAS
 Test condition: Species: mouse
 Strain: OF1
 No. of animals: 8 per treatment/control group
 Sex: Male
 Route of Administration: inhalation
 Dose: 250-288 ppm 1,2-DCB with or without pretreatment with ketones
 Exposure Period: 4 h
 Frequency of Treatment: once

20-AUG-2001	<p>GLP: no data Post Exposure Obs: centrilobular liver-cell injury was evaluated by glucose-6-phosphatase (G-6-Pase) staining intensity</p>	(48)
Type: Remark:	<p>other: hepatotoxicity Metabolism of 1,2-DCB by rat hepatic microsomes produced 2,3-dichlorophenol and 3,4-dichlorophenol as the major metabolites; dichlorophenols were further metabolised to their respective dichlorohydroquinone derivatives; minor conversion products of 1,2-DCB were 3,4-dichlorocatechol and 4,5-dichlorocatechol</p>	
Source: Test condition:	<p>NICNAS Species: rats Strain: Wistar Sex: Male Route of Administration: in vitro rat hepatic microsomes Dose: 0.8 mM (final concentration) Frequency of Treatment: once GLP: no data Post Exposure Obs.: identification of rat hepatic microsomal</p>	
Test substance:	<p>induced metabolism of 1,2-DCB 1,2-DCB 98.8% purity (1.04% impurity as an apolar fraction did not coincide with metabolite formation)</p>	
20-AUG-2001		(87)
Type: Remark:	<p>other: metabolism (human microsomes) Metabolism of 1,2-[14C]-DCB correlated well with CYP2E1 levels but not with other cytochromes tested (1A2, 2A6, 2B6, 2C9 or 3A4); 1,2-DCB metabolism was inhibited by approximately 90% in the presence of the CYP2E1 inhibitor, diethyldithiocarbamate</p>	
Source: Test condition:	<p>NICNAS Species: human hepatic microsomes Sex: male Route of Administration: in vitro Dose: 0.1 mM Frequency of Treatment: once GLP: no data Post Exposure Obs: 1,2-DCB metabolites with or without induction of CYP substrates including 2E1, 1A2, 2A6, 2B6, 2C9, and 3A4.</p>	
24-JUL-2001		(186)
Type: Remark:	<p>other: metabolites of 1,2-DCB in rats Analysis of urine and blood showed the presence of 2,3- and 3,4-dichlorophenyl methyl sulfoxides and 2,3- and 3,4-dichlorophenyl methyl sulfones; i.p. treated animals showed maximal amounts of 1,2-DCB in blood, liver and kidneys at 1 hour after administration declining rapidly over the next 12 hours at near exponential rates; estimated half-life of 1,2-DCB was 0.08, 0.04 and 0.02 hours for blood, liver and kidney respectively</p>	
Source: Test condition:	<p>NICNAS Species: rat Strain: Wistar Number of animals: 3-6 per treatment group Sex: Male Route of Administration: oral or intraperitoneal (i.p.) Dose: 500 mg/kg bw (oral); 1.36 mmol/kg (200 mg/kg bw; i.p.)</p>	

	<p>Testing Period: 1, 2, 4, 6, 12, 24, 48 and 72 h Frequency of testing: oral, once every other day for 10 days; i.p. once GLP: no data Post Exposure Obs: Estimate 1,2-DCB metabolites in blood, and urine following oral administration; estimate half-life of 1,2-DCB in blood, liver and kidney following i.p. administration</p>	
24-AUG-2001		(139)
Type:	other: protooncogene expression as a mechanism of delayed response to 1,2-DCB hepatotoxicity	
Remark:	Early and sustained increase in c-myc and Ha-ras expression was noted in F344 but not SD rats; compensatory liver regeneration consequent upon sub-threshold concentrations of 1,2-DCB (=0.6 ml/kg bw) in both strains is temporally concordant with hepatic c-myc and Ha-ras expression	
Source:	NICNAS	
Test condition:	<p>Species: rat Strain: Sprague-Dawley and F344 No. of animals: not stated Sex: M</p> <p>Route of Administration: intraperitoneal (i.p.) Dose: 0.6 and 1.2 ml/kg bw Frequency of Treatment: once GLP: no Post Exposure Obs: hepatic c-myc and Ha-ras expression following 1,2-DCB exposure</p>	
31-AUG-2001		(152)
Type:	other: renal effects	
Remark:	Overall, 1,2-DCB (3.4 mmol/kg bw) tissue distribution was mainly to fat, liver and kidney; 1,2-DCB was reversibly bound to alpha-2u-globulin in kidney cytosol; 1,2-DCB was covalently bound to renal alpha-2u-globulin and to liver and plasma high molecular-weight proteins; no effect in either sex on protein droplet formation	
Source:	NICNAS	
Test condition:	<p>Species: rat Strain: Fischer-344 No. of animals: 3-6 per treatment group Sex: Male Route of Administration: gavage Dose: Single dose of 3.4 mmol/kg or seven day doses of 0.8 or 2.0 mmol/kg bw Exposure Period: Frequency of Treatment: once GLP: no data Post Exposure Obs: Changes in renal alpha2u-globulin concentrations characterised by changes in protein droplet formation; cell proliferation evaluation determined by tritiated thymidine incorporation during DNA synthesis to measure spontaneous or 1,2-DCB induced mutagenesis</p>	
Test substance:	1,2-DCB HPLC grade (99.0%)	
31-AUG-2001		(65)
Type:		
Remark:	a single oral administration of o-dichlorobenzene at a dose level of 0.14 ml/kg bw (= ca. 182 mg/kg bw) to male rats resulted in centrilobular hepatic necrosis and increased serum alanine aminotransferase and aspar-	

Source: tate aminotransferase activities; hepatic cytochrome P-450 levels decreased steadily at dose levels above 0.04 ml/kg bw (> 52 mg/kg bw)
20-AUG-2001 Bayer AG Leverkusen (8)

Type: Centrilobular hepatic necrosis occurred at 172 mg/kg bw, and above; dose-dependent increases in serum AST and ALT; centrilobular vacuolar degeneration was noted in 98 mg/kg treated animals; dose-dependent decrease (20-50% c.f. untreated controls) in hepatic cytochrome P450 levels; relative liver weights increased for all doses
Remark:
Source: NICNAS
Test condition: Species: rat
Strain: Fischer-344
Number of animals: 1 per dose
Sex: M
Route of Administration: gavage
Doses: 6 - 1784 mg/kg bw (up to 25 dosages)
Exposure Period: 24 hr
Frequency of Treatment: once per animal per treatment group

Control Group: corn oil vehicle
GLP: no data
Post Exposure Obs: Serum concentrations of aspartate aminotransferase (AST), alanine aminotransferase (ALT), and alkaline phosphatase activities; hepatic P450 levels
Test substance: purity: 99%
24-AUG-2001 (7)

Type: o-dichlorobenzene when introduced directly into the hepatic portal circulation of male and female rabbits produced massive localised areas of liver necrosis
Remark:
Source: Bayer AG Leverkusen (59)
10-SEP-2001

Type: in vitro assay: rat liver slices were incubated in dynamic organ culture using different types of incubation media; 1 mM (= 147 mg/l) of o-dichlorobenzene produced no hepatotoxicity when incubated with Waymouths medium with 10 % fetal calf serum and glucose but was substantially toxic when incubated in Krebs-Henseleit buffer supplemented with glucose; by supplementation of the Krebs-Henseleit buffer with fetal calf serum the hepatotoxic response by o-dichlorobenzene was completely inhibited
Remark:
Source: Bayer AG Leverkusen (101)
24-AUG-2001

Type: vapour inhalation experiments: a nominal vapour concentration of 1000 ppm (= ca. 6.12 mg/l) of o-dichlorobenzene was found to be lethal for guinea pigs after a single exposure for 20 hours, and narcosis, as well as injury to the liver and kidneys, was noted in this animal species; the effects on rabbits were less (no further data)
Remark:
Source: Bayer AG Leverkusen (49)
24-AUG-2001

Type:
Remark: urinary metabolites of o-dichlorobenzene after i.p. administration into mice included hydroxy-, mercapto-, methyl sulphide- and dihydroxy-metabolites (no further data)

Source: Bayer AG Leverkusen
14-AUG-2001 (143)

Type:
Remark: male Fischer rats were treated i.p. with various doses (0.9-4.5 mmol/kg bw = 132-662 mg/kg bw) of o-dichlorobenzene (single administration); at 24 hours after dosing, the plasma activity of glutamic-pyruvate transaminase (an indicator of liver injury) was elevated; in preliminary experiments male Sprague-Dawley rats were administered o-dichlorobenzene (i.p.; doses: 1.8 or 5.4 mmol/kg bw = 265 or 794 mg/kg bw); Sprague-Dawley rats were more resistant to the hepatotoxicity of o-dichlorobenzene; the elevation of plasma glutamic-pyruvate activity was markedly lower than the elevation seen in Fischer rats

Source: Bayer AG Leverkusen
24-AUG-2001 (239)

Type:
Remark: 1,2-DCB did not alter either LDH release from or inhibition of glycogenolytic activity in rat hepatocytes compared to untreated controls

Source: NICNAS
Test condition: Species: Rat (hepatocytes)
Strain: Wistar
No. of animals: 3
Sex: Male
Route of Administration: ex vivo
Dose: 200 mM
Exposure (h): 20
Frequency of Treatment: once
GLP: no data
Post Exposure Obs: Hepatocyte viability and glycogenolytic activity: release of lactose dehydrogenase (LDH); inhibition of glycogenolytic activity

Test substance: 1,2-DCB was dissolved in 0.05% DMSO to a final concentration of 200 mM
10-SEP-2001 (265)

Type:
Remark: in vitro assay: the metabolism of o-dichlorobenzene (concentration: 0.5 mM = 73.5 mg/l) was investigated in dynamic organ culture of rat or human liver slices; metabolism was shown to proceed in a time-dependent manner for up to six hours; using rat liver slices, no sex differences could be observed; both rat and human liver slices metabolised the test substance to similar extents, although o-dichlorobenzene distributed into human liver slices to a greater extent than into rat liver slices (metabolites not specified)

Source: Bayer AG Leverkusen
24-AUG-2001 (290)

Type:
Remark: Dose-response studies: serum ALT levels and the hepatic

labelling index (a measure of cell proliferation assessed by incorporation of 5-bromo-2'-deoxyuridine (BrdU) were significantly increased at 300 and 800 mg/kg bw 1,2-DCB and histopathological findings showed areas of centrilobular hepatocyte swelling and necrosis in 300 mg/kg bw 1,2-DCB dosed animals; Time-course studies: serum ALT levels were maximal at day 1 and decreased thereafter to basal levels at day 4 while the labelling index which was absent at day 1 was maximal at day 3 and declined to basal levels at day 7; histopathology revealed hepatic injury at day 1 that was maximal at day 2 and which subsequently declined to undetectable levels at day 7

Source: NICNAS
Test condition: Species: mouse
Strain: B6C3F1
Number of animals: 5 per dose group
Sex: Male
Route of Administration: single intragastric (ig) administration
Dose: 120, 200 or 300 mg/kg/bw (dose-response); 300 mg/kg bw (time-course study)

Observation Period: 2 days (dose-response); 1,2,3,4, or 7 days (time-course)
Frequency of testing: once
GLP: no data
Post Exposure Obs: Acute hepatotoxicity assessed by serum alanine aminotransferase (ALT) activity; hepatic histology

Test substance: 1,2-DCB purity > 98%
10-SEP-2001 (261)

5.11 Experience with Human Exposure

Memo: 1,2-DCB exposure from dry cleaning fluid
Remark: The authors describe a case study of an 18 years old female, who, following chronic daily inhalational exposure to vapours of a dichlorobenzene solvent mixture consisting of 95 % 1,2-DCB and 5 % 1,4-DCB, presented with: fatigue, nausea, headache, bone marrow hyperplasia, severe acute haemolytic anaemia, leucocytosis and polynucleosis.

Source: NICNAS
20-AUG-2001 (103)

Memo: 1,2-DCB exposure from manufacture
Remark: Repeat medical examinations in male workers (number notspecified) exposed to prolonged exposures of 15 ppm 1,2-DCB(range 1 to 44 ppm) revealed no evidence of 1,2-DCB-dependent organic injury or of adverse haematological effects

Source: NICNAS
20-AUG-2001 (129)

Memo: 1,2-DCB in the environment
Remark: Levels of 1,2-DCB in human adipose tissue samples collected in the Tokyo (Japan) metropolitan area were not noticeably above the level of 0.01 ug/g fat; 1,2-DCB was not detectable in human blood in the Tokyo (Japan) area

Source: Bayer AG Leverkusen
05-SEP-2001 (176) (177)

- Memo: 1,2-DCB irritant effects
Remark: Irritation to the eyes and respiratory passages was reported in humans exposed to concentrations up to 100 ppm in wool-filling processes
Source: NICNAS
05-SEP-2001 (94)
- Memo: 1,2-DCB residue in breast milk of the General and Indigenous Canadian population
Remark: gas chromatograph analysis for residues of 1,2-DCB in breast milk of both indigenous and general canadian population revealed similar concentrations of 1,2-DCB in the breast milk of both populations
Source: NICNAS
06-AUG-2001 (74)
- Memo: 1,2-DCB residues in breast milk of Canadian women
Remark: a total of 210 (3-4 weeks after parturition) human breast milk samples from 5 different regions across Canada were analyzed; residues of 1,2-DCB were found in 69 % of the samples; the mean levels of 1,2-DCB were 3 ng/g milk and 84 ng/g milkfat
Source: NICNAS
06-AUG-2001 (169)
- Memo: 1,2-DCB residues in human blood samples from U.S. residents
Remark: screening and confirmational analyses were performed on human blood samples collected from potentially exposed residents of the Love Canal area of Niagara Falls, New York, USA (field samples) and from volunteers in the Research Triangle Park area of North Carolina (volunteer samples) for various organochlorine contaminants, including 1,2-DCB; 1,2-DCB residues fell in the range of 1-4 ppb (mean value = 3 ppb) in 25 % of the field blood samples and in the range of 3-4 ppb (mean value = 4 ppb) in 17 % of the volunteer blood samples
Source: NICNAS
20-AUG-2001 (42)
- Memo: 1,2-DCB urinary metabolites
Remark: Metabolites of 1,2-DCB detected were: 2,3- and 3,4-dichlorophenols and 3,4- and 4,5-dichlorocatechols
Source: NICNAS
Test condition: Gas chromatograph-mass spectroscopy was used to determine 1,2-DCB metabolites present in urine samples of 3 male workers exposed to 1,2-DCB (1-4 ppm)
24-AUG-2001 (153)
- Memo: Dietary intake of 1,2-DCB in Canada
Remark: Based on measured concentrations of 1,2-DCB in foods, dietary intake of 1,2-DCB was estimated at 108 ug per person and year
Source: NICNAS
05-SEP-2001 (75)
- Memo: Effect of 1,2-DCB atmospheric contamination in the working environment
Remark: "Severe toxic" effects of occupational inhalation exposure to 1,2-DCB 300 ppm (= ca. 1.836 mg/l) for 60 min at 100 ppm (= ca. 0.612 mg/l) illness reported; concentrations greater than 25 ppm (= ca. 0.153 mg/l) in workplace indicated

	unsatisfactory conditions (no further data)	
Source: 05-SEP-2001	NICNAS	(108)
Memo: Remark:	other: 1,2-DCB in drinking water and blood plasma 1,2-DCB was detected in blood plasma samples studied however no concentrations were stated	
Source: Test condition: 20-AUG-2001	NICNAS Gas chromatograph-mass spectroscopy was used to determine 1,2-DCB present in pooled blood plasma from eight human subjects	(90)
Memo: Remark:	other: Retrospective study Retrospective study examining possible causality in 7 individuals suffering serious blood borne disorders following workplace exposure to chlorinated benzene derivatives (mono, di and tri); coincidental relationship cannot be discounted	
Source: 20-AUG-2001	NICNAS	(202)
Remark:	o-dichlorobenzene was detected (concentrations in the parts-per-billion range) in human blood from a normal "unexposed" population	
Source: 24-AUG-2001	Bayer AG Leverkusen	(13)
Remark:	dichlorobenzene isomer(s) was (were) found in the breath (range of estimated levels: 60-5000 ng per cubic metre), blood (estimated levels: 0.15-68 ng per ml) and urine (estimated levels: 40-39000 ng per l) of an exposed pop- ulation (the dichlorobenzene isomer(s) was (were) not specified)	
Source: 19-AUG-1993	Bayer AG Leverkusen	(19)
Remark:	canal-diggers had inhaled vapours from the waste water of a dry cleaning plant utilizing o-dichlorobenzene; signs of toxicity were observable: irritation of the eyes and of the respiratory tract as well as nausea	
Source: 24-AUG-2001	Bayer AG Leverkusen	(91)
Remark:	o-dichlorobenzene is mentioned in a list of environmen- tal chemicals detectable in low concentrations in adip- ose tissue and/or milk of non-occupationally exposed humans (no further data)	
Source: 30-AUG-1993	Bayer AG Leverkusen	(106)
Remark:	several cases of chronic human exposure to solvent mix- tures (containing o-dichlorobenzene; composition of the mixtures partly unknown) are reported; in the exposed persons leukaemia and in a single case anaemia were diag- nosed; the findings are not clearly attributable to the exposure to o-dichlorobenzene	
Source: 04-JAN-1994	Bayer AG Leverkusen	(107)
Remark:	the mean levels of o-dichlorobenzene in human adipose tis-	

- sue and in human milk were determined; the following values were found: 9 ug/kg milk, 230 ug/kg milk fat and 13 ug/kg fat in adipose tissue
- Source: Bayer AG Leverkusen (135)
10-SEP-1993
- Remark: expired air samples have been collected from a carefully selected population of normal healthy human subjects under controlled experimental conditions; the samples were concentrated and analyzed by quantitative techniques which resulted in well-defined composite compositional and occurrence profiles of the organic constituents present in normal expired air; among 102 organic compounds, o-dichlorobenzene was identifiable in human expired air
- Source: Bayer AG Leverkusen (147)
17-SEP-1993
- Remark: paired whole blood and biopsy fat samples from a selected Canadian population (25 patients) were analyzed for 1,2-DCB; the median value of 1,2-DCB residues in blood was below the limit of detection (< 3.12 ng/g wet tissue); the median value of 1,2-DCB in biopsy fatty tissue was found to be 28.1 ng/g wet tissue; the median value of 1,2-DCB in blood lipids was found to be < 3 ng/g lipid; the median value of 1,2-DCB in adipose tissues was found to be 38 ng/g lipid.
- Source: NICNAS (168)
27-APR-2001
- Remark: the presence of 1,2-DCB residues in adipose tissue of Canadians was investigated by analysis of 108 human autopsy fat samples; the mean value of 1,2-DCB residues in adipose tissue was found to be 136 ng/g wet tissue; no significant differences in the residue levels of in adipose tissue were found with respect to region, gender or age
- Source: NICNAS (170)
27-APR-2001
- Remark: human olfactory threshold for o-dichlorobenzene: 0.003 mg/l
- Source: Bayer AG Leverkusen (210)
24-AUG-2001
- Remark: o-dichlorobenzene was applied on the flexor side of the forearm of probands (exposure time: 1 hour); ca. 15 minutes after the administration, the test substance induced strong burning at the site of application, which disappeared after removal of o-dichlorobenzene; at first a diffuse reddening was visible at the site of application; 24 hours after application this site was deep red coloured and covered with vesicles; later on a brownish pigmentation was observable, which was still visible after 3 months
- Source: Bayer AG Leverkusen (216)
11-OCT-1993
- Remark: human olfactory detection threshold for o-dichlorobenzene: 0.3 ppm (= ca. 0.00183 mg/l)
- Source: Bayer AG Leverkusen (221)
13-OCT-1993
- Remark: case report: a patient was overcome in a home treated with o-dichlorobenzene; after 2 days this patient became

- nauseated, suffered from shortness of breath and sleepiness, and 1 week later developed a haematuria of 2 weeks duration; it appears questionable, whether and to what extent o-dichlorobenzene was responsible for these symptoms
- Source: Bayer AG Leverkusen (187)
13-OCT-1993
- Remark: the air concentration level of 1,2-DCB where irritation to humans begins (threshold of irritation), was found to be 0.15 mg/l; odour threshold values were found to range between 0.012 mg/l and 0.3 mg/l (no further data)
- Source: NICNAS (225)
27-APR-2001
- Remark: vapours of o-dichlorobenzene are liable to cause such symptoms as headache in persons exposed to the fumes for an hour or so at a time (no further data)
- Source: Bayer AG Leverkusen (232)
14-OCT-1993
- Remark: an ad hoc list of neurotoxic chemicals in the Danish work environment has been developed and consists of those chemicals from the Danish list of threshold limit values (1985) which have been noted as having neurotoxic effects; 1,2-DCB is included in this list and has been assigned the risk index 4: chemical with a conspicuous risk of inducing severe and/or chronic damage to the nervous system during normal work with the substance (no further data)
- Source: NICNAS (237)
24-AUG-2001
- Remark: case report: a 40-year old man had worked for 22 years in the preparation of dyestuffs in dye-works; the list of products handled included various products (dyestuffs-phenols) and o-dichlorobenzene as main solvent; the patient suffered from purpura and intense anaemia; a marked hepatomegalia and a discreet splenic enlargement were the only examination signs; the blood count and the myelogram showed total medullar insufficiency; the diagnosis hesitated between myeloid leukosis and a myeloproliferative syndrome which was chosen because of the presence of young myeloid cells in the peripheral blood, of erythroblastosis, and especially from indications given by a medullar biopsy which showed positive myelofibrosis; this myelosis was very proliferative and its evolution was fatal within 4 months; the role of o-dichlorobenzene in the etiology of this haemopathy is debated
- Source: Bayer AG Leverkusen (257)
26-OCT-1993
- Remark: case report: a 30-year old woman was exposed to vapours of a disinfectant containing 54 % o-dichlorobenzene; she developed hepatitis and icterus (it is discussed if the hepatitis is due to an intoxication or to a viral infection)
- Source: Bayer AG Leverkusen (209)
27-OCT-1993
- Remark: in a review study, o-dichlorobenzene is listed among many other chemical substances which all are capable of inducing haemolytic anaemia in persons exposed occupationally (by an accident at industrial workplace) to the substance (no further data)

Source: Bayer AG Leverkusen (259)
06-AUG-2001

Remark: o-dichlorobenzene was occasionally detectable in exhaled human breath samples from U.S. residents; compound concentrations were also measurable in personal air and in outdoor air samples

Source: Bayer AG Leverkusen (280) (281) (282) (283)
10-NOV-1993

Remark: chromosome studies were done in 8 males and 18 females (laboratory workers) who were accidentally exposed for 4 work days (8 hours/day) to vapours of 1,2-DCB; the clinical symptoms included eye, nose and throat irritation (most individuals); 10 persons had severe headache, fatigue, nausea, dizziness; 1 individual developed partial facial edema; although there was no determination of the concentration of toxic vapours, the symptoms of most exposed individuals were consistent with those usually observed at concentrations above 100 ppm (ca. 0.60 mg/l); of the 1345

peripheral blood cells studied, 120 disclosed clastogenic chromosomal aberrations (8.92 %), 84 (6.25%) had single breaks and 86 (6.39%) had double breaks; a control group of 16 healthy individuals revealed 19 cells with clastogenic aberrations in 942 cells examined (2.02 %) while 9 (0.92%) had single breaks and 10 (1.06%) had double breaks; chromosome studies conducted 6 months later in 15 persons of the exposed group disclosed a significant reduction in both chromosomal aberrations (12 cells from 300 (4%)) and the number of single breaks (8 cells from 300 (2.67%))

Source: NICNAS (301)
05-SEP-2001

Remark: case report: a worker aged 47 had developed an eczematoid contact dermatitis of the hands, arms and face and was therefore physically examined; the patient was tested by dropping on the skin o-dichlorobenzene: two minutes after this was dropped on one arm intense erythema and edema developed at the site of application and for one-half inch surrounding it; later a large bullous lesion formed in the center of this area

Source: Bayer AG Leverkusen (89)
14-JAN-1994

Remark: urine samples collected from 8 volunteers for 36 h after exposure to 1,2-DCB in the range of 0.03-0.3 mg/l and, in one case up to 0.54 mg/l for two 4 h periods with a 45 min interval were analysed for the presence of isomeric dichlorophenylmercapturic acids; ethyl esters of 2,3-dichlorophenylmercapturic acid and 3,4-dichlorophenylmercapturic acid were detected in the urine, with a linear correlation found between urinary dichlorophenylmercapturic acid concentration and the level of 1,2-DCB exposure; a first-order excretion kinetic was determined for the two dichlorophenylmercapturic acids; the half lives of 3,4-dichlorophenylmercapturic acid and 2,3-dichlorophenylmercapturic acid were determined to be 5.9 +/- 1.7 h and 5.3 +/- 3.0 h respectively.

Source: NICNAS (302)
24-AUG-2001

Remark: Clinical features of 9 men chronically exposed to chlorobenzenes while working in a factory producing 1,2-, 1,3- and 1,4- DCB, and all of whom had direct contact with the chemicals through the skin and respiratory tract were found to include: polymorphic dermatosis in all patients, mainly comedones and cysts; some patients also had diffuse melanocytic discoloration, hyperpigmentation of the face, pigmentation of the lips, gums and oral mucosae, longitudinal lines on the fingernails, plantar hyperhydrosis or follicular hyperkeratosis; skin biopsies showed features typical of chloracne in all patients (comedones, cysts and follicular indifundibular enlargement), persisting for at least 2 years after leaving the company; all had conjunctivitis and reported chronic burning sensations of the eye; 7 had enlargement of and cysts in the Meibomian glands; all had gastrointestinal complaints, mostly nausea and occasionally vomiting, during working hours; all reported paresthesias, mostly in the lower extremities; diarrhea, irritability, insomnia and frequent headaches were also reported; liver function tests were abnormal in 8 patients while 5 had enlargement of the liver; findings of percutaneous liver biopsy included chronic inflammatory infiltrate in the sinusoids, portal and centrolobular areas, fatty degeneration of small and large fat droplets, granulomas, cholestasis, fibrosis and cirrhosis; 7 patients had significantly raised triglyceride and cholesterol levels; an electromyogram revealed a mixed polyneuropathy in all patients. Due to an insufficiency of data, a causal relationship between the symptoms described and 1,2-DCB exposure cannot be demonstrated

Source:
19-APR-2001

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