FOREWORD **INTRODUCTION**

1,2-DICHLOROETHANE

CAS N°: 107-06-2

SIDS Initial Assessment Report

for 14th SIAM

(Paris, France, March 2002)

Chemical Name:	**1,2-Dichloroethane**
CAS No :	**107-06-2**
Sponsor Country :	**Germany**

National SIDS Contact Point in Sponsor Country

Lead Organization:	
Name of lead organization:	BMU (Bundesministerium für Umwelt, Naturschutz und Reaktorsicherheit)
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History:	see next page
Testing:	No new SIDS testing (X) New SIDS testing ( )
Comments:	
last literature research:	Toxicology: 14.06.01; Ecotoxicology: 24.07.01
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Date of Circulation:	01. February 2002

OECD/ICCA - The BUA* Peer Review Process

Qualified BUA personnel (toxicologists, ecotoxicologists) perform a quality control on the full SIDS dossier submitted by industry. This quality control process follows internal BUA guidelines/instructions for the OECD/ICCA peer review process and includes:

- a full (or update) literature search to verify completeness of data provided by industry in the IUCLID/HEDSET

- Review of data and assessment of the quality of data

- Review of data evaluation

- Check of adequacy of selection process for key studies for OECD endpoints, and, where relevant, for non-OECD endpoints by checking original reports/publications

- Review of key study description according robust summaries requirements; completeness and correctness is checked against original reports/publications
  (if original reports are missing: reliability (4), i.e. reliability not assignable)

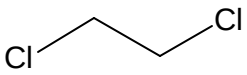
- Review of validity of structure-activity relationships

- Review of full SIDS dossier (including SIAR, SIAP and proposal for conclusion and recommendation for further work)

- In case of data gaps, review of testing plan or rationale for not testing

* BUA (GDCh-Beratergremium für Altstoffe): Advisory Committee on Existing Chemicals of the Association of German Chemists (GDCh)

SIDS INITIAL ASSESSMENT PROFILE

CAS No.	107-06-2
Chemical Name	1,2-Dichloroethane
Structural Formula	

SUMMARY CONCLUSIONS OF THE SIAR

Human Health

1,2-Dichloroethane has to be considered as harmful after inhalation and oral application and as uncritical after dermal exposure, based on the GHS system. LD_{50} values ranging from about 400 – 1000 mg/kg bw (oral), > 4000 mg/kg bw (dermal) and from approx. 4000 mg/m^3 (7 h) to >49,000 mg/m^3 (0.5 h). A respiratory 4-h NOAEL is approximately 1400 mg/m^3 in rats. However, a steep concentration-response relationship associated with sudden, often unexpected mortality is characteristic of 1,2-dichloroethane. Death is thought to occur through CNS (Central Nervous System) and cardiovascular depression.

Studies on primary irritation of the substance demonstrated a low irritation potential both to the skin and eyes. In contrast to other species tested, specifically dogs experienced corneal turbidity and oedema after single and repeated atmospheric exposure to systemically toxic concentrations (about 4000 mg/m^3), but not when exposed to lower ones.

No studies on contact allergy were located.

Several repeated dose toxicity studies following oral and inhalation exposure in rats and mice showed mild histopathological effects after inhalation in lung, liver and in the kidneys of rats and mice at high doses or, after gavage dosing, minimal local lesions of the kidney and the forestomach. A subchronic drinking-water study does not allow to derive a NOAEL because of the highly reduced water consumption by the test animals. The lowest NOAEL for subchronic oral exposure by gavage is assumed to be 120 and 150 mg/kg bw/d for male and female rats, respectively, based on treatment-related effects in the forestomach and clinical symptoms, while the chronic oral NOAEL of about 25 mg/kg bw is equivalent to the highest dose administered to rats for two years in the diet. For inhalation, studies are conducted on a broad spectrum of species. A two-year-study shows a NOAEL of 50 ppm in rats. At subchronic to chronic exposure to 200 ppm variable responses from unremarkable to toxic and lethal were observed even within the same species. Based on the GHS-system, 1,2-dichloroethane should be regarded as harmful following repeated inhalation exposure.

1,2-Dichloroethane is mutagenic and genotoxic in bacterial and mammalian *in vitro* test systems, but gave no evidence of *in vivo* mutagenic activity (mouse micronucleus and DL assay), while some *in vivo* genotoxic potential was demonstrated in mice. However, evidence of DNA damaging *in vivo* activity/genotoxicity is presented by positive results in SCE assay and single DNA strand-break analysis. The cytochrome-P450 and glutathione-dependent pathways are assumed to be responsible for the generation of intermediates capable of binding to and damaging DNA.

1,2-Dichloroethane was shown to produce carcinogenic effects at multiple sites in rats and mice of both sexes after oral gavage administration for 78 weeks (up to 195 and 300 mg/kg/d, respectively), but not after inhalation in both species exposed to a reasonably high concentration of 150 ppm (about 600 mg/m^3) for the same period of time. Based on the GHS-system, 1,2-dichloroethane has to be regarded as suspected human carcinogen. The route of application-specific expression of tumorigenesis may be explained by the difference in pharmacokinetics and dominance of metabolic pathways under either dosing mode: Systemically toxic inhalation concentrations result in significantly lower blood and organ levels than toxic gavage doses and, therefore, are expected to be (hypothetically) less likely to form oncogenic intermediates.

There was no evidence of 1,2-dichloroethane-induced impairment of reproductive performance in rats and mice including fertility of either sex and fetal viability parameters after repeated oral doses of 50 mg/kg bw/d (feed and

drinking water) and after inhalation exposure to up to 150 ppm in several one-and two-generation studies. Furthermore, no histopathological adverse effects on the gonads were reported in two oral long-term studies in rats and mice.

In Several investigations on developmental toxicity, no significant toxicity was noted in the offspring of rats receiving up to maternally toxic oral (gavage) and inhalation doses during pregnancy. The NOAELs for developmental effects were the highest doses employed, 240 mg/kg bw/d and 300 ppm, respectively.

In humans, incidental ingestion has been reported as cause of death; occupational dermal and inhalation exposure have produced marked systemic intoxication: primarily unspecific neurotoxic symptoms developed such as nausea, vomiting, headache, stupor, dysequilibrium, and - in fatal cases – coma followed by respiratory arrest. Severe cases also involved lesions of liver, kidney, and adrenal glands. High dermal and respiratory exposures caused skin and eye irritation. There have been no human case reports on skin sensitisation in the literature. In workers exposed to a mixture of vinyl chloride monomer (VCM) and 1,2-dichloroethane a statistically significant increase in SCE frequency of about 24 % in the higher exposed subgroup (20 individuals) was found. This increase was also obvious in non-smoking workers, and it was additionally shown that the SCE frequency was positively correlated with smoking but not with drinking habits and VCM exposure.

Environment

1,2-Dichloroethane has a water solubility of 8490 – 9000 mg/l, a vapor pressure of 81 hPa at 20°C and a log Kow of 1.45. According to a Mackay I model the atmosphere is the target compartment for the substance (~95 %), followed by water (~5 %). A Henry's law constant of 95.7 – 149 Pa * m^3/mol was determined. Due to its chemical structure the substance will not undergo both hydrolysis in water and photodegradation by direct sun-light. A half-life of 42 to 73 days was calculated for indirect photodegradation by hydroxyl radicals in the atmosphere. Field measurements confirmed, that the photodegradation in the atmosphere prevents the global distribution and the atmospheric enrichment of emissions, released by industry mainly in the northern hemisphere.

1,2-Dichloroethane is not biodegradable under non-adapted test conditions but it could be demonstrated that appropriately adapted bacteria or enrichment with degradation promoting factors lead to acceptable and fast biodegradation rates. However, under environmental conditions biodegradation is not likely to occur. No potential for bioaccumulation (measured BCF = 2) or geoaccumulation (measured Koc = 33) could be identified. In acute and long-term ecotoxicity tests with aquatic organisms the following results were found:

LC_{50} (96 h)	= 66 mg/l (*Micropterus salmoides*)
LC_{50} (96 h)	= 115 mg/l (*Limanda limanda*)
EC_{50} (24 h)	= 36 mg/l (*Artemia salina*)
EC_{50} (24 h)	= 150 mg/l (*Daphnia magna*)
EC_{50} (72 h)	= 189 mg/l (*Scenedesmus subspicatus*)
NOEC (32 d)	= 29 mg/l (*Pimephales promelas*)
NOEC (28 d)	= 11 mg/l (*Daphnia magna*, Reproduction)

All effect values are based on measured concentrations or were performed in closed systems.

Taking into account the results of the different chronic toxicity studies conducted in aquatic organisms and considering the lowest valid NOEC of 11 mg/l obtained in a chronic aquatic toxicity reproduction test conducted in *Daphnia magna* a PNEC of 1100 µg/l is being derived applying a safety factor of 10.

Exposure

The worldwide production volume of 1,2-dichloroethane exceeds 1,000,000 tonnes/year. The main uses are as chemical intermediate in the vinylchloride monomer (VCM) manufacture with a contribution of about 95%. The remaining 5% of produced 1,2-dichloroethane enter applications such as raw materials for ethyleneamines, tri- and tetrachloroethylene, extraction and cleaning solvent as well as lead scavengers for gasoline. Due to the increasing use of unleaded fuel the latter application is assumed to subside gradually. 1,2-Dichloroethane emissions to the aquatic environment and to the atmosphere come nearly exclusively from manufacturing industrial locations and only to a minor extent from its use as extraction and cleaning solvent and as lead scavenger, respectively. It is not clear, however, whether 1,2-dichloroethane is still being used in aircraft gasoline.

Production and handling of 1,2-dichloroethane takes place in closed systems and it is directly transported via pipelines during filling processes, e.g. loading of tanker ships. In all countries with production plants occupational exposure limit values are established, during maintenance operations personal protection is mandatory.

In 1993 it was reported that 150 tonnes were emitted to the atmosphere during production and processing in Germany by 9 production and/or processing sites. Releases into the hydrosphere were estimated to be about 4.46 t for 7 producers/processors.

European Product Registers have several entries of paints and lacquers, adhesives and fertilizers containing 1,2-dichloroethane. But according to national laws these products are only available for professional use.

RECOMMENDATION

The chemical is currently of low priority for further work.

RATIONALE FOR THE RECOMMENDATION AND NATURE OF FURTHER WORK RECOMMENDED

Human Health: The substance is currently of low priority for further work. Although hazardous properties have been identified for this substance (possible genotoxic and carcinogenic effects), the overall exposure in humans is low, as it is mostly used as a chemical intermediate. In some countries, where products for professional use containing 1,2-dichloroethane may still be available, further exposure assessment and if necessary risk assessment is recommended.

Environment: The substance is currently of low priority for further work. This can be concluded from the main use as chemical intermediate, the very low bioaccumulation potential and the low toxicity to aquatic organisms.

FULL SIDS SUMMARY

CAS NO: 107-06-2	SPECIES	PROTOCOL	RESULTS
PHYSICAL-CHEMICAL DATA			
2.1 Melting Point			-35.5 to –36°C
2.2 Boiling Point			83.5 – 84.1°C
2.3 Density			1.235 – 1.253 g/cm^3 (20°C)
2.4 Vapour Pressure			81.3 hPa at 20°C
2.5 Partition Coefficient (Log Kow)		measured	1.45
2.6 A. Water Solubility			8490 – 9000 mg/l at 20°C
B. pH			at °C
pKa			
2.12 Oxidation: Reduction Potential			MV
ENVIRONMENTAL FATE AND PATHWAYS			
3.1.1 Photodegradation		Calculated (acc. to Atkinson)	In air $T_{1/2}$ = 42 d (at a concentration of 1.5x10e6 radicals/cm^3 and a rate constant of 0.25x10e-12cm^3/moleculexsec)
		Calculated (acc. to Atkinson)	In air $T_{1/2}$ = 73 d (at a concentration of 5x10e5 radicals/cm^3 and a rate constant of 0.22x10e-12cm^3/moleculexsec)
3.1.2 Stability in Water			Not applicable, not hydrolysable
3.2 Monitoring Data		No up-to-date monitoring data available	In air : industrial locations: 21.4 µg/m^3 Non-industrial locations: 12.4 µg/m^3 In river water : 4.4 - 8.5 µg/l In drinking water :0.88 – 1.32 µg/l
		BUA report on 1,2-dichloroethane (data for 1993)	Emissions: In air : 150 t In water : 4.46 t
3.3 Transport and Distribution		Calculated (Mackay Level I v2.11)	In air : 95.03 % In water : 4.84 % In sediment : 0.00 % In soil : 0.12 % In biota : 0.00 %
		Estimated Henry's Law Constant	95.7 Paxm^3/mol at 20°C
		Experimental Henry´s Law Constant	149 Paxm^3/mol at 20°C
		Experimental Henry´s Law Constant	143 Paxm^3/mol at 25°C
3.5 Biodegradation		cf. IUCLID file „1,2-dichloroethane“ (Activated sludge, adapted, non-adapted and enriched)	Not biodegradable in soil and water under non-adapted conditions Biodegradable after adaptation and methane enrichment
3.7 Bioaccumulation		Estimation Method	BCF = 2.75 (log BCF = 0.44)
		Measured	BCF = 2 (log BCF = 0.30)

CAS NO: 107-06-2		SPECIES	PROTOCOL	RESULTS
ECOTOXICOLOGICAL DATA				
4.1	Acute/Prolonged Toxicity to Fish	Micropterus salmoides	static conditions, analytics	LC_{50} (96 h) = 66 mg/l
		Lepomis macro-chirus	EPA-660/3-75-009, closed system	LC_{50} (96 h) = 430 mg/l
		Limanda limanda	flow-through, analytics	LC_{50} (96 h) = 115 mg/l
		Pimephales promelas	EPA-660/3-75-009 flow-through, analytic	LC_{50} (96 h) = 116 mg/l
4.2	Acute Toxicity to Aquatic Invertebrates	Daphnia magna	OECD 202, analytics	EC_{50} (24 h) = 150 mg/l
		Artemia salina	No standard, similar to OECD 202; closed system; reduced salinity	EC_{50} (24h) = 36 mg/l
		Eliminius modestus	Closed system	LC_{50} (48h) = 186 mg/l
4.3	Toxicity to Aquatic Plants e.g. Algae	Scenedesmus subspicatus	OECD 201, closed system, analytic	EC_{50} (72h) = 189 mg/l
4.4	Toxicity to Microorganisms	Entosiphon sulcatum	toxicity threshold measurement; closed system	TT (72 h) = 1127 mg/l
		Pseudomonas putida	Similar to DIN 38412	TT (16 h) = 135 mg/l
4.5.1	Chronic Toxicity to Fish	Pimephales promelas	Preliminary Early-Life Stage Test, flow-through, analytic	NOECs (32 d) = 29 mg/l LOEC (32 d) = 59 mg/l
4.5.2	Chronic Toxicity to Aquatic Invertebrates (*Daphnia*)	Daphnia magna	ASTM Proposed Standard Practice (1979) semistatic, closed system, analytic	LOEC (28 d) = 21 mg/l (Reproduction) NOEC (28 d) = 11 mg/l (Reproduction)
4.6.1	Toxicity to Soil Dwelling Organisms	Eisenia fetida	EEC 79/831	LC_{50} (48 h) = 0.06 mg/cm^2
TOXICOLOGICAL DATA				
5.1.1	Acute Oral Toxicity	rat	Gavage	LD_{50} = 770 - 967 mg/kg bw
		mouse	Gavage	LD_{50} = 413 - 911 mg/kg bw
		rabbit	Gavage	LD_{50} = 910 mg/kg bw
5.1.2	Acute Inhalation Toxicity	Rat	Whole-body exposure	LC_{50} = 4100 mg/m^3/7.2h – 49400 mg/m^3/0.5h
		Rat	Derived from dose-response curve	LC_{50} = approx. 8000 mg/m^3/4 h
		Rat	Derived from dose-response curve	Acute NOAEL = approx. 1400 mg/m^3/4 h

CAS NO: 107-06-2		SPECIES	PROTOCOL	RESULTS
TOXICOLOGICAL DATA (cont´d)				
		Rat	Determined	Acute NOAEL = approx. 800 mg/m³/7 h = approx. 1200 mg/m³/3 h = approx. 4000 mg/m³/1.5 h
		mouse	Whole-body exposure	LC_{50} = 1080 mg/m³/6h
		guinea pig	Whole-body exposure	LC_{50} = 6400 mg/m³/7h
5.1.3	Acute Dermal Toxicity	rabbit	Occluded application	LD_{50} = 4890 mg/kg bw
5.2.1	Skin Irritation / Corrosion	rabbit	Occluded 4-h application (US Fed. Reg. 37, 1972)	not irritating
5.2.2	Eye Irritation / Corrosion	rabbit	Draize-Test	slightly irritating
5.4	Repeated Dose Toxicity	Rat	Feeding study, 2 yr, with special control of DCE stability in the diet	NOAEL = approx. 25 mg/kg bw/d (= highest dose tested)
		Rat	Drinking water, 13 wk, NTP protocol, GLP, 3 strains	NOAEL cannot be derived
		Rat	Gavage , 13 wk, NTP protocol, GLP	NOAEL = 120 mg/kg bw/d (m); 150 mg/kg bw/d (f) LOAEL = 240 mg/kg bw/d (m); 300 mg/kg bw/d (f)
		Mouse	Drinking water; 13 wk, NTP protocol, GLP	NOAEL = approx. 780 mg/kg bw/d (m); approx. 2500 mg/kg bw/d (f) LOAEL = approx. 2700 mg/kg bw/d (m)
		Rat	Inhalation: 30 wk, 7 h/d, 5 d/wk	NOAEL = 822 mg/m^3 (approx. 200 ppm) LOAEL = 1644 mg/m^3 (approx. 400 ppm)
		Rat	Inhalation: 17 wk, 7 h/d, 5 d/wk	NOAEL = 411mg/m^3 (approx. 200 ppm) LOAEL = 2055 mg/m^3 (approx. 500 ppm)
		Rat	Inhalation: 15 wk, 7 h/d, 5 d/wk	NOAEL = 420 mg/m^3 (102 ppm) LOAEL = 730 mg/m^3 (178 ppm)
		Rat	Inhalation: 78 wk	NOAEL = approx. 1012 mg/m^3 (150 ppm) (= highest dose tested)
		Rat	Inhalation: 2 yr	NOAEL = approx. 200 mg/m^3 (50 ppm) (= highest dose tested)
		Mouse	Inhalation: 78 wk	NOAEL = approx. 1012 mg/m^3 (150 ppm) (= highest dose tested)
		Rabbit	Inhalation (Screening): 25 wk, 7 h/d, 5 d/wk	NOAEL = 730 mg/m^3 (approx. 200 ppm)
		Rabbit	Inhalation (Screening) approx. 46 wk, 7 h/d, 5 d/wk	NOAEL = 1620 mg/m^3 (400 ppm)
		Rabbit	Inhalation (Screening): 17 wk, 6 h/d, 5 d/wk	NOAEL = approx. 400 mg/m^3 (100 ppm)
		Dog	Inhalation (Screening): 25 wk, 7 h/d, 5 d/wk	NOAEL = 1540 mg/m^3 (375 ppm)

CAS NO: 107-06-2		SPECIES	PROTOCOL	RESULTS
TOXICOLOGICAL DATA (cont´d)				
		Guinea pig	Inhalation: 49 wk, 7 h/d, 5 d/wk	NOAEL = 810 mg/m^3 (200 ppm)
		Guinea pig	Inhalation: approx. 14 wk, 7 h/d, 5 d/wk	NOAEL = 420 mg/m^3 (approx. 100 ppm)
		Guinea pig	Inhalation: 17 wk, 6 h/d, 5 d/wk	NOAEL = approx. 420 mg/m^3 (100 ppm)
		Monkey	Inhalation (Screening): 42 wk, 7 h/d, 5 d/wk	NOAEL = 405 mg/m^3 (approx. 100 ppm)
		Monkey	Inhalation (Screening): 25 wk, 7 h/d, 5 d/wk	NOAEL = 730 mg/m^3 (approx. 200 ppm)
5.5	Genetic Toxicity In Vitro			
A.	*Bacterial Test (Gene Mutation)*	S. typhimurium TA 1530, 1535, 1538	Ames-Test (without metabolic activation)	positive
		S. typhimurium TA 98, 100, 1535, 1537, 1538	Ames-Test (with and without metabolic activation)	2x negative
		S. typhimurium TA 98, 100, 1535, 1537, 1538	Ames-Test (with and without metabolic activation)	ambiguous
		S. typhimurium TA 1535	Ames-Test (with and without metabolic activation, including GSH source)	weakly positive
		S. typhimurium TA 98, 100, 1535, 1537, 1538	Ames-Test (with and without metabolic activation)	positive
		E. coli WP2 uvrA	Incubation at 37°C for 18 h (without metabolic activation)	ambiguous
B.	*Non-Bacterial In Vitro Test*	CHO-cells	HGPRT: TK$^{+/-}$-Test	positive (with metabolic activation) positive (without metabolic activation)
		AHH-1and TK6 human lympho-blastoid cell lines	HGPRT:TK$^{+/-}$-Test (without metabolic activation)	positive
		CHL-cells	Chromosome Aberration Test	positive (with metabolic activation) [no chromosome breaks or exchanges] negative (without metabolic activation)
		BALB/C-3T3 cells	Cell transformation with 3-MC as pos. control (without metabolic activation)	negative
		Primary rat hepatocytes	UDS-Test (without metabolic activation)	positive
5.6	Genetic Toxicity In Vivo	NMRI mouse	Micronucleus-Test: 2x i.p. dosing	negative
		Transgenic mouse, lymphoma prone	Micronucleus-Test: repeated oral dosing, 14 and 41 wk	negative
		Swiss mouse	SCE in bone marrow, i.p.	positive at 1 mg/kg bw and above

CAS NO: 107-06-2		SPECIES	PROTOCOL	RESULTS
TOXICOLOGICAL DATA (cont´d)				
		Swiss mouse	Dominant Lethal, oral, drinking water (max. dose approx. 50 mg/kg bw/d)	negative
		B6C3F1mouse	DNA-breaks/alkaline DNA elution: oral, i.p, inhalation	positive
		Drosophila melanogaster	SLRL-Test: oral feed, gas-phase	positive
		Drosophila melanogaster	SMART-Test: oral feed	positive
5.7	Carcinogenicity	F344 Rat (NCI, 1978)	Oral administration by gavage	positive: squamous cell carcinomas of the forestomach; hemangiosarcomas subcutaneous fibroma (m) mammary gland adenocarcinomas and fibroadenomas; hemangiosarcomas(f) high mortality at high dose
		B6C3F1 Mouse (NCI, 1978)	Oral administration by gavage	positive: alveolar/ bronchiolar adenomas, hepatocellular carcinomas (m) mammary gland carcinomas, pulmonary adenomas (f) high mortality at high dose
		SD Rat (Maltoni et al. 1980)	Inhalation: 7 h/d, 5 d/wk	negative: type and number of observable tumors were comparable to controls; high-dose toxicity at 250 ppm, but not at 150 ppm
		Swiss Mouse (Maltoni et al. 1980)	Inhalation: 7 h/d, 5 d/wk	negative: type and number of observable tumors were comparable to controls; high dose toxicity at 250 ppm, but not at 150 ppm
		SD Rat (Cheever et al. 1990)	Inhalation: 7 h/d, 5 d/wk	negative: type and number of observable tumors were comparable to controls; no toxicity observed
5.8	Toxicity to Reproduction	Rat	Repeated one-generation study: 2yr, diet, 250 and 500 ppm	NOAEL = 40-60 mg/kg bw/d (500 ppm) (General Toxicity) NOAEL = 40-60 mg/kg bw/d (500 ppm) (Repro. Tox. parental) NOAEL = 40-60 mg/kg bw/d (500 ppm) (Repro. Tox. F1)
		SD rat	One-generation study:Inhalation: 6 h/d, 5-7 d/wk, 60 d pre-mating exposure	NOAEL = 616 mg/m^3 (150 ppm) (General Toxicity) NOAEL = 616 mg/m^3 (150 ppm) (Repro. Tox. parental) NOAEL = 616 mg/m^3 (150 ppm) (Repro. Tox. F1)
		ICR mouse	Two-generation: drinking water, 5 wk(Fo) and 11 wk(F1) pre-mating exposure	NOAEL = approx. 50 mg/kg bw/d (General Toxicity) NOAEL = approx. 50 mg/kg bw/d (Repro. Tox. parental) NOAEL = approx. 50 mg/kg bw/d (Repro. Tox. F1/F2) *Note: NOAEL = upper dose tested*

CAS NO: 107-06-2		SPECIES	PROTOCOL	RESULTS
TOXICOLOGICAL DATA (cont´d)				
5.9	Developmental Toxicity/ Teratogenicity	SD rat	Oral gavage	NOAEL = approx.160 mg/kg bw/d (General Toxicity) NOAEL = approx. 160 mg/kg bw/d (Embryotoxicity) NOAEL = approx. 240 mg/kg bw/d (Fetotoxicity) NOAEL = approx. 240 mg/kg bw/d (Teratogenicity)
		SD rat	Inhalation: 7 h/d	NOAEL = approx. 400 mg/m^3 (100 ppm) (General Toxicity) NOAEL = approx. 400 mg/m^3 (100 ppm) (Embryo-/Fetotoxicity) NOAEL = approx. 400 mg/m^3 (100 ppm) (Teratogenicity)
		New Zealand white rabbit	Inhalation: 7 h/d	LOAEL <400 mg/m^3 (<100 ppm)?? (General Toxicity) NOAEL = approx. 1200 mg/m^3 (300 ppm) (Embryotoxicity) NOAEL = approx. 1200 mg/m^3 (300 ppm) (Teratogenicity)
		SD rat	Inhalation: 6 h/d	NOAEL = approx. 1000 mg/m^3 (250 ppm) (General Toxicity) NOAEL = approx. 1200 mg/m^3 (300 ppm) (Embryo-/Fetotoxicity) NOAEL = approx. 1200 mg/m^3 (300 ppm) (Teratogenicity)
5.11	Experience with Human Exposure		Hazardous Substances Data Bank (HSDB) literature search	Substance is a central nervous system depressant. Severe ingestions may lead to damage of the liver, kidneys and adrenal glands. Gastrointestinal hemorrhage may occur. Conjunctival congestion and burning sensation, weakness, bronchial and pharyngeal symptoms, metalic taste in mouth, headache, dermatographism, nausea, liver pain, tachycardia, and dyspnea after effort have been reported after dermal contact and after inhalation.

SIDS Initial Assessment Report (SIAR)

1. IDENTITY

1.1. General Substance Information

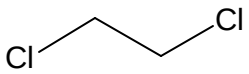
CAS No. 107-06-2

Chemical Name 1,2-Dichloroethane

Other Names ethylenedichloride; glycol dichloride

Molecular Weight 98.96

Molecular Formula $C_2Cl_2H_4$



Substance Type halogenated aliphatic hydrocarbon

1.2. Physical and Chemical Properties

1,2-Dichloroethane is a clear, colourless, oily liquid (melting point – 35.5 to - 36°C, boiling point 83.5 to 84.1°C), which is highly flammable (flash point 13°C) . It is readily soluble in water (8490 - 9000 mg/l at 20°C) and has a density of 1.235 – 1.253 g/cm^3 (20°C) as well as a high vapour pressure (81.3 hPa at 20°C). The measured log K_{ow} value of 1.45 indicate no little affinity for lipophilic matrices.

2. GENERAL INFORMATION ON EXPOSURE

1,2-Dichloroethane is being produced by several manufacturers in each of the three main regions Europe, United States and Japan. The annual worldwide production volume of the substance exceeds 1,000,000 tons. –In Europe, 14 producers are known.
1,2-Dichloroethane is mainly used (with a contribution of 95 %) as a chemical intermediate in the production of vinylchoride monomer which in turn is used in the manufacture of polymers. The remaining 5 % are used as an intermediate in the production of ethylenediamines, tri- and tetrachloroethylene and in other fields of application, i.e. as extraction and cleaning solvent and as lead scavenger in gasoline. The application as a lead scavenger, however, is known to disappear in OECD countries due to the increasing use of unleaded fuels. It is not clear whether 1,2-dichloroethane is still finding use in aviation gasoline where environmental exposure may be implied. However, its structural analogue 1,2-dibromoethane is still used as gasoline additive both in vehicles and aircrafts. Other former applications were described as diluent in pesticides, grain fumigant and in paint, coatings and adhesives. Reported applications in glues or cosmetics are assumed not to exist anymore due to the proven toxic effects of the substance.

European product registers contain entries of products with 1,2-dichloroethane as ingredients. Product types are paints and lacquers (concentrations between 1 and 100 %), adhesives (concentrations between 10 and 50 %) and fertilizers (concentrations below 1 %).

Due to information submitted by both the sponsor and co-sponsors, 1,2-dichloroethane is produced and handled in closed systems or directly transported via pipelines during filling processes, e.g. loading of tanker ships.
Internally produced 1,2-dichloroethane is being processed almost quantitatively onsite and converted to vinyl chloride monomer.

Releases into the environment are expected to occur mainly during production and processing of 1,2-dichloroethane as well as during use of products containing the substance. Additional releases may occur from the use as extraction and cleaning solvent and as lead scavenger in gasoline.

Information on exposure from production of the chemical in the Sponsor country at one company is available. In 1999, 240 kg 1,2-dichloroethane were released into the waste water treatment plant. The exhausts from this production site were connected to thermal exhaust purification plants. In 1999 about 10 to 15 t 1,2-dichloroethane were emitted into the atmosphere due to failure of the thermal purification plant (Wacker Chemie GmbH, 2001: personal communication).

The following exposure information is taken from the BUA report 163 (1995) :
In 1993 about 150 t 1,2-dichloroethane were emitted into the atmosphere during production and processing in Germany by 9 production and/or processing sites. Releases into the hydrosphere were estimated to be about 4.46 t for 7 producers/processors. For two companies there are no data about emission into the hydrosphere.

No information is available about environmental releases from other applications.

Several exposure measurements performed by analysis of the atmosphere within the production facility of vinylchloride during the years 1995 through 1999 yielded 1,2-dichloroethane concentrations ranging from 0.5 to 15.3 mg/m^3 (0.122 to 3.72 ppm) with an average value of 4.59 ± 3.83 mg/m^3 (1.12 ± 0.93 ppm). During filling processes in tanks no worker exposure does result since all steps are conducted via pipelines. In addition, filling of the material into barrels is not an intended mode for storing the substance.

Another important exposure scenario is being given during maintenance procedures, i.e. high pressure cleaning of facilities and filter exchanges. Exposure measurements have been undertaken during these processes, too, with values determined being in the range of <2 to 151 mg/m^3 (0.49 to 36.7 ppm). It should be stressed that workers are expected to be PPE (personal protective equipment including respiratory protection) during these operations.

2.1 Environmental Exposure and Fate

According to a Mackay level I model calculation 1,2-dichloroethane is mainly distributed to air (95.0 %) and to a lesser extent into water (4.8%) while all other compartments such as soil, sediment, suspended matter and biota make no substantial contributions (Mackay 1999) (input values see IUCLID). The relative high degree of distribution into air is based on the high vapour pressure and the high volatility of the substance from water as indicated from the calculated and experimentally determined Henry's Law constants of 95.7 Pa * m^3/mol (Mackay 1999) and 149 Pa * m^3/mol, respectively (Ashworth et al. 1988).
Based on the high vapour pressure and volatility of the substance, 1,2-dichloroethane entering aquatic systems would be transferred to the atmosphere through volatilisation. Results of laboratory experiments yielded half-lives in water ranging from 0.5 – 4 hours. A half-life of 1.4 hours for the removal from running river water was found in outdoor experiments conducted under controlled conditions. These results indicate that 1,2-dichloroethane is expected to be rapidly removed from aqueous media by volatilisation (De Rooij et al. 1998). Nevertheless the low affinity for soil may pose a risk of groundwater contamination.

Different investigations have been undertaken to study the biodegradability of 1,2-dichloroethane. However, there are no standardized screening studies on ready or inherently biodegradation available. In the various non-guideline studies which were mostly conducted according to generally acceptable principles it could be shown that the material is not biodegradable when non-adapted, non-acclimated conditions were used. In contrast biodegradation occurred when adapted or induced micro-organisms were used. Under abiotic conditions biodegradation of 1,2-dichloroethane is too slow to be an important environmental fate process (Barbash and Reinhard 1989).

Based on both the water solubility and high volatility, adsorption to soil and sediments is not expected, which is supported by an experimentally determined K_{OC}-value of 33 for silt loam. The substance rapidly percolates through sandy soil (HSDB 2000).

Due to its chemical structure, the substance will not undergo both hydrolysis in water and photo-degradation by direct sun-light. At an atmospheric concentration of $1.5 * 10^6$ hydroxyl radicals/cm^3 and a rate constant of $0.25 * 10^{-12}$ cm^3/molecule * sec the half-life of 1,2-dichloroethane can be estimated to be about 42 days assuming a 12-h light-cycle (AOPwin v1.90, SRC-AOP for Microsoft Windows). The products arising from photo-oxidation are carbon dioxide and hydrogen chloride (HSDB 2000). With an atmospheric concentration of $5 * 10^5$ hydroxyl radicals/cm^3 and a rate constant of $0.22 * 10^{-12}$ cm^3/molecule * sec the half-life of 1,2-dichloroethane can be estimated to be about 73 days. Field measurements confirmed that the photo-degradation in the atmosphere prevents the global distribution and the atmospheric enrichment of emissions, released by industry mainly in the northern hemisphere (Class et al. 1986).

A value for Ozone Depletion Potential of < 0.001 was calculated for 1,2-dichloroethane (Nimitz et Skaggs 1992). Even though 1,2-dichloroethane has a high half-life in air, disadvantageous effects to the ozone concentration in the atmosphere are not expected.

Taking into consideration the measured octanol/water partition coefficient of 1.45, no potential for bioaccumulation/bioconcentration can be identified (Veith, G.D. et al. 1980). This is supported by calculated and experimentally determined bioconcentration factors of 2 – 2.75 (Barrows et al. 1980; BCFWIN v2.14 - SRC-BCF for Microsoft Windows).

2.2 Human Exposure

2.2.1 Occupational Exposure

Since the material is produced in closed systems, stored and filled in tanks via pipeline no direct worker exposure does result. In occupational settings, however, exposure towards 1,2-dichloroethane might be given during sampling processes for analytical purposes (i.e. quality control). Exposure measurements performed in the course of working place surveillance during the years 1995 through 1999 yielded 1,2-dichloroethane concentrations ranging from 0.5 to 15.3 mg/m^3 (0.122 to 3.72 ppm) with an average value of 4.59 ± 3.83 mg/m^3 (1.12 ± 0.93 ppm). The exposures were mainly caused by sampling procedures with open systems. During filling processes in tanks no worker exposure does result since all steps are conducted via pipelines. In addition, for filling of the material into containers closed systems are applied.

Another important exposure scenario is being given during maintenance procedures, i.e. high pressure cleaning of facilities and filter exchanges. Exposure measurements have been undertaken during these processes, too, with values determined being in the range of <2 to 151 mg/m^3 (0.49 to 36.7 ppm). It should be stressed that workers of the maintenance crew, usually 10 – 20 workers per shift, were mandatory equipped with PPE (personal protective equipment including respiratory protection) during these operations for about 3 – 5 days/year

For 1,2-dichloroethane working place limit values have been established in various countries including the region of the U.S. and Japan (Table 1).

Table 1: Working place limit values for 1,2-dichloroethane.

Country	Type of limit value	Value (ppm)
Denmark	OEL (skin notation)	1
France	OEL	10
Germany	TRK (technical standard value)	5
Japan	TLV	10
Netherlands	MAC	1.5
UK	MEL	5
US	TLV	10

2.2.2 Consumer Exposure

1,2-dichloroethane is almost exclusively used as a chemical intermediate in the production of polymers. However, it has been reported to be a constituent of leaded fuel as a scavenger for the removal of lead which implies exposure of individuals during filling processes. It is not known, however, whether 1,2-dichloroethane is still used as aviation gasoline as it is the case with its structural analogue 1,2-dibromoethane. In addition, no direct information is available for 1,2-dichloroethane as to the concentrations which may occur during filling process of vehicles and aircrafts. Figures given for release of 1,2-dibromoethane are 0.4 – 1.5 t/a in the production of aircraft gasoline formulations including distribution and consumption of aviation gasolines. During storage, transfer and transport of vehicle gasoline emissions ranging from 0.48 – 1.9 t/a were

reported and evaporation from vehicle tanks and carburettors was estimated to be about 3.7 t/a (BUA supplement report No. 223). In 1989 total release of 1,2-dibromoethane resulting form consumption of carburettor fuel into the atmosphere was estimated to be 20 – 76 t/a.

According to the Guideline 76/769/EC, which has been adapted in the national legislation of the EC-Memberstates, products containing more than 0.1% of 1,2-dichloroethane are not permitted for consumer use, with the conclusion, that consumer exposure from products can be excluded.

2.2.3 Indirect Exposure via the Environment

Since no up-to-date monitoring are available and no sources for deriving such data have been disclosed environmental background data from the mid seventies to the late eighties determined at several European locations are being described to illustrate exposure situations for the different compartments air, river water and drinking water, respectively.

In air, mean 1,2-dichloroethane concentrations of 21.4 µg/m^3 including industrial locations and 12.4 µg/m^3 without industrial locations have been found in 1986 near Hamburg (Bruckmann, P. et al. 1988; Hamburger Umweltbehoerde 1988). The highest 1,2-dichloroethane concentrations were found in river water of the Rhine river with a sampling site dependent range of 4.4 - 8.5 µg/l thereby representing worst case conditions when comparing typical values determined in different coastal waters/estuaries (< 0.005 – 6.4 µg/l) and other river waters (< 0.5 µg/l) (Meijers 1988). Drinking water samples taken from the river Rhine in 1975 contained 1,2-dichloroethane concentrations of 0.88 – 1.32 µg/l depending on the previous treatment of the water, i.e. ozone treatment of filtered raw water or char coal filtration / purification, respectively (Stieglitz et al. 1976).

Environmental background data have also been established for air and river water in Japan in the year 1988. Concentrations determined were in the range of 45 – 2,200 ng/m^3 and 0.082 – 13.9 µg/m^3 for air and river waters, respectively (Ministry of the Environment, Japan 1999).

On the basis of the low bioconcentration factors determined no potential for bioaccumulation via the food chain does exist.

3. HUMAN HEALTH HAZARDS

3.1 Effects on Human Health

3.1.1 Mode of action of the chemical, toxicokinetics and metabolism

- **General**

The substance is well absorbed by all routes of exposure and rapidly distributed throughout the body with preferential affinity to adipose tissues, but is readily released from all compartments without signs of accumulation. The greatest part undergoes extensive metabolism, followed by rapid excretion of metabolites into the urine, another fraction mainly eliminated unchanged by exhalation (overall approx. 90 % within 48 h) (Mitoma et al., 1985; Reitz et al., 1982; Tsuruta ,1975; Yllner, 1971 ; Jakobson et al. 1982).

- **Systemic absorption and elimination characteristics**

After 6-h inhalation (150 ppm, Osborne-Mendel rats), the maximum blood concentration (after 2 to 3 h) was 8 to 10 µg/ml and disappeared by 80 % within 30 min and by more than 97 % within 80 min (Spreafico et al., 1980). Single oral application of 150 mg/kg bw (gavage, SD rats) caused peak blood levels after 15 min between 30 to 44 µg/ml, i.e. 4 – 5x higher than after inhalation, and it took about 3 h to reach the maximum level seen with inhalation (Reitz et al., 1982). Based upon the rapid elimination rate, DCE is expected to be quantitatively removed under either test condition. However, oral gavage application tends to create a prolonged state with blood concentrations significantly higher than during an inhalation cycle of 6 to 7 h comparable body burdens.

- **Blood levels and toxicity**

Several blood levels in rabbits and dogs following 6- to 7-h inhalation exposure towards concentrations of 1000 to 3000 ppm were published by Heppel et al. (1946): They ranged from 8 to 30 µg/ml (average 23 µg/ml) at 1000 ppm in dogs and 20 to 40 µg/ml at 1500 ppm in rabbits and dogs to 40 µg/ml and higher at 3000 ppm in rabbits. No data have been reported at lower exposures for these species.

The DCE blood level of 8 – 10 µg/ml after 6-h inhalation of 150 ppm in rats (Reitz et al., 1982) may represent a non-toxic to toxic threshold dose in these rats under these conditions (see also: Spreafico et al., 1980; Maltoni et al., 1980). The corresponding blood level of DCE was at 30 µg/ml after single 6-h exposure to 250 ppm (Spreafico et al., 1980).

After prolonged inhalation, Spreafico et al. (1980) found 1.4 µg DCE/ml blood after single 6-h exposure in SD rats, while after long-term exposure to 50 ppm, a lower level of 0.22 – 0.28 µg/ml (unchanged DCE) was detected in the blood of 2-year old SD rats when measured 15 and 135 min after the final 7-h exposure (Cheever et al., 1990). There appears to be a shift in kinetics due to prolonged exposure and/or age of the animals.
In the 2-years study, after the 50-ppm exposure the blood levels thus obtained were about 1.4 µg/ml, about 5 times higher than with DCE alone (Cheever et al., 1990).

For oral administration, only gavage data are available: doses of 25, 50, and 150 mg/kg bw produced peak blood levels at 13, 30, 67 µg/ml, respectively (Spreafico et al., 1980). Reitz et al. (1992) found 30 – 44 µg/ml in blood of Osborne-Mendel rats given a dose of 150 mg/kg bw by gavage. There are no blood data on corresponding doses administered in drinking water. The different DCE levels in the blood and liver which are expected to be considerably higher after gavage administration than after drinking water consumption represent invasion kinetics comparable to that associated with inhalation.

These data suggest that a blood level of 5 - 10 µg/ml may be considered as a critical threshold level in rats under these conditions (here: Osborne-Mendel and SD) beyond which saturation of metabolic pathways may give rise to toxicity (Reitz et al., 1982) (IARC, 1999). The relevance of metabolic saturation and overstress of liver metabolic capacity for the formation of oncogenic intermediates is still hypothetical (Spreafico et al., 1980, p. 22).

- **Saturation kinetics**

The elimination of DCE from the body is a saturable process and has been shown by over-proportionate increases in tissue levels of DCE, reduction of elimination rates, and by depression of the metabolising capacity, thereby concomitantly increasing the fraction of unmetabolised substance in exhaled air (Reitz et al, 1982,Tab. 1).

After single 6-h inhalation exposure, the fivefold increase in the exposure concentration (from 50 to 250 ppm) led to a multifold enhancement of DCE in tissues (Spreafico et al., 1980, Fig. 3 A,B, Tab. 6): about 23x (blood), 20x (liver), 35x (lung), and 27x (adipose tissue). Thereby, the tissue-specific elimination half-lives of approx. 10 to 13 min increased at a factor of 1.7 to 2 at maximum in liver and blood, respectively, but in adipose tissue insignificantly from about 23 to 28 min.
After single oral doses of 25, 50 and 150 mg/kg bw (gavage), no such exponential increases were seen for DCE in the blood and tissues, but ratios of the respective AUCs (Areas Under the Curve) after 150 vs. 25 mg/kg bw determined in blood and the liver were 16 and 8 rather than 6 as expected from the ratio of both doses.

- **Distribution characteristics after gavage dosage and inhalation**

Appreciable amounts of DCE accumulated in the various tissues in SD rats after an oral dose of 25 mg/kg bw, but only very little after 50 ppm (6 h) (Spreafico et al., 1980): tissue peak levels at 50 ppm were about 1/10, in liver about 1/30 of that at 25 mg/kg bw, even more striking for the corresponding AUCs. With increasing doses, tissue disposition goes up more or less linearly, but resulting in substantial liver levels. However, after inhalation exposure, the liver values at 250 ppm were only similar to those found at the oral dose of 25 mg/kg bw and were about ¼ of the peak concentration and about 1/8 of the AUC observed at 150 mg/kg bw. In relation to the low liver burden, DCE concentration in adipose tissue appeared to be very high.

Overall, the kinetic parameters (including AUC and peak tissues levels) derived from the study by Spreafico et al. (1980) suggest that the inhalation of 50 ppm (6 h) correlated to an oral dose (gavage) significantly below 25 mg/kg bw, and 250 ppm to a dose between 25 and 50 mg/kg bw.

This implies that during inhalation exposure to apparently high DCE concentrations (e.g. 250 ppm), the liver burden appears to be low without noticeable metabolic limitation, whereas oral bolus treatments tend to overstress liver metabolic capacities. [see: Maltoni et al., 1980/Spreafico et al., 1980 and NCI, 1978] [see 3.1.8].

- **Metabolism and toxicity**

About 50 – 86 % of absorbed DCE undergoes metabolism and subsequent urinary excretion. Only a minor portion of the substance, i.e. 4 – 18 % is metabolically converted to carbon dioxide while 8 - 42 % is being exhaled as parent compound (Mitoma et al. 1985; Reitz et al. 1982; Tsuruta 1975; Yllner 1971). Urinary metabolites consisted mainly of thiodiacetic acid, the corresponding sulfoxide and S-carboxymethylcysteine. Small amounts of chloroacetic acid and very low concentrations of S,S´-ethylene-bis-cysteine and chloroethanol were also found in urine (Guengerich et al., 1980).

The two metabolic routes involved in the biotransformation of 1,2-dichloroethane are oxidation by mixed-function-oxidases, i.e. enzymes of the cytochrome P 450 family, and glutathione-S-transferase mediated glutathione(GSH) conjugation, respectively. In SD rats, depletion of hepatic GSH was found to be substantial after a single oral, maximally tolerated dose (MTD) of 625 mg DCE /kg: less than 10 % of the GSH level in untreated control livers was recovered after 18 h post-treatment, which represented by far the highest GSH loss as compared with other structure-related compounds concurrently tested in this study (Moody and Smuckler, 1986).

Both metabolic pathways lead to the formation of reactive intermediates with chloroacetaldehyde and chloroethanol being produced by cytochrome P 450 dependent metabolism and an episulfoniumion being formed by glutathione conjugation. The reactive species formed are both capable of binding to DNA and are suspect of being responsible for in- vivo genotoxic and carcinogenic activity of 1,2-dichloroethane (Guengerich et al. 1980) (Storer et al. 1984).

This is supported by the observation that after absorption of comparable doses of DCE, five times higher peak plasma levels were observed after oral administration as compared to inhalation which was accompanied by about a five times higher binding of radiolabeled DCE-borne compounds in the liver DNA after oral treatment than after inhalation (Reitz et al. 1982). The 5-fold increase in DNA-binding was explained by a saturation of the oxidative and detoxifying, GSH-dependent metabolism occurring after administration by gavage, but not after inhalation because of the different invasion and distribution kineti.

3.1.2 Acute Toxicity

The acute toxicity of 1,2-dichloroethane was investigated by the oral, dermal and inhalation route, respectively. By the oral or inhalation route of administration the material proved to be moderately toxic and virtually non-toxic after dermal application to the animals tested.

After oral administration to rats, LD_{50}-values determined were in the range of 770 -967 mg/kg bw. Signs of toxicity were characterised by lung congestion, pale kidneys and livers as well as congestion of the blood vessels in the intestines. was reported, too (Mellon Inst. Industr. Research, 1986; Smyth et al., 1969). A single maximum tolerated dose (MTD) of 625 mg/kg (oral, gavage) in SD rats was reported to produce liver effects: a slight decrease in hepatic porphyrin and cytochrome-P450 content and a more pronounced in the activity of hepatic aminolaevulinic acid dehydratase and the level of glutathione (Moody and Smuckler, 1986).

In mice, LD_{50}-values determined were 413 – 911 mg/kg bw, in rabbits an LD_{50}-value of about 910 mg/kg bw, and in dogs an LD_{50}-value of >2500 mg/kg bw was reported (Barsoum and Saad, 1934; Heppel et al., 1945; Mellon Inst. Industr Research, 1986; Munson et al. 1982). The solvent was reported to act as a cardiac depressant in dogs, but deaths occurred through respiratory arrest prior to cardiac failure (Barsoum and Saad, 1934).

After acute inhalation exposure to DCE, LC_{50}-values obtained in rats were about 4100 mg/m³/7.2 h to 49400 mg/m³/0.5h (Spencer et al. 1951). In compliance with these results, another 6-h LC_{50} was found at about 1650 ppm (= 6670 mg/m^3) (Bonnet et al., 1980). A 4-h LC50 (rat) of about 8000 mg/m^3 (= 1900 ppm) can be derived from a concentration-response graph (Spencer et al., 1951). In mice, the LC_{50} after a six-hour exposure was determined to be 272 ppm (= 1080 mg/m³) (Gradiski et al. 1978), and in guinea pigs an LC_{50} of 6400 mg/m³/7 h was reported (Heppel et al. 1945). In principal, other available acute data in rats, mice and rabbits which lack a sufficient data base to establish a defined LC_{50} (Heppel et al., 1945; Frankovitch et al., 1986) are consistent with those findings.

The comprehensive study by Spencer et al. (1951, Tab. 1) provides the following non-lethal concentration-time exposures in female rats (post-exposure observation for 2 to 3 weeks):

Determinations of LC_0:

- 300 ppm (approx. 1200 mg/m^3) [7 h] ,
- 1500 ppm (approx. 6200 mg/ m^3) [2 h],
- 3000 ppm (" 12400 mg/ m^3) [0.5 h]

Determinations of NOAELs (based on blood parameters and histopathology) (Spencer et al., 1951: Tab. 2):

- 200 ppm (approx. 800 mg/ m^3) [7 h];
- 300 ppm (" 1200 mg/ m^3) [3 h] (but effects at 5.5h)
- 1000 ppm (" 4000 mg/ m^3) [1.5 h] (but effects at 3 h).

A 4-h LC_0 of about 3000 mg/m^3 and an acute 4h NOAEL of about 1400 mg/ m^3 can be estimated from given concentration-response graphs (Spencer et al., 1951: Chart 1).

In particular after inhalation, a steep concentration-response relationship associated with sudden, often unexpected mortality was characteristic of DCE (see Bonnet et al., 1986; Gradiski et al., 1978; Spencer et al., 1951; Mellon Inst. Industr. Research, 1987). For example, among dose groups of SD rats covering just an increment of 400 ppm DCE (from 1300 to 1700 ppm), mortality increased steeply from about 17 to 75% % (Bonnet et al., 1986, Fig. 1), and the mortalities observed in male albino rats were 0/10 animals at 500 mg/kg, 3/10 at 630 mg/kg bw after 1 to 5 days, 5/10 at 795 mg/kg after 1 day and 8/10 at 1000 mg/kg bw after 2 to 3 days. Similar results were seen with rabbits and mice (Mellon Inst. Industr. Research, 1987).

The mean LD_{50}-value for an acute dermal toxicity study after application of 1,2-dichloroethane under occluded conditions to rabbits was 4890 mg/kg bw with a 95 % confidence interval of 4270 – 5600 mg/kg bw (Mellon Inst. Industr. Research, 1987).

Regardless of the route of administration chosen, signs of toxicity in rats, mice, guinea pigs and rabbits after administration of high doses are described by liver damage (fatty degeneration and haemorrhagic necrosis, increased hepatic enzyme activities and reduction of glutathione levels), kidney damage (congestion, haemorrhage, necrosis, interstitial oedema, dilatation of renal tubules, fatty degeneration of the tubular epithelium and hypertrophy of tubular cells) and damage to the lungs (congestion, haemorrhage, oedema, fluid in the pleural and peritoneal space).

Conclusion: According to the lethal doses determined in rodents after oral administration and inhalation DCE has to be considered as harmful acc. to GHS. The substance may be considered uncritical after dermal application.

3.1.3 Skin Irritation

DCE failed to produce any signs of irritation when applied to the skin of 6 rabbits in an early skin irritation test which, however, has been conducted according to current standards (occluded 4-h exposure, intact skin acc. to FDA Rev., Fed. Reg. 37, No. 244, 1972, USA) (Stauffer Chemical, 1973).

A second test revealed moderate irritation on the intact and scarified skin of rabbits (primary irritation index 4.7 of max. 8 scores), but the test design and conditions apparently corresponded to the genuine Draize assay using occluded 24-h exposure (Duprat et al., 1976).

A third non-standard test on skin of guinea pigs treated with 1 ml of the neat material for up to 16 hours under occluded conditions (cover-glass limited skin area approx. 3.1 cm^2) produced mild signs of irritation after 4- and 16-h exposure, but none after 15 or 60 minutes. Effects were microscopically characterized as slight degenerative changes in the epidermis, slight focal karyopyknosis, slight perinuclear oedema in the region of cells with pyknotic nuclei, spongiosis and junctional separation (Kronevi et al. 1981).

This test design does not allow to correlate the microscopically identified changes with those classical, macroscopic indicators for irritation which are common under the current classification system.

Conclusion: Overall, topically applied DCE produced no or only slight irritation to skin.

3.1.4 Eye Irritation

The eye irritating properties of DCE were investigated in rabbits, dogs and guinea pigs. Rabbits were administered 0.1 ml of the pure substance into the conjunctival sac. Moderate lacrimation, abrasion of the corneal epithelium and mild to moderate catarrhal conjunctivae were observable. In addition, regenerating keratitis was evident on day 7 which disappeared after another seven days. In this study the substance was judged to be slightly irritating, based on an overall Draize-score ranking with 7 of max. 110 scores (Duprat et al. 1976).
In another rabbit study, 0.1 ml of the neat material was applied into the conjunctival sac. Slight reddening in 2/6 animals as well as annular conjunctival swelling in one animal was observable. All symptoms were reported to have disappeared completely within three days (Stauffer Chemical 1973).

After single inhalation exposure to 1000 and 1500 ppm (4110 and 6165 mg/m^3) of DCE for 7 h, dogs experienced corneal turbidity and oedema, an effect not found in other species tested but a fox (among them cats, monkeys, rabbits, and chickens and various rodents) (Heppel et al., 1944): At a concentration of 1000 ppm, symmetric turbidity of the corneas was observed in 8/10 dogs, while at the toxic concentration of 1500 ppm, 1/6 dogs showed corneal damage, one developed faint turbidity and 4/6 showed intense clouding of both corneas which cleared within one week in one animal. Resistance to the cornea effects of DCE developed and remained unchanged even after cessation of exposure for two to four weeks. Prolonged exposure to 400 ppm (about 1600 mg/m^3) for 25 weeks gave no evidence of eye damage, whereas during exposure to the toxic concentration of 1000 ppm (about 4000 mg/m^3) corneal opacity was prominent (Heppel et al., 1946).

Guinea pigs were exposed to concentrations of 600 to about 70000 ppm (2500 to about 29,000 mg/m^3) of DCE. Eye and nose irritation (squinting and lacrimation), for example, occurred after exposure to toxic concentrations of 2000 to 4000 ppm within less than 10 min, but no signs of irritation and intoxication, but occasional retching in 1/18 animals were reported at 1200 ppm (approx. 5000 mg/m^3) after exposure of several hours (Sayer et al., 1930).

Conclusion: Overall, instilled DCE produced no or only slight to transiently moderate irritation to eyes.

Other assays using atmospheric exposure suggest that significant irritancy or locally noxious effects do only emerge at concentrations which already produce other systemic intoxication:

1. The species-specific effect on the eye of dogs following atmospheric exposure was not observed during exposure to 400 ppm for up to 25 weeks. This concentration is distinctly higher than for general systemic intoxication after prolonged exposure to DCE (see below).

2. The clinical rather than pathologically relevant irritation reflexes in guinea pigs noted during 8-h exposure to 1200 ppm atmospheric DCE may be appropriate to set an acute irritation threshold concentration. Also this concentration clearly falls within or above the range of acute toxicity (see above: 3.1.2, Spencer et al., 1951).

3.1.5 Skin Sensitization

No animal data are available as to the examination of the possible skin sensitizing properties of DCE.

3.1.6 Repeated Dose Toxicity

The toxicity of DCE was investigated in several oral studies in rats and mice for 2 years (Alumot et al., 1976) and 13 weeks (Morgan et al., 1990/NTP, 1991) (Munson et al., 1982) and inhalation studies in rats and mice (Heppel et al., 1946; Spencer et al., 1951; Hofmann et al., 1971; Maltoni et al., 1980/Spreafico et al., 1980) and in guinea pigs, rabbits, cats, dogs, and monkeys (Heppel et al., 1946; Spencer et al., 1951).

- **Oral administration**

In a non-standard oral study, which included mating intervals of treated females with untreated males, average doses of 12.5 and 25 mg /kg bw/d were administered with especially fumigated and preserved feed (250 and 500 ppm, respectively) to male and female locally bred rats for two years. No impairment of feed consumption and body weight development was observable. By 14 months, all animals including controls began to suffer from chronic respiratory disease causing mortality rates to increase. Examination of liver weights, hepatic fat content, various serum parameters did not support any effect on liver and kidney function (Alumot et al. 1976). According to the results of this study, the NOAEL is defined to be 25 mg/kg bw/d. In the previous range-finding study, no effects but slight increases in hepatic total fat and in triglycerides ($p<0.05$) were found after feeding of about 80 mg CDE/kg bw/d for 7 weeks. The NOAEL was 30 mg/kg bw/d (Alumot et al., 1976).

In a comprehensive standard 13-week drinking water study comprising three strains of rats (Fischer 344, Osborne-Mendel and Sprague-Dawley rats) and concentrations of 500 to up to 8000 mg/l, corresponding to doses of about 50 and 730 mg/kg bw/d, resp.), no substance related mortalities, no clinical signs of toxicity, no abnormalities of blood-chemical parameters, were evident in all five dose groups of either sex. Minimal histological lesions appeared only in female F344 rats as a dose-dependent increase in renal tubular regeneration. Increases in the absolute and relative weights of kidneys and livers were observable throughout ($p<0.05$ or <0.01). Body weight gain and water consumption were reduced in dose-related manner, the latter by 50 - >60 % at maximum in all strains (Morgan et al. 1990; NTP 1991).
Because of the high reduction of water consumption, a NOAEL cannot be established and is also not given by the authors of the study.
In a 13-week gavage study conducted in F344 rats, equivalent DCE doses between 18 and 480 mg/kg bw/d (5d/wk) produced substantial higher toxicity than in the drinking-water study, demonstrated by pronounced clinical signs of intoxication (tremor, hypersalivation, ruffled fur as well as dyspnoea) and high mortality (90 to 100 % at the higher dose levels). No substance-related abnormalities of blood-chemical parameters, and histopathological organ changes were detectable, including renal tubular regeneration, except minimal to mild hyperplasia and inflammation of the mucosa of the forestomach in the second highest dose group of males ($P<0.05$) as well as necrosis of the thymus and cerebellum in the second highest dose group of males and in the highest dose group of females ($P<0.05$). Increases in the absolute and relative kidney and liver weights were observable in all dose groups to a different extent (Morgan et al. 1990; NTP 1991).

The NOAEL is assumed to be 120 and 150 mg/kg bw/d for male and female F344 rats, respectively, based on treatment-related effects in the forestomach and clinical symptoms. A LOEL is at 18 - 30 mg/kg bw/d, the lowest dose tested, based on significant increases in liver and kidney weight in females and males, respectively, which is considered as biologically relevant, but not pathological.

DCE given to male and female B6C3F1 mice for 13 weeks via the drinking water at doses of up to 8000 mg/l, corresponding to about 4200 – 4900 mg/kg bw/d, caused minimal to moderate organ toxicity, only observed in the kidneys of male animals and characterised by hyaline urinary cylinders, dilatation of the tubules and focal mineralisation in the renal papilla of all dose groups. In the highest dose group of females, 9/10 animals died (NTP 1991). A NOAEL cannot be established because of renal tubular regeneration in male mice:
0/10 (contr.), 1/10 (500 mg/l), 2/10 (1000 mg/l), 2/10 (2000 mg/l), 8/10 (4000 mg/l), and 9/10 (8000 mg/l). For females, the NOAEL is about 2500 mg/kg/d, based on mortality. No NOEL was established: The LOEL of about 240 - 250 mg/kg bw/d is based on absolute and relative increases in kidney weights already evident in 500-mg groups and considered as substance-related, but not yet pathological.

A further 13-week drinking-water study on male and female CD1-mice which was mainly focussed on immunotoxic aspects and comprised other parameter not generally covered in a standard study, gave equivocal evidence of adverse effects on both humoral and cell-mediated immunity at concentrations of 20, 200, and 2000 mg/l (Munson et al. 1982): There was a dose-dependent declining trend in haemagglutination titer which was not statistically significant ($p<0.05$). The NOAEL referring to immune responsiveness was the highest dose tested, correspondingly about 190 mg/kg bw/d, while the NOEL can be assumed to be 24 mg/kg bw/d, based on the absence of depression of body–weight gain.

- **Administration by Inhalation**

Several early subchronic to chronic inhalation studies realised largely consistent results after exposure to concentration levels ranging from 100 to 400 ppm (approx. 400 and 1600 mg/m^3, respectively) for about 15 weeks, 7h/d, and 5d/wk (Heppel et al., 1946), for 17 weeks, 6h/d, and 5d/wk (Hofmann et al., 1970), and for more than 40 weeks, 7h/d, and 5d/wk (Spencer et al., 1951). The studies partly including several rat strains of either sex (Wistar, SD, Osborne-Mendel) comprised clinical, blood-chemical as well as microscopic/histopathological examinations, the latter mostly limited to main organs.
In line with these previous observations were those made in the comprehensive 18-months inhalation study by Maltoni et al. (1980)/Spreafico et al. (1980) on SD rats exposed to concentrations of 5, 10, 50, and 150 (250) ppm [see also Carcinogenicity]. Further support is provided by another, special 2-year study including exposure of male and female SD rats to 50 ppm of neat DCE, 7 h/d, 5 d/wk (Cheever et al., 1990) [see also Carcinogenicity].

The toxicity profile of DCE elaborated in rats is further supplemented by more or less well founded, but on the whole reliable findings in other species including rabbits and guinea pigs (Heppel et al., 1946; Spencer et al., 1951; Hofmann et al., 1970), dogs (Heppel et al., 1946), and monkeys (Heppel et al., 1946; Spencer et al., 1951). Yet, other limited screening studies performed on cats (Heppel et al., 1946; Hofmann et al., 1970) and mice (Heppel et al., 1946) are available, but are dismissed here, because they appear not to add new information to that known from the other results. All these investigations covered similar concentration ranges and exposure periods like those employed in the rat studies.

Marked signs of toxicity eventually associated with substantial reduction in survival were evident at a level of 200 ppm in rats (Heppel et al., 1946), guinea pigs, and monkeys (Heppel et al., 1946;

Spencer et al., 1951), but not in rabbits and dogs (Heppel et al., 1946; Spencer et al., 1951). Contrary to Heppel et al. (1946), Spencer et al. (1951) reported less pronounced or no significant adverse effects in guinea pigs and rats, respectively, after prolonged exposure to 200 ppm of DCE, while this exposure level is missing in the work of Hofmann et al. (1970). In the study by Heppel et al. (1946), about 100 ppm) produced no signs of toxicity in rats (strain not specified) receiving 74 exposures (about 15 weeks; 7 h/d, 5 d/wk), whereas already 200 ppm caused significant toxicity associated with early mortality in Osborne-Mendel and Wistar rats (<6 and < 27 days, respectively).

In principal, the toxic pattern was similar to that found after oral ingestion, including hepatic fatty degeneration and proliferative changes in the renal tubular epithelia, but, more often than not, involving lung damage, too, such as congestion and hemorrhage.
The occurrence of deaths at toxic levels was very variable, either already within the time of 4 to 9 exposures or also not until 27 to 44 or even beyond 70 exposures within the same treated group. The unequivocal cause of mortality was never clear, and deaths often came about quite unexpected and abruptly: post-mortem, they could not be related to the generally low degree of the organ lesions discovered. It was assumed that ultimately respiratory arrest and/or cardiovascular failure lead to death.

In the long-term study by Maltoni et al. (1980), the top-exposure level had to be lowered after a few weeks due to overt signs of intoxication, which underlines that the critical atmospheric DCE-exposure level is supposed to be in the range of 200 ppm (approx. 800 mg/m^3).

The findings by Maltoni et al. (1980) and Cheever et al. (1990) that no significant to marginal treatment-related effects were seen at 150 ppm, but none at 50 ppm over 18 or 24 month, respectively, in rats lends support for a NOAEL of 50 ppm (approx. 200 mg/m^3).

Conclusions from repeated studies by the oral and inhalation route
In conclusion, from the majority of investigations, the following NOAELs and LOAELs can be derived:
50 ppm (= approx. 400 mg/m^3) and 200 ppm (= approx. 800 mg/m^3) after prolonged inhalation exposure to all animal species under test. In the 2-years study (Cheever et al., 1990) 50 ppm (the only selected concentration) was the NOAEL, however, this for technical (one concentration only) rather than for scientific, toxicological reasons.

In the 2 oral rodent studies, the lowest subchronic NOAEL (13 wk) was at 120 mg/kg bw/d and the respective LOAEL at approx. 240 mg/kg bw/d, based on treatment-related effects in the forestomach and clinical symptoms. All corresponding values found in mice were significantly higher or of the same order: Likewise, the NOAEL (subchronic) for immunotoxic response of about 190 mg/kg bw/d is of the same order and thus no determinant factor.
The apparent NOAEL in the 2year feeding study (Alumot et al., 1976) was defined by the top dose of 25 mg/kg bw/d. The previous dose-finding study suggested treatment-related effects on lipid homeostasis in the liver after subacute exposure at about 80 mg/kg bw/d. Therefore, this observation appears to confirm that a NOAEL for chronic oral exposure at 25 mg/kg bw/d is reasonable. These derivations are also in harmony with the toxicokinetic data [see 3.1.1].
Because of a high reduction in water consumption, no NOAEL could be found in a drinking-water study over 13 weeks comprising three strains of rats. The authors of the study state, that because of limitations in the solubility and palatability of 1,2-dichloroethane, it was not possible to obtain a high enough dose in drinking water to see biologically significant toxic effects in rats.
Based on the GHS (OECD, 2001), DCE can be presumed as harmful after repeated exposure.

3.1.7 Genetic Toxicity

- **Bacterial test(s) in vitro**

The mutagenicity of DCE was investigated in several AMES-tests under standard and preincubation conditions using *S. typhimurium* strains TA98, 100, 1530, 1535, 1537 and 1538 both in the presence and absence of a metabolic activation system. Apart from a few exceptions (King et al., 1979; Principe et al., 1981), the test material was demonstrated to be mutagenic in *S. typhimurium* strains TA1530 and 1535 both with and without metabolic activation regardless of the concentrations used in the studies available, and it was noted that in the presence of activating factors the mutagenic response was enhanced. In contrast the compound did not induce point mutations in *S. typhimurium* strains TA98, 100, 1537 and 1538, respectively, both with and without metabolic activation (Barber et al., 1981; Brem et al. 1974; Guengerich et al., 1980; King et al., 1979; Nestmann et al., 1980; Principe et al., 1981). In a reverse mutation assay conducted in *E.coli* WP2 uvrA, 1,2-dichloroethane was only weakly mutagenic in the absence of a metabolic activation system at concentrations < 990 µg/ml (Hemminki et al., 1980).

- **Non-bacterial test(s) in vitro**

The genotoxicity of DCE was studied in a series of in vitro assays using mammalian cells (CHO / CHL-cells and human AHH-1/TK6 lymphoblastoid cell lines) and investigating different end points such as unscheduled DNA-synthesis (UDS), chromosomal aberrations (CA), gene mutations (HGPRT / TK ± -test) and cell transformations.

In the HGPRT-assay performed in CHO cells, dose-related gene mutation was noted both in the absence and presence of metabolic activation at substance concentrations of about 100 - 5000 µg/ml (1 – 50 mM) as derived from a loss of the thymidine-kinase activity (Tan and Hsie, 1981). The same result was obtained in the HGPRT assays using the human AHH-1 and TK6 lymphoblastoid cell-lines at concentrations of ≥100 and ≥500 µg/ml, respectively, both in dose-related manner without metabolic activation (Crespi et al., 1985).

In CHL fibroblasts, DCE was shown to increase the incidence of chromosomal aberrations (chromatid breaks and exchanges, no chromosome breaks) in the presence of metabolic activation at concentrations of ≥1000 µg/ml after 6-h exposure with no effect at 0.5 mg/ml, while without metabolic activation no effects were obvious at 200 - 4000 µg/ml after 24- and 48 hours, while an ambiguous result was found at 6000 µg/ml (Sofuni et al. 1985).

In primary rat hepatocytes, significant induction of unscheduled DNA-synthesis was reported at concentrations of >13 µg/ml in the absence of metabolic activation (Williams et al., 1989). Unscheduled DNA-synthesis reportedly induced in human lymphocytes is based on an unsuitable test method using [3H]-TdR incorporation (Perocco and Prodi, 1981): Hydroxyurea-induced suppression of replicative DNA synthesis is no reliable means to discriminate unscheduled from semi-conservative DNA replication, including that of mitochondria. Furthermore, an appropriate positive control substance was not included in the test. The calculation of the so-called DNA-repair value is obscure

In a cell transformation experiment conducted in BALB/C-3T3-cells, no mutagenic effects were observed at concentrations from 5 to 50 µg/ml without metabolic activation (Tu et al. 1985).

- **Genetic toxicity in vivo**

DCE was subject to several in vivo mutagenicity studies in which endpoints such as induction of micronuclei (MN), sister chromatid exchanges (SCE), germ cell mutations, DNA-breakage as well

as sex-linked-recessive-lethal mutations and somatic mutations and recombinations in *Drosophila melanogaster* have been investigated.

In a presumably well conducted micronucleus test in male and female NMRI mice, no increases in the number of micronucleated PCEs were noted in bone marrow cells 6 hr after the last dose when the maximum possible dose of 396 mg/kg bw of the material was given twice in an interval of 24 hr by i.p. injection; the dose was selected from previous toxicity testing ranging from non-toxic to approximate lethal doses. (King et al. 1979). Likewise, a second well conducted micronucleus test on lymphoma-prone transgenic mice (Eμ-PIM-1) using repeated oral dosing of DCE *(200 mg/kg in males and 300 mg/kg in females, due to toxicity reduced to 100 and 150 mg/kg bw, respectively)* in corn oil by gavage failed to demonstrate any deleterious effect on peripheral polychromatic and normochromatic erythrocytes after exposure for 14 and 41 weeks (Armstrong and Galloway, 1993).

Likewise, a second well conducted micronucleus test on lymphoma-prone transgenic mice (Eμ-PIM-1) using repeated oral dosing of DCE in corn oil by gavage failed to demonstrate any deleterious effect on peripheral polychromatic and normochromatic erythrocytes after exposure for 14 and 41 weeks (Armstrong and Galloway, 1993).

A third micronucleus was negative after single i.p. injection of 100 mg/kg bw into male CBA mice. But the result may be of limited value because of use of one relatively low single dose and the late sampling time of 30 hrs (Jenssen and Ramel, 1980).

In an SCE study on bone marrow cells of male Swiss mice, animals were administered DCE in groundnut oil (peanut) by i.p. injection at doses of 0, 0.5, 1.0, 2.0, 4.0, 8.0 and 16 mg/kg bw. The material led to a dose-dependent increase in the number of SCEs at 1.0 mg/kg bw and above ($p < 0.01$ at 2 mg/kg bw and higher). A DCE dose of 4 mg/kg bw caused doubling of the spontaneous SCE rate (background: approx. 3 events per cell). At 0.5 mg/kg bw, no increase in the number of SCEs was observable. No positive control was included (Giri and Que-Hee 1988).

Within the scope of a two-generation reproduction study, a dominant lethal test was undertaken twice in male Swiss mice of the first (F1) and second (F2) descendants generation which had been delivered from pre-treated parents (F0 and F1). After administration of DCE in drinking water (0; 0.03; 0.09 or 0.29 mg/ml), those repeatedly treated F1 and F2 males were mated to virgin females. There was no evidence of increases in pre- and post-implantation losses, no significant effects on the number of foetal implants and viable foetuses. Therefore, the ability of DCE to produce genotoxic effects on germ cells of male mice is considered unlikely (Lane et al., 1982). However, the incomplete documentation of the dosage regimen and does not allow a firm conclusion on these results.
The selection of relatively low doses do not allow a firm conclusion on these results.

Investigations were performed in male B6C3F1 mice to study the DNA-breaking potential of DCE (in-vivo/in-vitro DNA unwinding assay): Single doses of the substance were administered orally, by i.p. injection and by inhalation, and the presence of single strand breaks and alkali labile sites in isolated hepatic double-strand DNA was examined by using the in-vitro alkaline DNA-elution technique (Storer et al., 1984).
After 4-hr oral and i.p. application of DCE, sublethal and subtoxic doses of 100 to 200 mg/kg bw (oral) as well as of 150 to 300 mg/kg bw (i.p.) were able to induce DNA damage demonstrated by a distinct decrease in the double-strand fractions as compared to the vehicle controls. After 4-h inhalation exposure, no such effect was found at subtoxic concentrations up to 500 ppm (approx. 2000 mg/m^3), whereas clear DNA damage occurred at (hepato-) toxic and lethal exposures to 1000 and 2000 ppm. The differences can be explained by the completely different invasion and elimination kinetics for the various exposure routes (see 3.1.1).

In *Drosophila melanogaster,* 1,2-dichloroethane produced significant increases in somatic mutations (SMART-test) as well as germ-cell mutations (SLRL-test) both after feed and gas-phase exposure (Kramers et al. 1991) (King et al. 1979) (Ramel et al. 1990; Romert et al. 1990). Furthermore, mutagenic effects after feed administration were enhanced after pretreatment with the cytochrome P 450 inducer phenobarbital and reduced after pretreatment with the glutathione-*S*-transferase inhibitor buthionine sulfoximine (Ramel et al. 1990; Romert et al. 1990).

Conclusion
DCE was weakly mutagenic in bacterial tests systems, but was shown to produce clear mutagenic effects in mammalian cytogenetic and gene mutation assays. Metabolic activation is primarily required to cause these effects, which is in line with the known metabolism of the material involving the cytochrome-P450- and the glutathione-dependent pathways, where both pathways were considered as possible steps step in the bioactivation cascade leading to reactive metabolites.

The results of available in-vivo studies failed to show a mutagenic potential of DCE, as three MN and one questionable DL assay were negative. However, evidence of DNA damaging in-vivo activity/genotoxicity is presented by positive results in SCE assay and single DNA strand-break analysis.

DCE is no mutagen acc. to GHS (OECD, 2001), because there is no experimental evidence for DCE to cause mutations in germ cells.

3.1.8 Carcinogenicity

In the oral gavage study by NCI (1978), Osborne-Mendel rats of both sexes received 47 and 95 mg/kg bw/d (time-weighted doses, intermittent, 78 wk, 5d/wk) dissolved in corn oil by. Two control animal groups (20 animals/sex each) were included, one group being vehicle treated and the other one untreated. Evaluation of the results included comparison of tumour incidences in treated animals against matched control animals, and against pooled vehicle control animals from experiments with different chemicals which were conducted in parallel in the same room. The only clinical symptom during the first year of treatment was respiratory impairment while body weights, general appearance and behaviour were comparable to controls. Chronic pneumonia aggravated during the second year and was identified in 60-95% of all control and test animals. Mortality rates were increased in the high dose groups at 50% of males by week 55 and of females by week 57. By week 75, 84% of males and 80% of females were dead. Survival of the low dose rats was similar to that of the vehicle controls (males: 52 % survived until week 82; females: 50 % until week 85).

Significantly increased tumour incidences were seen in males as substantiated by haemangiosarcomas of the circulatory system, fibromas of subcutaneous tissue, and squamous cell carcinomas of the forestomach (significant only high dose).
In females, haemangiosarcomas of the circulatory system, mammary gland adenocarcinomas (significant only high dose), and mammary gland fibroadenomas significantly at low dose) were seen. In addition 7 cases of unusual tumours were seen in various organs, and rats bearing metastatic tumours especially in the high dose groups (National Cancer Institute 1978; Ward 1980).

In the corresponding second chronic oral study (NCI (1978) using B6C3F1 mice receiving time-weighted doses of 97 and 195 mg/kg bw/d (males) and 149 and 299 mg/kg bw/d (females), a significant increase in mortality rates was seen only in high dose females (32 %); mortality of low dose females (72 %) was similar to vehicle controls (20%) after 80 weeks. Clinical symptoms from study week six were abscesses at body and extremities as well as generalised and local alopecia. Behaviour of treated groups was comparable to controls throughout the study period.

Significant tumour increases in high dose males were located in lung (alveolar/bronchiolar adenoma) and liver (hepatocellular carcinoma). Significant differences in both low- and high-dose females were seen in incidences of mammary gland carcinomas and of alveolar/bronchiolar adenomas. Also, a trend suggesting substance-related increases in the incidence of uterine carcinomas and squamous cell carcinomas of the forestomach in females and hepatocellular carcinomas in males was noted (National Cancer Institute 1978; Ward 1980).

However, both studies share several limitations such as dosage adjustment, intermittent, higher-than-average dosing, poor survival in the top-dose group (in particular in rats) with a reasonable non-toxic low–dose group missing, unclear quality of the test substance, and treatment time too short.

No differences in tumour formation were seen in two apparently well-designed inhalation studies with groups of 90 animals, Sprague-Dawley rats and Swiss mice of both sexes (Maltoni et al., 1980/Spreafico et al., 1980). The animals were exposed to DCE concentrations of 5, 10, 50 and 150 – 250 ppm (corresponding to 21, 41, 206 and 617 – 1028 mg/m^3) for 78 consecutive weeks, 7 hr/d, 5 d/wk. Due to pronounced signs of toxicity especially in mice, the highest concentration was reduced to 617 mg/m^3 after a few weeks.

Apart from toxicity at 250 ppm, no clinical signs were noted in any group. In mice, survival rates were slightly reduced in the two highest dose groups (43.9 and 38.9 % vs. 47.4 % in controls), while in rats survival rates were not changed even in the high dose group (17.2 % vs. 18.9 % in controls). In neither study were specific types of tumours and relevant changes in the incidence of the tumours normally occurring in the strain of rats and mice used. An apparent, slight increase of mammary fibromas and fibroadenomas was statistically significant in the 250-150, 50 and 5 ppm female rat groups, but is to be considered incidental.

In mice, no differences between treated and control groups as to the type and the number of tumours was noted in any of the dose groups.

In conclusion, based on toxicokinetic data, 150 ppm can be assumed to be the reasonable upper tolerable exposure concentration in such a long-term study (Spreafico et al., 1980) [see 3.1.1]. Inhaled DCE was not carcinogenic in male and female Sprague Dawley rats nor in male and female Swiss mice under the conditions of the experiment including a limited exposure time of 78 weeks only (Maltoni et al. 1980). However, due to the above mentioned shortcomenings of the study, a final evaluation cannot be drawn from these data.

In another long-term rat inhalation study with sole exposure to 50 ppm DCE (2 yr, 5d/wk, 7 h/d) no tumor formation was noted in either sex (Cheever et al. 1990). 50 ppm was the occupational standard at that time. In this study, blood levels were determined to be in the range of 0.2-0.3 µg/ml immediately after the 7h-inhalation exposure. In animals receiving a combined 1,2-dichloroethane/disulfiram treatment blood levels were approx. 5-fold increased, and tumour incidence was significantly increased in several organs (liver, skin, testes). Thus inhibition of the ethanol metabolism pathway enzymes increased both blood levels and tumour incidence.

Overall, two long-term carcinogenicity studies in rat and mice showed tumours in an number of organs (mammary gland adencarcinomas, squamous cell carcinomas of the forestomach and hemangiosarcomas) after oral DCE administration by gavage but not after inhalation.

The differences in the carcinogenic response after oral administration and inhalation may be explained at least partly on the basis of toxicokinetics and metabolic pathways of the substance [see 3.1.1]. Despite the shortcomings of the oral studies, the results have to be considered as relevant. Due to the short exposure time of the inhalation study, the inhalation data do not permit a final evaluation.

Based on the GHS system (OECD, 2001), DCE has to be regarded as suspected human carcinogen.

3.1.9 Reproductive/Developmental Toxicity

- **Reproductive Toxicity**

In a 2-year "repeated one-generation study" with male and female rats fed DCE in the diet at 250 and 500 mg/kg feed, no differences in parental fertility, litter data, and pup data (survival, body weights) compared to controls were seen during F0-pregnancies from number 1 through 5. NOAELs for both parental and F1 reproductive effects were estimated to be the top dose in the range of 50 mg/kg bw/d, taking into account substance losses due to evaporisation (Alumot et al. 1975). This result is confirmed by a similarly designed two-generation study in male and female ICR mice having received comparable doses of DCE in drinking water of 5 – 50 mg/kg bw/d for 5 weeks during premating of the Fo and 11 weeks of the F1 generation). Adult mice (F0 and F1b) showed no significant changes in water consumption, body weight or fertility index and gestation index (number of females with live litters/number of females pregnant) but 'inexplicable' sporadic increases in mortality occurred (details not given). Among the offspring of F0 and F1b animals (F1a, F1b, F2a), no significant changes were seen in mean litter size, mean post-natal body weights (measured on days 7, 14 and 21), or survival (measured on days 4 and 21) and it was reported that there was no evidence of dose-dependent gross pathology or congenital external, visceral or skeletal malformations although no details or data were given. According to the results of the two-generation study in mice the NOAEL for general and parental toxicity as well as for the F1 and F2 offspring is 50 mg/kg bw/d in each case (Lane et al. 1982).

The reproductive toxicity of DCE was also investigated in a one-generation study in male and female rats after inhalation exposure to 0, 25, 75 and 150 ppm (corresponding to 0, 103, 308 and 617 mg/m^3) for 60 exposures (5/wk, 6 h/d) during the premating period and another 116 exposures (7/wk; 6 h/d) for the remainder, but sparing the pregnancy and lactation period for the F0-females.
Neither the parental nor the F1 animals did reveal any treatment-related changes in clinical and pathological parameters or reproductive performance (Murray et al., 1980 ; Rao et al., 1980).
NOAELs from this study are 150 ppm for both parental animals and F1-offsprings and also for signs of general toxicity.

All three studies failed to exhibit clear toxic signs at the doses applied: therefore, evaluation as to reproduction performances is only possible under this restriction.

The reproductive toxicity of 1,2-dichloroethane was investigated in a one-generation study in male and female Sprague-Dawley rats after inhalation exposure towards 0, 25, 75 and 150 ppm (corresponding to 0, 103, 308 and 617 mg/m^3), respectively. The premating period was 60 days for both sexes and the mating regimen was one male each with one female for a period of four days to produce the F1a-generation. The F1a-generation was necropsied between postnatal day 21 and 25. Seven days after the last F1a litter was sacrificed parental animals were remated and the produced F1b-litter was necropsied between postnatal days 21 and 25 as well. Maternal exposure was discontinued only from gestation day 21 until lactation day four.
Adult animals did not reveal any clinical signs of intoxication and no treatment-related changes in food consumption or body weights were reported. Relative organ weights of liver, kidneys, testes, uterus and ovaries of all dose groups were comparable to controls, too.

In the offspring (both F1 generations) no changes in the fertility indices, in the number of pups/litter, gestation survival, pup survival indices on days, 1, 7, 14 and 21, sex ratio at day 21, neonatal body weight and growth was observable. No substance related macroscopical and histopathological changes of liver and kidneys and external, visceral and skeletal malformations or retardations/variations were evident in both F1-generations (Murray et al. 1980 ; Rao et al 1980a). The NOAEL derivable from this study is 150 ppm for both parental animals and F1-offsprings and signs of general toxicity.

- **Developmental Toxicity**

Developmental toxicity / teratogenicity studies were performed in rats and rabbits by the inhalation and oral route of exposure.
In two well conducted studies using pregnant SD rats either exposed to 150, 200, 250, and 300 ppm (6h/d) or to 118, 158, 198, 238 mg/kg bw/d (corn oil, gavage) from day 6 through 20 p.c., no treatment-related differences were seen in mean litter size, foetuses per litter, in numbers of implantations, incidence of resorptions, foetal body weight and the incidence of malformations length, sex ratio as compared to controls at maternally non-toxic doses/concentrations of either exposure regimen, except some embryolethal effects (increase in non-viable implants and resorption sites per litter), significant in the oral dose-groups of 200 mg/kg bw and higher ($p<0.05$). Distinct maternal toxicity was indicated by intermittent delayed weight gains and expressed by a decrease in the absolute weight gain of dams and by three and two stillborn/not viable litters delivered at 240 mg/kg and 300 ppm, respectively (Payan et al., 1995).
Accordingly, the NOAELs(inhalation/oral) were at 250 ppm and 160 mg/kg bw/d for maternal general toxicity, and 300 ppm for embryo-/fetotoxicity/teratogenicity, and at 240 mg/kg bw/t for fetotoxicity/teratogenicity, but at 160 mg/kg bw/d for embryotoxicity, respectively.

In the limited inhalation rat study by Rao et al. (1980) using only two concentrations of 100 and 300 ppm, the NOAEL was 100 ppm for maternal as well as developmental toxicity, while the high exposure level showed overt toxicity (10/16 dams dead). An intermediate, less maternally toxic levels appears to be missing in order to identify the appropriate NOAEL. In the respective inhalation study conducted in rabbits (Rao et al., 1980), the NOAEL for developmental effects proved to be at 300 ppm with unclear maternal toxicity, as several dams died at either exposure level without signs of intoxication.

In principal, the observations of the latter are in line with those of the more comprehensive studies by Payan et al. (1995).

Conclusion: Overall, three generation studies by the oral or inhalation route in rats and mice gave no evidence of impairment of the parental reproductive performance and pre- and postnatal viability and development of the progeny. In four oral or inhalation studies in rats and rabbits, intrauterine development of embryos and fetuses was not significantly affected up to maternally toxic doses. Based on the GHS system (OECD, 2001), DCE has not to be regarded as reproductive or developmental toxicant

3.1.10 Human data

In humans it is reported that DCE is a central nervous depressant and effects are manifested by unspecific symptoms such as nausea, vomiting, headache, lightheadedness and weakness to stupor, dysequilibrium, coma, and respiratory arrest. In severe cases, central nervous system signs appear first within several hours of exposure and are followed by a quiescent period. On the second day, oliguria and hepatic transaminasemia may develop. Severe ingestions produce widespread organ damage (especially kidney, liver, and adrenal gland) as well as gastrointestinal bleeding. No concentrations where these effects occur were given in the reference (Ellenhorn and Barceloux, 1988).

Agricultural workers received exposure dermally and via inhalation (4-60 ppm) resulting from fumigation practices. Ninety of 118 workers reported symptoms including conjunctival congestion and burning sensation, weakness, bronchial and pharyngeal symptoms, metallic taste in mouth, headache, dermatographism, nausea, liver pain, tachycardia, and dyspnoea after effort. Liver function measurements showed abnormality in 40 out of 56 (HSDB 2000).

After intermittent immersion of the hands into DCE the development of a severe dermatitis is described which is in accordance with the materials defatting, degreasing properties (Wirtschafter and Schwartz, 1939).

In a study conducted in 71 workers (51 test, 20 control subjects) employed at a vinyl chloride manufacturing plant in China the genotoxicity of DCE in humans as assessed by sister chromatic exchange (SCE) rates was investigated. Workers were exposed to a mixture of vinyl chloride monomer (VCM) and DCE and three exposure categories were defined: low VCM/low DCE (VCM: 0.25 - 0.39 ppm; DCE: 0.20 - 0.29 ppm); low VCM/moderate DCE (VCM: 0.16 - 0.27 ppm; DCE: 0.69 - 1.31 ppm); moderate VCM/moderate DCE (VCM: median of 1.63 ppm; DCE: median of 0.77 ppm). A not significant 7-% increase in SCE frequencies as compared to controls was found in the low VCM/low DCE group (23 individuals) and a statistically significant increase of about 24 % in the low VCM/moderate DCE group (20 individuals). It was contended that relatively small amounts of DCE cause an increase in SCE frequency. This increase was also obvious in non-smoking workers, and it was additionally shown that SCE frequency was positively correlated with smoking but not with drinking habits amid VCM exposure in this study (Cheng et al. 2000).

4. Hazards to the Environment

4.1 Aquatic effects

The acute aquatic toxicity of 1,2-dichloroethane to fish has been investigated in several species of fresh water fish. The material showed a minimum 96 h LC_{50} of 66 mg/l in a static test with *Micropterus salmoides* with analytical monitoring and a maximum 96 h LC_{50} of 430 mg/l in a closed static test with *Lepomis macrochirus* (Rinehart, W.E. 1971; Buccafusco et al. 1981). Most of the available studies are static or semi-static studies and most of them are conducted without analysis of the test concentrations. These tests are not considered for the assessment due to the high volatility of 1,2-dichloroethane.

The acute toxicity of 1,2-dichloroethane to aquatic invertebrates was studied in several static and semistatic tests. Only such tests were considered for the assessment that were performed in closed systems or with analytical monitoring of the test substance concentration. The lowest EC_{50} value for freshwater invertebrates of 150 mg/l was found in a 24h test with Daphnia magna. In this test the substance concentration was analytically monitored. Additional investigations with the marine species *Artemia salina* yielded a 24h- EC_{50}-value of 36 mg/l, in a test system with a reduced salinity of 25 %.

The toxicity of 1,2-dichloroethane was investigated in different algal species. The 72 h measured EC_{50} of 189 mg/l was obtained on *Scenedesmus subspicatus*, tested in a system controlling volatile losses (capped vessels) and is considered to be the lowest EC_{50}-value for growth inhibition of algae (Freitag et al. 1994). A corresponding NOEC is not available but, based on this EC_{50}, it is, however, unlikely that the NOEC would be lower than NOEC obtained on *Daphnia magna* (28d NOEC of 11 mg/l for reproduction, see table 2). For the longer-term algae studies there is no information whether the algae were within the exponential growth phase during the whole test. Therefore, these data cannot be used for the effect assessment.

In addition, long-term tests are available with fish and Daphnia. In an embryo-larval study with *Pimephales promelas* a 32d-MATC related to wet weight of 29 - 59 mg/l based on measured concentrations was found under flow-through conditions. Eggs used were 24 hr old (Ahmad 1984). From the MATC a NOEC of 29 mg/l can be derived.
In a 28d-reproduction test conducted under semistatic closed conditions with *D. magna* the LOEC-values determined for reproduction and growth were 21 ± 1.7 and 72 ± 4.8 mg/l and the NOEC-values determined for reproduction and growth were 11 ± 0.8 and 42 ± 2.4 mg/l (based on measured concentrations), respectively (Call et al. 1983).

The lowest effect value of 11 mg/l was found in a long-term test with Daphnia magna. This value is used as basic value for the derivation of the PNECaqua. As long-term tests with fish and daphnids are available and as it can be assumed that algae are not more sensitive to 1,2-DCE than daphnids an assessment factor of 10 is applied resulting in a PNECaqua of 1.1 mg/l.

Table 2: Summary table on ecotoxicity data of 1,2-dichlorethane

Species	Duration d (days) h (hours)	Type of study	Criterion (LC50/EC50 NOEC)	Concentration (mg/l)	Reference
ACUTE TOXICITY TO FISH					
1. FRESHWATER					
Pimephales promelas	96 h	F-T; A	LC50	116	Ahmad 1984 ; Walbridge et al. 1983
Pimephales promelas	96 h	F-T; A	LC50	118	Veith et al. 1983
Lepomis macrochirus	96 h	S; A	LC50	94	Rinehart 1971
Micropterus salmoides	96 h	S; A	LC50	66	Rinehart 1971
Poecilia reticulata	7 d	SS; N; C	LC50	106	Koenemann 1981
Lepomis macrochirus	96 h	S; N; C	LC50	430	Buccafusco et al. 1981
Pimephales promelas	96 h	F-T; A	LC50	136	Brooke et al. 1985
2. SALTWATER					
Limanda limanda	96 h	F-T; A	LC50	115	Pearson and McConnell 1975

CHRONIC TOXICITY TO FISH					
1. FRESHWATER					
Pimephales promelas	32 d	F-T; A	NOEC LOEC (survival-hatching)	29 59	Ahmad 1984
Oncorhynchus kisutch	21 d	SS; A	LOEC (hatching)	56	Reid et al. 1982
CHRONIC TOXICITY TO FISH					
2. SALTWATER (NO DATA AVAILABLE					
ACUTE TOXICITY TO INVERTEBRATES					
1. FRESHWATER					
Daphnia magna	48 h	A; C	EC50 LC50	155-183 268-315	Ahmad 1984; Call et al. 1983; Richter et al. 1983
Daphnia magna	24 h	A	EC50	150	Freitag et al. 1994
Daphnia magna	48 h	N; C	EC50	324	Kuehn et al. 1989
Daphnia magna	24 h	N; C	LC50	250	Le Blanc 1980
Daphnia magna	48 h	N; C	LC50	220	Le Blanc 1980
2. SALTWATER					
Artemia salina	24 h	S; N; C	EC50	36	Foster and Tullis 1985
Artemia salina	24 h	S; N; C	EC50	320	Price et al. 1974
Eliminius modestus	48 h	N; C	EC50 (larvae)	186	Pearson and McConnell 1975
CHRONIC TOXICITY TO INVERTEBRATES					
1. FRESHWATER					
Daphnia magna	28 d	SS; A; C	NOEC LOEC (reproduction)	11 21	Ahmad 1984; Call et al. 1983; Richter et al. 1983
2. SALTWATER (NO DATA AVAILABLE)					
TOXICITY TO ALGAE					
1. FRESHWATER					
Scenedesmus subspicatus	72 h	A; C	EC50	189	Freitag et al. 1994
Scedenesmus subspicatus	96 h	A; C	EC50	213	Behechti et al., 1995
2. SALTWATER (NO VALID DATA AVAILABLE)					
TOXICITY TO MICROORGANISMS					
Entosiphon sulcatum	72 h	N, C	TT (72 h)	1127	Bringmann et al. 1980
Pseudomonas putida	16 h	N, C	TT (16 h)	135	Bringmann et al. 1980
Activated sludge	24 h	N, C	IC50	2780	Tang et al. 1990

Fish/Invertebrates: All endpoints of the tests are based on survival/mortality. Other effects are explicitly mentioned in the table.
Algae: All endpoints of the tests are based on growth
A = analysis; C = closed system or controlled evaporation; N = nominal concentration; S = static; SS = semistatic;
F-T = flow-through

4.2. Terrestrial Effects

The effects of 1,2-dichloroethane on the earth worm *Eisenia fetida* has been investigated. Animals were exposed in the dark for 48 hr towards the material by means of a filter paper. A 48 hr LC_{50}-value of 60 µg/cm^2 was derived from this investigation (Neuhauser et al. 1985; Neuhauser et al. 1986). No PNECsoil can be derived from this study due to the use of filter paper instead of soil.

4.3 Other Environmental Effects

In the cell multiplication inhibition test the effect of 1,2-dichloroethane on micro-organisms was studied. In the bacterial strain *Pseudomonas putida* the toxicity threshold (TT) after a16 hr exposure period has been determined to be 135 mg/l (Bringmann and Kuehn 1976; 1977b; 1980). The same test design was applied to the protozoa *Entosiphon sulcatum* with a toxicity threshold of 1127 mg/l after 72 h (Bringmann and Kuehn 1980). In the course of a closed bottle test the toxicity towards activated sludge from a local WWTP was studied. The cumulative oxygen demand has been measured over 24 hr and the concentration leading to a 50 % reduction in oxygen consumption was determined. A 24 hr IC_{50} of 2780 mg/l was derived from this investigation indicating only very little toxicity on activated sludge (Tang et al. 1990).

5. CONCLUSIONS AND RECOMMENDATIONS

5.1 Conclusions

Several manufacturers in each of the three main regions Europe, Japan and USA produce 1,2-dichloroethane with an worldwide annual production volume exceeding 1,000,000 tons. The material is primarily being used as an intermediate in the production of vinyl chloride monomer (with a contribution of 95 %) which is converted to polyvinyl chloride. The remaining 5 % are used as an intermediate in the production of ethylenediamines, tri- and tetrachloroethylene and in other fields of application, i.e. as extraction and cleaning solvent and as lead scavenger in gasoline. Due to the increasing use of unleaded fuel the latter application is expected to decline steadily in OECD countries which in turn leads to a subsiding exposure via this route. Therefore, exposure of consumers towards the substance is not being assumed to be of importance because no other consumer applications are known or intended. It is not clear whether 1,2-dichloroethane is still finding use as aviation gasoline where environmental exposure may be implied. However, its structural analogue 1,2-dibromoethane is still used as gasoline additive both in vehicles and aircrafts. Other former applications were described as diluent in pesticides, grain fumigant and in paint, coatings and adhesives. Reported applications in glues or cosmetics are assumed not to exist anymore due to the proven health effects of the substance.
Consequently, since 1,2-dichloroethane is used predominantly as a chemical intermediate exposure towards the material is given mainly in occupational settings where the inhalation route represents the most relevant pathway for uptake.

Releases into the environment are expected to occur mainly during production and processing of 1,2-dichloroethane as well as during use of products containing the substance. Additional releases may occur from the use as extraction and cleaning solvent and as lead scavenger in gasoline.

Since no up-to-date measurements are available concentrations of the substance measured during the mid seventies and late eighties in the environment for air, river water and drinking water to reflect environmental exposure situations were presented. Highest concentrations were found in river water of the river Rhine ranging form 4.4 – 8.5 µg/l and lowest levels were determined in air ranging from 12.4 – 21.4 µg/m^3. Comparable measurements performed in Japan in 1988 yielded 1,2-dichloroethane concentration ranges of 0.082 – 13.9 µg/m^3 and 45 – 2200 ng/m^3 for river waters and air, respectively.

According to a Mackay level I calculation the material is predominantly distributed in air (95.0%) and only to a minor portion into water (4.8 %) which is supported by both the high vapour pressure and the volatility of 1,2-dichloroethane. Based on a calculation according to Atkinson the substance is being degraded in the atmosphere by photochemically produced hydroxyl radicals with a half life of about 42 days at a hydroxyl radical concentration of $1.5 * 10^6$ radicals/cm^3 and about 73 days at a hydroxyl radical concentration of $5 * 10^5$ radicals/cm^3, respectively. In light of the calculated half-lives in water ranging from 6 – 300 years hydrolysis is not an important pathway of degradation in water. Due to the half-lives in the atmosphere, emissions are not globally distributed and are not enriched in the atmosphere. The compound is not biodegradable under non-adapted test conditions but it could be demonstrated that appropriately adapted bacteria or enrichment with degradation promoting factors lead to acceptable and fast biodegradation rates. However, under environmental conditions biodegradation is not likely to occur. The measured n-octanol / water partition coefficient of 1.45 demonstrates no potential for bioaccumulation/bioconcentration.

Physico-chemical data are referenced from reliable handbooks and are in accordance with those in other review publications.

Both acute and long-term ecotoxicity tests are available with aquatic organisms from three and two trophic levels, respectively. Due to the volatility of 1,2-dichloroethane, only those tests were considered for the assessment that were performed under flow-through or semi-static conditions, in closed systems or with analytical monitoring of the test substance concentration.

The lowest effect values in short-term tests were found for Micropterus salmoides (96 h-LC50 = 66 mg/l), Daphnia magna (24 h-EC50 = 150 mg/l), Artemia salina (24 h-EC50 = 36 mg/l) and Scenedesmus subspicatus (72 h-EC50 = 189 mg/l). In long-term aquatic toxicity studies effect values were found for Pimephales promelas (32 d-NOEC = 29 mg/l) and Daphnia magna (28d-NOEC = 11 mg/l). A PNEC of 1100 µg/l was calculated on the basis of the lowest valid NOEC of 11 mg/l obtained in a chronic aquatic toxicity reproduction test conducted in *Daphnia magna* applying an assessment factor of 10.

After acute oral administration or inhalation, DCE has to be considered as harmful and as uncritical after dermal exposure, based on the GHS system. Oral LD_{50} values are ranging from about 400 to 1000 mg/kg bw and LC_{50}-values of 4100 mg/m³/7.2 h – 49400 mg/m³/0.5h. A dermal LD_{50} was high at about 5000 mg/kg bw in rabbits. After acute inhalation, a 4-hour LC_{50} can be estimated to be at 8000 mg/m^3 (approx. 2000 ppm), a 4- and 7-hour NOAEL to be at 1400 and 800 mg/m³, respectively (approx. 350 and 200 ppm, resp.) in rats.

Steep concentration-response relationships associated with sudden and often delayed mortality were characteristic of acute DCE exposure without evident organ lesion causing the death.

Experimental evidence gives no rise to evaluate DCE as a skin or eye irritant, although after atmospheric exposure the specific corneal damage observed in dogs cannot be completely dismissed. DCE showed a low irritation potential.

No studies on contact allergy were located

DCE was examined after prolonged oral and inhalation exposure in rats and mice:
Concerning the subchronic oral studies, a drinking-water study does not allow to derive a NOAEL because of the highly reduced water consumption by the test animals. In a 13 week gavage study the NOAEL is assumed to be 120 and 150 mg/kg bw/d for male and female rats, respectively, based on treatment-related effects in the forestomach and clinical symptoms. For chronic oral exposure (2 years), the top dose of 25 mg/kg bw/d was void of any adverse effect. This can be adopted as a reasonable chronic NOAEL, also supported by toxicokinetic deliberations that suggest a blood level significantly below 10 µg DCE/ml which has been proposed as a toxic threshold concentration in blood in two rat strains under the conditions of the experiment. Following inhalation, all studies conducted on a broad spectrum of species including rats, rabbits, guinea pigs, and dogs, and monkeys are consistent with a NOAEL of 200 mg/m^3 (approx. 50 ppm) for a subchronic to chronic time period of exposure, whereas at 200 ppm variable responses from unremarkable to toxic and lethal were observed even within the same species (e.g. rats or guinea pigs).
Based on the GHS system (OECD, 2001), DCE should be classified as harmful following repeated inhalation exposure.

DCE was mutagenic in bacterial and mammalian in-vitro test systems: Positive results were obtained in gene mutation assays and a cytogenetic assay. In vivo, no mutagenic potential was elicited in three mouse micronucleus assays.
Yet, evidence of DNA damaging in-vivo activity and genotoxicity was demonstrated by positive results in an SCE assay (mice) and DNA strand-break analysis (mouse liver). It is worth while

mentioning that DNA destabilisation was not evident at a sub-toxic to low toxic inhalation exposure level (500 ppm/4 h = approx. 2000 mg/m^3/4 h).
However, DCE is no mutagen to be classified acc. to GHS (OECD, 2001), because there is no experimental evidence for DCE to cause mutations in germ cells.

The oral administration of DCE for 78 weeks by gavage proved to be carcinogenic in either sex of Osborne-Mendel rats and B6C3F1 mice at bolus doses of 50 mg/kg bw/d and higher, but not after 78-week inhalation of up to 150 ppm in SD rats and Swiss mice. Based on the GHS system (OECD, 2001), DCE has to be classified as suspected human carcinogen.
The route of application-specific expression of tumorigenesis may be explained by different pharmacokinetic processes [see: 3.1.1]: After absorption of comparable doses of DCE, five times higher peak plasma levels were observed after oral administration as compared to inhalation which was accompanied by about a five times higher binding of radiolabeled DCE-borne compounds in the liver DNA after oral treatment than after inhalation (Reitz et al. 1982). The 5-fold increase in DNA-binding was explained by a saturation of the oxidative and detoxifying, GSH-dependent metabolism occurring after administration by gavage, but not after inhalation because of the different invasion and distribution kinetics.

Likewise, the negative finding in the in-vivo genotoxicity study on the DNA damaging potential of DCE in B6C3F1 mice (see above and 3.1.7) may provide a further piece of evidence that inhalation exposure of DCE may harbour a smaller potential for producing deleterious effects on DNA than oral administration by gavage.

Reproductive performance in rats and mice including fertility of either sex and fetal viability parameters was not impaired after repeated oral doses of 50 mg/kg bw/d (feed and drinking water) and after inhalation exposure to up to 150 ppm in several generation studies. Furthermore, no histopathological adverse effects on the gonads were reported in two oral long-term studies in rats and mice. In summary, all these observations appear to provide sufficient confidence for no concern over DCE-induced toxicity on reproduction.

In two well conducted investigations on developmental toxicity, no significant toxicity was noted in the offspring of rats receiving up to maternally toxic oral (gavage) and inhalation doses during pregnancy. The NOAELs for developmental effects were the highest doses employed, 240 mg/kg bw/d and 300 ppm, respectively. Results of previous, more limited studies in rats and rabbits are consistent with those observations.
Based on the GHS system (OECD, 2001), DCE is no candidate for classification with respect to reproductive toxicity.

However, intoxications through skin penetration of DCE have been reported in human workers. However, despite long experience with the use of DCE in the industry and consumer applications in former times, there have been no human case reports on skin sensitisation in the literature.
In a study conducted in 71 workers (51 test, 20 control subjects) employed at a vinyl chloride manufacturing plant in China the genotoxicity of DCE in humans as assessed by the change in sister chromatic exchange (SCE) rates was investigated. Workers were exposed to a mixture of vinyl chloride monomer (VCM) and DCE and three exposure categories were defined: low VCM/low DCE (VCM: 0.25 - 0.39 ppm; DCE: 0.20 - 0.29 ppm); low VCM/moderate DCE (VCM: 0.16 - 0.27 ppm; DCE: 0.69 - 1.31 ppm); moderate VCM/moderate DCE (VCM: median of 1.63 ppm; DCE: median of 0.77 ppm). A not significant 7-% increase in SCE frequencies as compared to controls was found in the lower (23 individuals) and a statistically significant increase of about 24 % in the higher exposed subgroup (20 individuals). It was contended that relatively small amounts of DCE cause an increase in SCE frequency. This increase was also obvious in non-smoking workers, and it

was additionally shown that SCE frequency was positively correlated with smoking but not with drinking habits in this study (Cheng et al. 2000).

5.2 Recommendations

Concerning the environment, the substance is currently of low priority for further work. This can be concluded from the main use as chemical intermediate, the very low bioaccumulation potential and the low toxicity to aquatic organisms.

Concerning human health, the substance is currently of low priority for further work unless there is worker or consumer exposure due to the possible genotoxic and carcinogenic effects. The recommendation is based on limited exposure information.

Further work might be necessary in member countries with a different exposure situation.

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I U C L I D Data Set

Existing Chemical	:	ID: 107-06-2
CAS No.	:	107-06-2
EINECS Name	:	1,2-dichloroethane
EC No.	:	203-458-1
TSCA Name	:	Ethane, 1,2-dichloro-
Molecular Formula	:	C2H4Cl2

Producer related part

Company	:	Wacker - Chemie GmbH
Creation date	:	17.11.2000

Substance related part

Company	:	Wacker - Chemie GmbH
Creation date	:	17.11.2000
Status	:	
Memo	:	
Printing date	:	27.06.2002
Revision date	:	
Date of last update	:	27.06.2002
Number of pages	:	1
Chapter (profile)	:	Chapter: 1, 2, 3, 4, 5, 6, 7, 8, 10
Reliability (profile)	:	Reliability: without reliability, 1, 2, 3, 4
Flags (profile)	:	Flags: without flag, confidential, non confidential, WGK (DE), TA-Luft (DE), Material Safety Dataset, Risk Assessment, Directive 67/548/EEC, SIDS

1.0.1 APPLICANT AND COMPANY INFORMATION

Type : other: Cooperating Panel
Name : American Chemistry Council
Contact person :
Date :
Street :
Town :
Country :
Phone :
Telefax :
Telex :
Cedex :
Email :
Homepage :

Flag : Critical study for SIDS endpoint
25.01.2002

Type : other: Cooperating Panel
Name : EURO CHLOR
Contact person :
Date :
Street :
Town :
Country :
Phone :
Telefax :
Telex :
Cedex :
Email :
Homepage :

Remark : European Cooperating Panel consists of the following companies:

Dow Chemicals
Elf Atochem
Enichem
EVC
ICI Chlor Chemicals
Norsk Hydro
Solvay
Tessenderlo Chemie
Vestolit

Flag : Critical study for SIDS endpoint
25.01.2002

Type : other: Cooperating Panel
Name : Vinyl Environment Council, Japan
Contact person :
Date :
Street :
Town :
Country :
Phone :
Telefax :
Telex :

Cedex	:	
Email	:	
Homepage	:	
Remark	:	Japanese Cooperating Panel consists of the following companies: ---------- Asahi Glass Central Chemicals Kaneka Kashima VCM Shin Dai-Ichi Vinyl Shin-Etsu Chemicals Tokuyama Tosoh V-Tech
Flag	:	Critical study for SIDS endpoint

25.01.2002

Type	:	lead organisation
Name	:	WACKER CHEMIE GMBH, Burghausen, Germany
Contact person	:	
Date	:	14.11.2000
Street	:	Johannes-Hess-Str. 24
Town	:	84489 Burghausen
Country	:	Germany
Phone	:	+49 8677 83-5586
Telefax	:	+49 8677 83-5590
Telex	:	
Cedex	:	
Email	:	
Homepage	:	
Flag	:	Critical study for SIDS endpoint

25.01.2002

1.0.2 LOCATION OF PRODUCTION SITE, IMPORTER OR FORMULATOR

1.0.3 IDENTITY OFRECIPIENTS

1.0.4 DETAILS ON CATEGORY/TEMPLATE

1.1.0 SUBSTANCE IDENTIFICATION

1.1.1 GENERAL SUBSTANCE INFORMATION

Purity type	:	
Substance type	:	organic
Physical status	:	liquid
Purity	:	> 99 % w/w
Colour	:	
Odour	:	

Source : Wacker Chemie GmbH, Burghausen, Germany.
Reliability : (1) valid without restriction
Flag : Critical study for SIDS endpoint
09.08.2001

1.1.2 SPECTRA

1.2 SYNONYMS AND TRADENAMES

1, 2-Dichloroethan

Attached document : Synonyms are:
1, 2-Dichloroethane
1,2-Bichloroethan
alpha, beta-Dichloroethan
DCE; 1,2-ethylene dichloride
Dichloro-1,2-ethane
Dichloroethane
EDC
ethane, 1,2-dichloro
Glycol dichloride
Flag : Critical study for SIDS endpoint
25.01.2002

1.3 IMPURITIES

Purity :
CAS-No : 79-00-5
EC-No : 201-166-9
EINECS-Name : 1,1,2-trichloroethane
Molecular formula :
Value : <= .5 % w/w

Source : Wacker - Chemie GmbH, Burghausen, Germany
Reliability : (4) not assignable
Secondary Literature
Flag : non confidential
14.08.2001 (1)

Purity :
CAS-No : 75-35-4
EC-No : 200-864-0
EINECS-Name : 1,1-dichloroethylene
Molecular formula :
Value : <= .2 % w/w

Source : Wacker - Chemie GmbH, Burghausen, Germany
Reliability : (4) not assignable
Secondary Literature
Flag : non confidential
09.08.2001 (1)

Purity :
CAS-No : 56-23-5
EC-No : 200-262-8

EINECS-Name : carbon tetrachloride
Molecular formula :
Value : ca. .11 % w/w

Source : Wacker - Chemie GmbH, Burghausen, Germany
Reliability : (4) not assignable
Secondary Literature
Flag : non confidential
09.08.2001 (1)

Purity :
CAS-No : 75-00-3
EC-No : 200-830-5
EINECS-Name : chloroethane
Molecular formula :
Value : <= .1 % w/w

Source : Wacker - Chemie GmbH, Burghausen, Germany
Reliability : (4) not assignable
Secondary Literature
Flag : non confidential
09.08.2001 (1)

Purity :
CAS-No : 71-43-2
EC-No : 200-753-7
EINECS-Name : benzene
Molecular formula :
Value : ca. .05 - .112 % w/w

Source : Wacker - Chemie GmbH, Burghausen, Germany
Reliability : (4) not assignable
Secondary Literature
Flag : non confidential
09.08.2001 (1)

Purity :
CAS-No :
EC-No :
EINECS-Name : dichlorethanisomers
Molecular formula :
Value : ca. .037 % w/w

Source : Wacker - Chemie GmbH, Burghausen, Germany
Reliability : (4) not assignable
Secondary Literature
Flag : non confidential
09.08.2001 (1)

Purity :
CAS-No : 75-34-3
EC-No : 200-863-5
EINECS-Name : 1,1-dichloroethane
Molecular formula :
Value : ca. .0356 % w/w

Source : Wacker - Chemie GmbH, Burghausen, Germany
Reliability : (4) not assignable
Secondary Literature
Flag : non confidential

09.08.2001 (1)

Purity :
CAS-No : 79-01-6
EC-No : 201-167-4
EINECS-Name : trichloroethylene
Molecular formula :
Value : ca. .034 % w/w

Source : Wacker - Chemie GmbH, Burghausen, Germany
Reliability : (4) not assignable
Secondary L iterature
Flag : non confidential
09.08.2001 (1)

Purity :
CAS-No : 156-60-5
EC-No : 205-860-2
EINECS-Name : trans-dichloroethylene
Molecular formula :
Value : ca. .018 - .052 % w/w

Source : Wacker - Chemie GmbH, Burghausen, Germany
Reliability : (4) not assignable
Secondary Literature
Flag : non confidential
09.08.2001 (1)

Purity :
CAS-No : 7647-01-0
EC-No : 231-595-7
EINECS-Name : hydrogen chloride
Molecular formula :
Value : ca. .01 % w/w

Source : Wacker - Chemie GmbH, Burghausen, Germany
Reliability : (4) not assignable
Secondary Literature
Flag : non confidential
09.08.2001 (1)

Purity :
CAS-No : 67-66-3
EC-No : 200-663-8
EINECS-Name : chloroform
Molecular formula :
Value : ca. .007 % w/w

Source : Wacker - Chemie GmbH, Burghausen, Germany
Reliability : (4) not assignable
Secondary Literature
Flag : non confidential
09.08.2001 (1)

Purity :
CAS-No : 75-01-4
EC-No : 200-831-0
EINECS-Name : chloroethylene
Molecular formula :
Value : ca. .003 % w/w

Source : Wacker - Chemie GmbH, Burghausen, Germany
Reliability : (4) not assignable
Secondary Literature
Flag : non confidential
14.08.2001 (1)

1.4 ADDITIVES

Purity type :
CAS-No :
EC-No :
EINECS-Name : Alkylamines
Molecular formula :
Value :
Function of additive :

Source : Wacker - Chemie GmbH, Burghausen, Germany
Reliability : (4) not assignable
Secondary Literature
Flag : non confidential
09.08.2001 (139)

1.5 TOTAL QUANTITY

Quantity : > 1000000 - tonnes in 2000

Source : Wacker Chemie GmbH, Burghausen, Germany.
Reliability : (4) not assignable
Secondary literature
13.06.2002

1.6.1 LABELLING

Labelling : as in Directive 67/548/EEC
Specific limits : yes
Symbols : F, T, ,
Nota : E, ,
R-Phrases : (45) May cause cancer
(11) Highly flammable
(22) Harmful if swallowed
(36/37/38) Irritating to eyes, respiratory system and skin
S-Phrases : (53) Avoid exposure - obtain special instructions before use
(45) In case of accident or if you feel unwell, seek medical advice immediately (show the label where possible)

Flag : Critical study for SIDS endpoint
26.01.2002

1.6.2 CLASSIFICATION

Classified : as in Directive 67/548/EEC
Class of danger : carcinogenic, category 2
R-Phrases : (45) May cause cancer

Specific limits :

Flag : Critical study for SIDS endpoint
25.01.2002

Classified : as in Directive 67/548/EEC
Class of danger : harmful
R-Phrases : (22) Harmful if swallowed
Specific limits :

Flag : Critical study for SIDS endpoint
26.01.2002

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

Flag : Critical study for SIDS endpoint
25.01.2002

Classified : as in Directive 67/548/EEC
Class of danger : irritating
R-Phrases : (36/37/38) Irritating to eyes, respiratory system and skin
Specific limits :

Flag : Critical study for SIDS endpoint
25.01.2002

1.6.3 PACKAGING

1.7 USE PATTERN

Type of use : type
Category : Use in closed system

25.01.2002

Type of use : industrial
Category : Chemical industry: used in synthesis

25.01.2002

Type of use : industrial
Category : Polymers industry

25.01.2002

Type of use : use
Category : Intermediates

25.01.2002

Type of use : use

Category : other: raw material for the production of trichloroethylene and tetrachloroethylene; extraction and cleaning solvent, lead scavenger for gasoline

25.01.2002

1.7.1 DETAILED USE PATTERN

1.7.2 METHODS OF MANUFACTURE

1.8 REGULATORY MEASURES

1.8.1 OCCUPATIONAL EXPOSURE LIMIT VALUES

Type of limit : MAC (NL)
Limit value : 1.5 ml/m3

25.01.2002 (106)

Type of limit : MEL (UK)
Limit value : 20 mg/m3

Remark : 5ppm (8hr TWA)
Skin notation (sk) listed against OEL - can be absorbed through skin.

25.01.2002

Type of limit : TLV (US)
Limit value : 40 mg/m3

25.01.2002

Type of limit : TRK (DE)
Limit value : 20 mg/m3

Remark : Classified as carcinogenic to human. Substance listed in MAK list appendix III A2.

25.01.2002

Type of limit : other: OEL-Denmark
Limit value : 4 mg/m3

Remark : Skin
25.01.2002

Type of limit : other: OEL-France
Limit value : 40 mg/m3

25.01.2002

Type of limit : other: TLV-Japan
Limit value : 10 ml/m3

25.01.2002

1.8.2 ACCEPTABLE RESIDUES LEVELS

1.8.3 WATER POLLUTION

Classified by : KBwS (DE)
Labelled by : KBwS (DE)
Class of danger : 3 (strongly water polluting)

Reliability : (1) valid without restriction
25.01.2002 (92)

1.8.4 MAJOR ACCIDENT HAZARDS

Legislation : Stoerfallverordnung (DE)
Substance listed : yes
No. in Seveso directive :

Reliability : (1) valid without restriction
25.01.2002

1.8.5 AIR POLLUTION

Classified by : TA-Luft (DE)
Labelled by : TA-Luft (DE)
Number : 3.1.7 (organic substances)
Class of danger : I

Reliability : (1) valid without restriction
25.01.2002

1.8.6 LISTINGS E.G. CHEMICAL INVENTORIES

1.9.1 DEGRADATION/TRANSFORMATION PRODUCTS

1.9.2 COMPONENTS

1.10 SOURCE OF EXPOSURE

1.11 ADDITIONAL REMARKS

1.12 LAST LITERATURE SEARCH

Type of search : External
Chapters covered : 3, 4, 5
Date of search : 17.11.2000

25.01.2002

1.13 REVIEWS

Memo : 1,2 Dichloroethane (IARC)

Remark : Update of the last data review published in 1979. The TS was classified in 1987.

Result : Human data (epidemiological studies, some cases of accidental exposure) and experimental data are reviewed and evaluated.
Experimental animal studies reviewed covered
- absorption, distribution, metabolism, excretion
- toxic effects
- genetic, reproductive and developmental effects
- carcinogenicity after oral, inhalative and dermal exposure

Brief summary of presented data and evaluation:
- Human exposure is mainly given during production of vinyl chloride. The TS is no longer registered as a fumigant. Low levels have been detected in ambient and urban air, groundwater and drinking-water.
- Human carcinogenicity was examined in 5 cohort studies and one nested case-control study. All studies included workers with exposure to multiple agents and could not examine the risk associated with 1,2-dichloroethane.
- Animal carcinogenicity was seen after oral, inhalative and dermal exposure. However, data from inhalation experiments are conflicting.
- Absorption and metabolism is given in humans and animals.
Two major metabolic pathways are identified in rat and mouse, i.e. via cytochrome P450 and via glutathione-S-transferase.
- No teratogenicity was seen in rats, rabbits or mice.
- Binding to DNA, RNA, proteins was seen. Mutagenicity in bacterial and mammalian cells was demonstrated.

Overall, there is sufficient evidence in experimental animals for the carcinogenicity of 1,2-dichloroethane.
Evidence for the carcinogenicity in humans is inadequate.
1,2-dichloroethane is possibly carcinogenic to humans and classified in Group 2B.

Conclusion : There is sufficient evidence in experimental animals for the carcinogenicity of 1,2-dichloroethane. Evidence for the carcinogenicity in humans is inadequate.
1,2-dichloroethane is possibly carcinogenic to humans (Group 2B)

Reliability : (4) not assignable
4b Secondary literature.
Reliability is deemed high since the reported experimental data were repeatedly subjected to a scientific evaluation process.

15.05.2002 (85)

Memo : Toxicological profile for 1,2-Dichloroethane (ATSDR; Draft)

Result : The monograph provides extensive peer-reviewed information on Health Effects, Mechanisms of action, Toxicokinetics, Human Exposure Data, Analytical Methods, and Regulations derived from toxicological risk assessment.

Experimental animal studies reviewed cover
- absorption, distribution, metabolism, excretion
- toxic effects including neurological and immunological effects

- genetic, reproductive and developmental effects
- carcinogenicity after oral, inhalative and dermal exposure

A chronic minimal risk level (MRL) of 0.6 ppm was calculated from the NOAEL for liver pathology in a 2-yr study with rats exposed to 50 ppm (Cheever et al., 1990). An intermediate oral MRL of 0.2 mg/kg/d was based on the LOAEL of 58 mg/kg/d for increased kidney weights in rats exposed to the TS in drinking water for 13 wk (NTP 1991).

EPA has derived an oral cancer slope factor from the NCI study (1978) which corresponds to drinking water unit risk of 2.6xE-06 per (µg/L), and an inhalation unit risk of 2.5xE-06 per (µg/m³) (page 114).

EPA has classified 1,2-dichloroethane in Group B2 (possibly carcinogenic to humans), based on the sufficient evidence for carcinogenicity in animals.

Conclusion : Sufficient evidence exists for carcinogenicity of 1,2-dichloroethane in experimental animals.
US EPA has classified 1,2-dichloroethane in Group B2, as possibly carcinogenic to humans.

Unit risk and Minimum Risk Levels for oral and inhalation exposure were calculated.

Reliability : (4) not assignable
4b Secondary literature.
Reliability is deemed high since the reported experimental data were subjected to a scientific evaluation process.

Flag : Risk Assessment
10.05.2002 (11)

Memo : 1,2-Dichloroethane (CICAD)

Result : The review summarizes animal study results and provides guidance on human health protection and emergency action in terms of International Chemical Safety Card.

Provides estimates for daily intake inhalation and oral uptake in the range of 0.123 µ/kg/d (section 6.2) and identifies air as the principal source of exposure.

It was stated that indirect exposure from the environment is approx. 300 times less those values which were derived as guidance values from animal data on the basis of a margin 5000 -50 000-fold less than the estimated carcinogenicity potency. Guidance value for air would be 3.6-20 µg/m³, and the value for ingestion would be 1.2-6.8 µg/kg/d (these values correspond to a risk of 1:10E05) It was also stated that risk might be overestimated as inhaled 1,2-dichloroethane is less potent than when ingested.

Conclusion : Sufficient evidence exists for carcinogenicity of 1,2-dichloroethane in experimental animals. US EPA has classified 1,2-dichloroethane in Group B2, as possibly carcinogenic to humans.

"Essentially negligible risk levels" for oral and inhalation exposure were compared with exposure in the general environment which was found to be up to approx. 300 times less than the guidance levels.

This margin of safety might be larger since guidance levels were derived from oral exposure studies: since the major exposure of humans is given from inhaled air, and since inhaled 1,2-dichloroethane has a lower carcinogenic potency than when ingested, risks associated with the guidance level may be overestimated.

Reliability : (4) not assignable
4b Secondary literature.
Reliability is deemed high since the reported experimental data were subjected to a scientific evaluation process.
Flag : Risk Assessment
10.05.2002 (187)

Memo : 1,2-Dichlorethan (BUA)

Reliability : (4) not assignable
Flag : Risk Assessment
16.05.2002 (1)

Memo : 1,2-Dichloroethane (SMACS)

22.05.2002 (192)

Memo : 1,2-Dichloroethane (HSE)

22.05.2002 (66)

Memo : 1,2-Dichloroethane (IPCS; EHC 176)

23.05.2002 (86)

2.1 MELTING POINT

Value : = -36 °C
Sublimation :
Method : other
Year :
GLP :
Test substance :

Source : WACKER CHEMIE GMBH, Burghausen, Germany
Reliability : (4) not assignable
Secondary Literature
Flag : Critical study for SIDS endpoint
09.08.2001 (84) (121)

Value : -35.5 °C
Sublimation :
Method :
Year :
GLP : no data
Test substance :

Source : Wacker - Chemie GmbH Burghausen
Reliability : (4) not assignable
Secondary Literature
Flag : Critical study for SIDS endpoint
27.06.2002 (57)

2.2 BOILING POINT

Value : = 82.9 °C at 1000 hPa

Source : WACKER CHEMIE GMBH, Burghausen, Germany
Reliability : (4) not assignable
Secondary Literature
09.08.2001 (139)

Value : 83.5 - 84.1 °C at 1013 hPa

Source : WACKER CHEMIE GMBH, Burghausen, Germany
Reliability : (4) not assignable
Secondary Literature
Flag : Critical study for SIDS endpoint
14.08.2001 (7) (8) (52) (70) (84) (105) (181) (185)

2.3 DENSITY

Type : density
Value : = 1.282 g/cm³ at 0 °C

Source : WACKER CHEMIE GMBH, Burghausen, Germany
Reliability : (4) not assignable
Secondary Literature
09.08.2001 (70) (139)

Type : density
Value : = 1.26 g/cm³ at 15 °C

Source : WACKER CHEMIE GMBH, Burghausen, Germany
Reliability : (4) not assignable
Secondary Literature
09.08.2001 (70)

Type : density
Value : 1.235 - 1.253 g/cm³ at 20 °C

Source : WACKER CHEMIE GMBH, Burghausen, Germany
Reliability : (4) not assignable
Secondary Literature, Handbook data
Flag : Critical study for SIDS endpoint
09.08.2001 (52) (70) (139) (185)

2.3.1 GRANULOMETRY

2.4 VAPOUR PRESSURE

Value : = 33.3 hPa at 0 °C

Source : WACKER CHEMIE GMBH, Burghausen, Germany
Reliability : (4) not assignable
Secondary Literature
Flag : Non confidential
09.08.2001 (52) (139)

Value : = 53.3 hPa at 10 °C

Source : WACKER CHEMIE GMBH, Burghausen, Germany
Reliability : (4) not assignable
Secondary Literature
Flag : Non confidential
14.08.2001 (7) (181)

Value : 85.3 - 87 hPa at 20 °C

Source : Wacker - Chemie GmbH, Burghausen, Germany
Reliability : (4) not assignable
Secondary Literature, Handbook data
Flag : Non confidential
10.05.2002 (52) (105) (139)

Value 81.3 h Pa at 20°C

Source : WACKER CHEMIE GMBH, Burghausen, Germany
Reliability : (4) not assignable
Secondary Literature/Handbook data
Flag : Critical study for SIDS endpoint
28.06.2002 (181)

Value : 105 - 116 hPa at 25 °C

Source : Wacker - Chemie GmbH, Burghausen, Germany

Reliability : (4) not assignable
Secondary Literature
Flag : non confidential
10.05.2002 (157) (170) (185)

2.5 PARTITION COEFFICIENT

Partition coefficient :
Log pow : = 1.45 at 23 °C
pH value :
Method : other (measured): LSC (liquid scintillation counting)
Year : 1980
GLP :
Test substance :

Source : Wacker - Chemie GmbH, Burghausen, Germany
Test condition : Test temperatures: 23 +/- 1.5°C.
A mixture of octanol and water was shaken for 30 min and separated by centrifugation. The 14C-labeled test compound was dissolved in the organic phase, octanol-saturated water was added. The sealed tube was equilibriated during several 5 min shaking periods and centrifuged for 30 min at 10000 rpm.
Both layers were sampled and analyzed through liquid scintillation counting. The concentration in water was far below the solubility limit.

Two test runs were made with only one concentration.
Reliability : (2) valid with restrictions
No details as to the purity of the substance used. Method applied generally accepted.
Flag : Critical study for SIDS endpoint
10.05.2002 (13)

Partition coefficient :
Log pow : = 1.45 at 20 °C
pH value :
Method : other (measured): Flask shaking method
Year : 1980
GLP :
Test substance : no data

Remark : Study was conducted in the course of an experimental determination of bioconcentration factors on fish.
Source : Wacker - Chemie GmbH, Burghausen, Germany
Test condition : Analysis of test solutions by RP-HPLC

1 mg/ml solutions of the test substance in water or octanol were equilibrated against the other solvent. After shaking the solution in closed tubes both phases were separated by centrifugation at 27000 rpm for 30 min and analyzed.
Reliability : (2) valid with restrictions
No further information as to the identity and purity of the substance measured, no details regarding conduct of study and analytical procedures. Method used generally accepted.
Flag : Critical study for SIDS endpoint
10.05.2002 (179)

Partition coefficient :
Log pow : = 1.46 at °C

pH value	:	
Method	:	other (calculated): CLOGP3 (Leo & Weininger 1984)
Year	:	1991
GLP	:	no data
Test substance	:	
Source	:	Wacker - Chemie GmbH, Burghausen, Germany
Reliability	:	(2) valid with restrictions Generally accepted method
09.08.2001		(24)
Partition coefficient	:	
Log pow	:	= 1.48 at °C
pH value	:	
Method	:	other (calculated): according to Leo et al.
Year	:	1971
GLP	:	no data
Test substance	:	
Source	:	Wacker - Chemie GmbH, Burghausen, Germany
Reliability	:	(4) not assignable Secondary literature
14.08.2001		(179)
Partition coefficient	:	
Log pow	:	= 1.48 at °C
pH value	:	
Method	:	other (measured): according to SRC PhysProp Database
Year	:	
GLP	:	no data
Test substance	:	
Source	:	Wacker - Chemie GmbH, Burghausen, Germany
Reliability	:	(4) not assignable Secondary literature
10.05.2002		(157)
Partition coefficient	:	
Log pow	:	= 1.76 at °C
pH value	:	
Method	:	other (calculated): according to Rekker
Year	:	1977
GLP	:	no data
Test substance	:	
Source	:	Wacker - Chemie GmbH, Burghausen, Germany
Reliability	:	(2) valid with restrictions accepted calculation method
09.08.2001		(78) (80) (98)

2.6.1 SOLUBILITY IN DIFFERENT MEDIA

Solubility in	:	Water
Value	:	= 8.73 g/l at 0 °C
pH value	:	
concentration	:	at °C
Temperature effects	:	
Examine different pol.	:	

pKa : at 25 °C
Description :
Stable :

Source : Wacker - Chemie GmbH, Burghausen, Germany
Reliability : (4) not assignable
Secondary literature
13.06.2002 (139)

Solubility in : Water
Value : = 9.2 g/l at 0 °C
pH value :
concentration : at °C
Temperature effects :
Examine different pol. :
pKa : at 25 °C
Description :
Stable :

Source : Wacker - Chemie GmbH, Burghausen, Germany
Reliability : (4) not assignable
Secondary literature
13.06.2002 (181)

Solubility in : Water
Value : 8.49 - 9 g/l at 20 °C
pH value :
concentration : at °C
Temperature effects :
Examine different pol. :
pKa : at 25 °C
Description :
Stable :

Source : Wacker - Chemie GmbH, Burghausen, Germany
Reliability : (4) not assignable
secondary literature/handbooks for physical-chemical parameters and manufacturer data
Flag : Critical study for SIDS endpoint
13.06.2002 (7) (52) (70) (84) (113) (139) (170) (181)

Solubility in : Water
Value : 8.95 g/l at 35 °C
pH value :
concentration : at °C
Temperature effects :
Examine different pol. :
pKa : at 25 °C
Description :
Stable :

Source : Wacker - Chemie GmbH, Burghausen, Germany
Reliability : (4) not assignable
Secondary literature
13.06.2002 (139)

Solubility in : Water
Value : 10.3 g/l at 56 °C
pH value :
concentration : at °C

Temperature effects :
Examine different pol. :
pKa : at 25 °C
Description :
Stable :

Source : Wacker Chemie GmbH, Burghausen, Germany
Reliability : (4) not assignable
Secondary literature
13.06.2002 (139)

2.6.2 SURFACE TENSION

2.7 FLASH POINT

Value : ca. 13 °C
Type : closed cup
Method : other: DIN 51755
Year : 1974
GLP : no data
Test substance :

Source : Wacker - Chemie GmbH, Burghausen, Germany
Reliability : (4) not assignable
secondary literature
Flag : Critical study for SIDS endpoint
10.05.2002 (139) (170)

Value : 18 °C
Type : open cup
Method : Directive 84/449/EEC, A.9 "Flash point"
Year : 1986
GLP : no data
Test substance :

Source : Wacker - Chemie GmbH, Burghausen, Germany
Reliability : (4) not assignable
Secondary literature
06.05.2002 (83)

2.8 AUTO FLAMMABILITY

Value : 412.6 - 440 °C at
Method : other: no data
Year : 1978
GLP : no data
Test substance :

Source : Wacker - Chemie GmbH, Burghausen, Germany
Reliability : (4) not assignable
Secondary literature
Flag : Critical study for SIDS endpoint
09.08.2001 (5) (84) (139)

2.9 FLAMMABILITY

Result : highly flammable
Method :
Year : 1991
GLP : no data
Test substance :

Source : Wacker - Chemie GmbH, Burghausen, Germany
Reliability : (4) not assignable
Secondary literature
Flag : Critical study for SIDS endpoint
24.01.2002 (83)

2.10 EXPLOSIVE PROPERTIES

Remark : upper explosive limit: 16 Vol.-% at 20°C
Source : Wacker - Chemie GmbH, Burghausen, Germany
Reliability : (4) not assignable
Secondary literature
Flag : non confidential
09.08.2001 (7) (121) (139)

Remark : lower explosive limit: 6.2 Vol.-% at 20 and 25°C
Source : Wacker - Chemie GmbH Burghausen
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Reliability : (4) not assignable
Secondary literature
Flag : non confidential
24.01.2002 (7) (121) (139)

2.11 OXIDIZING PROPERTIES

2.12 DISSOCIATION CONSTANT

2.13 VISCOSITY

2.14 ADDITIONAL REMARKS

3.1.1 PHOTODEGRADATION

Type	:	air
Light source	:	
Light spectrum	:	nm
Relative intensity	:	based on intensity of sunlight
INDIRECT PHOTOLYSIS		
Sensitizer	:	OH
Conc. of sensitizer	:	1000000 mg/l
Rate constant	:	.00000000000022 cm³/(molecule*sec)
Degradation	:	50 % after 35.6 day(s)
Deg. product	:	
Method	:	other (calculated)
Year	:	
GLP	:	
Test substance	:	
Remark	:	With a sensitizer concentration of 500 000 molecules/cm3 a half life of 73 days is calculated. In Pearson et al. (Pearson, C.R. (1982): C1 and C2 Halocarbons. In: Hutzinger, O. (ed.), The Handbook of Environmental Chemistry, Vol. 3 part B, Springer-Verlag, Berlin, 69 - 88) the half life for photochemical degradation of 1,2-dichloroethane is given with 56 days (8 weeks).
Source	:	Wacker Chemie GmbH
Reliability	:	(1) valid without restriction Accepted calculation method
Flag	:	Critical study for SIDS endpoint

14.06.2002 (46) (73) (150)

Type	:	air
Light source	:	
Light spectrum	:	nm
Relative intensity	:	based on intensity of sunlight
INDIRECT PHOTOLYSIS		
Sensitizer	:	OH
Conc. of sensitizer	:	1500000 molecule/cm³
Rate constant	:	= .000000000000255 cm³/(molecule*sec)
Degradation	:	= 50 % after 41.9 day(s)
Deg. product	:	
Method	:	other (calculated)
Year	:	2000
GLP	:	no data
Test substance	:	no data
Source	:	Wacker Chemie GmbH, Burghausen, Germany
Reliability	:	(2) valid with restrictions Well accepted calculation method
Flag	:	Critical study for SIDS endpoint

14.06.2002 (6)

Type	:	air
Light source	:	
Light spectrum	:	nm
Relative intensity	:	based on intensity of sunlight
INDIRECT PHOTOLYSIS		
Sensitizer	:	OH

Conc. of sensitizer : 300000 molecule/cm³
Rate constant : .00000000000022 cm³/(molecule*sec)
Degradation : = 50 % after 121.5 day(s)
Deg. product :
Method : other (measured): Field Observation
Year : 1985
GLP : no data
Test substance : no data

Remark : Measurement: atmosphere (location: west wind drift, atlantic ocean)
Source : Wacker - Chemie GmbH, Burghausen, Germany
Test condition : no temperature given.
Reliability : (1) valid without restriction
Flag : non confidential
14.06.2002 (46)

Type : air
Light source :
Light spectrum : nm
Relative intensity : based on intensity of sunlight
INDIRECT PHOTOLYSIS
Sensitizer : OH
Conc. of sensitizer : 3000000 molecule/cm³
Rate constant : .00000000000022 cm³/(molecule*sec)
Degradation : = 50 % after 12.2 day(s)
Deg. product :
Method : other (measured): Field Observation
Year : 1985
GLP : no data
Test substance : no data

Remark : Measurement: atmosphere (location: intertropical convergence - area with calm in the equator region between northeast- and southeast trade wind)
Source : Wacker - Chemie GmbH, Burghausen, Germany
Test condition : During the cruise of a research vessel from Capetown to the North Sea air samples of the lower troposphere were collected, covering the south-easterly tradewind system (20°S- 2°S), the intertropical convergence (2°S - 4°N), the northern tradewinds (6°N - 27°N), the subtropical high pressure area (27°N - 36°N) and the region of the westwind drift. Further samples were collected on the Bermudas and the Azores. The samples were analyzed by high-resolution gaschromatography (detection limit 4 pptv).

In the southern hemisphere, above the tradewind system and on the Bermudas no 1,2-DCE could be detected. In the northern hemisphere the concentration was in the range of 15 - 30 pptv.

From the measured pattern of chlorinated hydrocarbons in the northern and southern hemisphere follows, that only compounds with long atmosheric half-lives are subject of the interhemispheric exchange. The results are in accordance with the assumed average OH -radical concentrations of 0.3x10exp6/cm3 in the westwind belt of the north-hemisphere and 3x10exp6/cm3 in the region of the marine intertropical convergence.
Reliability : (1) valid without restriction
Flag : Critical study for SIDS endpoint
27.06.2002 (46)

Type : air
Light source :

Light spectrum	:	nm
Relative intensity	:	based on intensity of sunlight
INDIRECT PHOTOLYSIS		
Sensitizer	:	
Conc. of sensitizer	:	
Rate constant	:	= .00000000000022 cm³/(molecule*sec)
Degradation	:	% after
Deg. product	:	
Method	:	other (measured)
Year	:	1976
GLP	:	no data
Test substance	:	other TS
Result	:	From the plotted OH concentration as a function of the length of the reaction zone (equivalent to reactant inlet position) for different reactant concentrations (16 measurements) the average rate constant 22x10exp -14cm3/(molecules x s) was calculated. The estimated total error is 23 %.
Source	:	Wacker - Chemie GmbH, Burghausen, Germany
Test condition	:	Measurements were performed in a conventional discharge flow system in which OH -radicals are generated in a helium carrier gas stream by the fast reaction of H with NO2. Typical concentrations are about 10exp9-10exp11molecules/cm3 for OH and 8x10exp12-6x10exp15 for reactant molecules. The gas temperature is 296 K. Hydroxyl radicals are measured with a laser magnetic resonance spectrometer.
Test substance	:	The purity of the test substance was >99.99 % (analyzed)
Reliability	:	(1) valid without restriction
Flag	:	Critical study for SIDS endpoint

14.06.2002 (82)

3.1.2 STABILITY IN WATER

Type	:	abiotic
t1/2 pH4	:	at °C
t1/2 pH7	:	= 23 - 300 year at 15 °C
t1/2 pH9	:	at °C
t1/2 pH 7	:	= 6 - 64 year at 25 °C
Deg. product	:	
Method	:	other: Measured
Year	:	1989
GLP	:	no data
Test substance	:	no data
Result	:	Either in the presence or in the absence of Na2S the overall reaction rate was strictly of pseudo first order to the substrate concentration. The hydrolysis is accelerated by phosphate buffer and bisulfide as well. The calculated activation energies were used to extrapolate the rate constants to 15 °C, which is more typical to groundwater conditions. The smaller activation energy for the reaction with HS- gives this reaction path more importance at lower temperatures.

	Half lives in years	
	T=25°C	T=15°C
Zero buffer (extrapolated)	64	300
50 mM phosphate buffer	37	170
50 mM phosphate buffer, 1 mM total sulfide	6	23

1 mM total sulfide equals 0.51 mM HS- at 25°C and 0.43 mM HS- at 15°C

From a reference half lives in distilled water of 72 yrs(25°C) and 310 yrs (15°C) are reported.

Source : Wacker - Chemie GmbH, Burghausen, Germany
Test condition : At temperatures of 25, 37.5, 50, 62.5 and 87.5 °C the rate constants of the dehalogenation of 1,2 -dichloroethane in phosphate buffe r at pH=7 were measured in sealed ampules. Additionally the effect of the bisulfide anion HS- was measured, which is a most common nucleophile in aquatic environments containing very low oxygen concentrations
Reliability : (2) valid with restrictions
Study well documented meets generally accepted scientific principles.
Flag : Critical study for SIDS endpoint
13.06.2002 (14)

3.1.3 STABILITY IN SOIL

Type :
Radiolabel :
Concentration :
Soil temperature : °C
Soil humidity :
Soil classification :
Year :

Remark : The information on the stability and degradation of 1,2 -dichloroethane in soil is included in section 3.5 ("Biodegradation")
Source : Wacker Chemie GmbH, Burghausen, Germany.
Flag : non confidential
26.01.2002

3.2.1 MONITORING DATA

Type of measurement : background concentration
Media : air
Concentration :
Method :

Remark : The relationship between soil contaminated with volatile organic compounds and indoor air quality was examined. Measurements in the soil and indoor air were taken in 77 houses built on different types of contaminated soils.
Result : In- and outdoor concentrations:
In the Netherlands (time period: May 1984 - November 1985) the indoor and outdoor air of houses not being built on contaminated ground was investigated. The indoor concentrations in the crawl space and in the living rooms were 3400 and 2500 µg/m3 DCE, respectively. Samples of outdoor air gave concentrations of 4900 µg/m3.

A relationship of soil contamination and indoor air quality was found in seven houses.

Comparing soil concentrations:
The mean concentration of DCE in soil near reference houses was 11 mg/kg, in soil near contaminated grounds (former gaswork sites, harbor sludge dumps, general waste dumps and areas contaminated with spills from dry cleaners and garages)a concentration of 30 mg/kg was measured. Soil samples were taken at two places and two different depths.

Source : Wacker Chemie GmbH, Burghausen, Germany
Reliability : (2) valid with restrictions
Study well documented, meets generally accepted scientific principles
Flag : Critical study for SIDS endpoint
18.05.2002 (96)

Type of measurement : background concentration
Media : surface water
Concentration :
Method :

Remark : River water:
In 1986 a concentration of 8.5 µg/l dichloroethane was measured in the river Rhine near Lobith (dutch border) as the highest DCE-content in one out of 97. All other measured concentrations were < 1 µg/l. In Lek near Hagestein (at Rhine-km 940) a concentration of 4.4 µg/l DCE was measured as the highest DCE-content in one out of 50 samples. All other measured values were < 1 µg/l.
Source : Wacker Chemie GmbH, Burghausen, Germany
Reliability : (2) valid with restrictions
Study well documented, meets generally accepted scientific principles.
Flag : Critical study for SIDS endpoint
10.08.2001 (114)

Type of measurement : background concentration
Media : other: rain water
Concentration :
Method :

Remark : Rain water:
In Ulm the 1,2-dichloroethane-concentration in the air immediately before start of rain was < 0.00015 ug/l in a measurement conducted in September 1985. Rain contained 0.01 µg 1,2-dichloroethane/l (2 samples).
Source : Wacker - Chemie GmbH, Burghausen, Germany
Reliability : (2) valid with restrictions
Flag : Critical study for SIDS endpoint
25.01.2002 (47)

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

Remark : In the course of measurements performed in the United Kingdom at Southampton city, Marchwood and in a village 0.05 µg, 0.42 µg and 0.04 µg 1,2-dichloroethane/l could be determined.
Source : Wacker - Chemie GmbH, Burghausen, Germany
Reliability : (2) valid with restrictions
Flag : Critical study for SIDS endpoint
14.05.2001 (22)

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

Remark : Drinking water:
During measurements of the municipal water supply (one week/month) 6 % of 315 samples contained average 1,2-dichloroethane concentrations of 0.5 µg/l (minimum: 0.1 µg/l; maximum: 56.7 µg/l) Location: Santiago de Compostela, Spain; Time period: February until June 1987
Source : Wacker Chemie GmbH, Burghausen, Germany
Reliability : (2) valid with restrictions
Flag : Critical study for SIDS endpoint
14.05.2001 (145)

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

Remark : In bank filtrate samples of the river Rhine (pretreatment of a small proportion with about 1 mg chlorine; total chlorine consumption occurred) 1,2-dichloroethane concentrations of 0.35 µg/l were determined from November 1975 until January 1976. Ozone treated filtered raw water (2 mg/l ozone) contained 0.88 1,2-dichloroethane/l. Not chlorinated drinking water (samples taken from the river Rhine after charcoal filter purification) contained 1.32 µg/l 1,2-dichloroethane.
Source : Wacker Chemie GmbH, Burghausen, Germany
Reliability : (2) valid with restrictions
Flag : Critical study for SIDS endpoint
14.05.2001 (159)

Type of measurement : background concentration
Media : other: coastal and river waters/estuaries
Concentration :
Method :

Remark : Location Year of measurement mean concentration (µg/l)

-COASTAL WATERS AND ESTUARIES

Tees estuary (UK)	1992	0.72 - 4.02
Mersey estuary (UK)	1992	< 0.05
other estuaries (UK)	1992	< 0.05
River estuaries (UK)	1993	< 0.01 (max 0.03)
North sea, open sea(NL)	1983-84	< 0.005)
North sea coast, 9 sites	1983-84	0.05
Rhine estuary (NL)	1983-84	max. 0.647
Elbe estuary (DE)	1993	< 1
Weser estuary (DE)	1993	< 1
Seine estuary (FR)	1995	< 1

RIVER WATERS

Elbe, Schnackenburg (DE)	1981-82	< 0.15 (max .2.1)

Ruhr, km 124-46 (DE)	1983-86	0.03 (max. 0.1)
Emscher (DE)	1988-91	5.6-<5
Rhine (Bad Honnef, Kleve, Düsseldorf)	1990	< 5
Rhine, DE/NL-border	1990/93	< 0.1; max. 0.57
Rhine affluents (DE)	1987	< 5
Ijsselmeer/Maas (NL)	1990-91	max. 2
Ijsselmeer, Andijk (NL)	1991	< 2
Lekwater, Hagestein (NL)	1991	< 0.1
Rhine (NL)	1983	0.2
Rhine, Lobith (NL)	1991	0.3
Meuse, Eijsden (NL)	1992/93	1 - < 2
Meuse, Keizersveer (NL)	1993	< 2
Meuse, Tailfer (BE)	1993	0.2
Schelde, Doel (BE)	1992/93	< 0.085 - < 2
Seine river (FR)	1995	< 2

Source : Wacker Chemie GmbH, Burghausen, Germany.
Reliability : (2) valid with restrictions
Flag : Critical study for SIDS endpoint
14.08.2001 (50)

Type of measurement : background concentration
Media : other: river water and air
Concentration :
Method :

Remark : No data available concerning the location of the Japanese rivers and the specific sampling sites.
Result : In 1988 the concentration of 1,2-dichloroethane was measured in Japanese river waters.

Number of measurements: 144
Number of times detected: 66

Concentration range determined: 0.02 - 3.4 ppb (µl/m3) =
0.082 - 13.9 µg/m3

Detection limit: 0.02 ppb (= 0.082 µg/m3)
In 1988 the concentration of 1,2-dichloroethane was measured in the air of Japan.

Number of measurements 68
Number of times detected: 39

Concentration range determined: 11.3 - 550 ppt (nl/m3) =
45 - 2,200 ng/m3

Detection limit: 40 ng/m3 (10 ppb)

Source : WACKER CHEMIE GmbH, Burghausen, Germany.
Reliability : (4) not assignable
Secondary literature
25.01.2002 (44)

Type of measurement : other: background concentration
Media : air
Concentration :
Method :

Remark : The concentration of 1,2-dichloroethane in houses,outdoor and the concentration of personal exposure was measured 1998 in Japan.

in house : 0.5 µg/m³ (average; max.value: 11.5 µg/m³)
outdoors : 0.5 µg/m³ (average; max.value: 17.1 µg/m³)
personal exposure: 0.8 µg/m³ (average; max.value: 75.0 µg/m³)

Reliability : (4) not assignable
Secondary literature

26.01.2002 (124)

Type of measurement : other: background concentration/contaminated sites
Media : air
Concentration :
Method :

Remark : For December 1981 the distribution of 1,2 -dichloroethane in the northern and southern hemisphere is given as follows:

Location 1,2-dichloroethane (µg/m3)

Northern hemisphere
eastern pacific : 0.152

Southern hemisphere
eastern pacific : 0.058

Global mean : 0.103

Typical 1,2-dichloroethane concentrations in industry areas are 21 and 37 ug/m3.

Source : Wacker Chemie GmbH, Burghausen, Germany
Reliability : (2) valid with restrictions
Flag : Critical study for SIDS endpoint

10.08.2001 (151)

Type of measurement : other: emissions at production sites
Media : other: air and water
Concentration :
Method :

Remark : In 1993 about 150 t 1,2-dichloroethane were emitted into the atmosphere during production and processing in Germany by 9 production and/or processing sites. Releases into the hydrosphere were estimated to be about 4.46 t for 7 producers/processors. For 2 companies there are no data about emission into the hydrosphere.

Source : Wacker Chemie GmbH, Burghausen, Germany.
Reliability : (4) not assignable
Secondary literature

25.01.2002 (1)

Type of measurement : other:concentration at contaminated site/background concentration
Media : air
Concentration :
Method :

Remark : Concentration at contaminated site/background concentration.
Starting in April 1986 twenty-five measurements at twelve different sampling sites each have been conducted in different urban districts of the city of Hamburg for a time period of one year.

Annual mean values at all sampling sites (including industrial locations): 21.38 ug/m3;
Annual mean values without industrial locations : 12.4 ug/m3;

At one industrial site (lubricating oil refinery) peak values of 529 ug/m3 (annual mean value 119 ug/m3) were measured. In city regions with a heavy traffic load (22000 cars/d) near industrialised harbour areas, peak values of 1560 µg/m3 were measured.

Source : Wacker Chemie GmbH, Burghausen, Germany
Reliability : (2) valid with restrictions
Study well documented, meets generally accepted scientific principles.
Flag : Critical study for SIDS endpoint
11.05.2002 (40) (69)

3.2.2 FIELD STUDIES

3.3.1 TRANSPORT BETWEEN ENVIRONMENTAL COMPARTMENTS

Type : adsorption
Media : water - soil
Air : % (Fugacity Model Level I)
Water : % (Fugacity Model Level I)
Soil : % (Fugacity Model Level I)
Biota : % (Fugacity Model Level II/III)
Soil : % (Fugacity Model Level II/III)
Method : other: Calculated
Year : 1980

Remark : On the basis of the water solubility of 1,2-dichloroethane a soil adsorption coefficient Koc of 43 can be estimated indicating high mobility in soil.
Source : Wacker - Chemie GmbH, Burghausen, Germany
Reliability : (2) valid with restrictions
Acceptable calculation method
Flag : Critical study for SIDS endpoint
25.01.2002 (93)

Type : adsorption
Media : water - soil
Air : % (Fugacity Model Level I)
Water : % (Fugacity Model Level I)
Soil : % (Fugacity Model Level I)
Biota : % (Fugacity Model Level II/III)
Soil : % (Fugacity Model Level II/III)
Method : other: no data
Year : 2000

Result : Based on both the water solubility and high volatility adsorption to soil and sediments is not expected which is supported by an experimentally determined KOC-value of 33 for silt loam. The substance rapidly percolates through sandy soil.
Source : Wacker - Chemie GmbH , Burghausen, Germany
Reliability : (4) not assignable
Data were described in secondary literature.
Flag : Critical study for SIDS endpoint
08.08.2001 (2)

Type : volatility

Media : water - air
Air : % (Fugacity Model Level I)
Water : % (Fugacity Model Level I)
Soil : % (Fugacity Model Level I)
Biota : % (Fugacity Model Level II/III)
Soil : % (Fugacity Model Level II/III)
Method : other: no data
Year : 1975

Result : As indicated by the Henry´s law constant, 1-2-dichloroethane e ntering aquatic systems would be transferred to the atmosphere through volatilization. In laboratory experiments, a half-live in water of 0.5- 4 hours has been reported.
Source : Wacker - Chemie GmbH, Burghausen, Germany
Reliability : (4) not assignable
Data taken from secondary literature without access to original information to prove generation of result.
14.08.2001 (50)

3.3.2 DISTRIBUTION

Media : air - biota - sediment(s) - soil - water
Method : Calculation according Mackay, Level I
Year :

Method : Version: 2.11

Input Parameters:
Molecular Mass (g/mol): 98.96
Temperature (°C): 20
Log Kow : 1.45
Water Solubility (g/m³) 9000
Water Solubility (mol/m³): 90.9
Henry´s Law Constant (Pa*m³/mol): 95.7
Vapour Pressure (Pa) : 8700
Melting Point (°C) : -35.5

Remark : Estimated distribution of 1,2-DCE in the environment according to Mackay.
Result : Distribution of 1,2-dichloroethane in the environment based on a calculation according to Mackay, Level I:

Compartment	Concentration (percent)
air	95.03
biota	0.00
soil	0.12
sediment	0.00
water	4.84

Source : Wacker Chemie GmbH, Burghausen, Germany
Reliability : (2) valid with restrictions
Generally accepted calculation method
Flag : Critical study for SIDS endpoint
13.06.2002 (107)

Media : other: fat - air

Method : other (measurement): Gas -Phase Vial Equilibration Technique, modified
Year : 1989

Result : The partition coefficient for 1,2-dichloroethane in fat/air is 344 (37°C).
Source : Wacker - Chemie GmbH, Burghausen, Germany
Reliability : (2) valid with restrictions
Study well documented, meets generally accepted scientific principles.
Flag : Critical study for SIDS endpoint
10.08.2001 (62)

Media : other: persistence in water
Method :
Year :

Remark : As indicated by the figure of the Henry´s law constant, 1,2-dichloroethane entering aquatic systems would be transferred to the atmosphere through volatilization. In laboratory experiments, a half-life in water of 0.5– 4 hours has been reported.

In a controlled outdoor experiment the half-life for the disappearance from running river water was found to be 1.4 hours.

In light of these values a rapid disappearance of 1,2-dichloroethane by volatilization to the atmosphere from water is being expected.
Source : Wacker - Chemie GmbH, Burghausen, Germany
Reliability : (1) valid without restriction
Flag : Critical study for SIDS endpoint
14.08.2001 (50)

Media : water – air
Method : other (measurement)
Year : 1975

Result : The partition coefficient for 1,2-dichloroethane in water/air is 26.4
Source : Wacker - Chemie GmbH, Burghausen, Germany
Test condition : Temperatur: 20 Grad C
Reliability : (3) invalid
Documentation insufficient
Flag : non confidential
10.08.2001 (131)

Media : water - air
Method : other (calculation)
Year : 1977

Remark : According to Thomas (1982) 1,2-dichloroethane has to be considered readily volatile from water. Therefore, a translocation of 1,2-dichloroethane from aqueous solutions into the atmosphere is very likely to occur.
Result : The calculated Henry´s law constant is:

at 20°C: 111 Pa x m3 x mol-1
at 25°C: 96 Pa x m3 x mol-1
at 25°C: 104 Pa x m3 x mol-1
at 25°C: 124 Pa x m3 x mol-1
Source : Wacker Chemie GmbH, Burghausen, Germany
Reliability : (2) valid with restrictions
Flag : Critical study for SIDS endpoint
07.05.2002 (108) (169)

Media : water - air

Method : other (calculation): calculation according to a well established method
Year : 2001

Result : The volatility of 1,2-dichloroethane from water was calculated to be 95.7 Paxm3/mol based on a water solubility of 9,000 mg/l, a vapour pressure of 8,700 Pa and a molecular weight of 99.
Source : Wacker - Chemie GmbH, Burghausen, Germany
Reliability : (2) valid with restrictions
Calculation of the volatility from water (Henry´s Law Constant) according to a well established and accepted method.
Flag : Critical study for SIDS endpoint
31.01.2002 (107)

Media : water - air
Method : other (measurement)
Year : 1977

Result : The evaporation half life was 28,0 min, from which a partition coefficient of 0,0273 or 67 Pa x m3 x mol-1 is calculated.
Test condition : The half-lives of evaporation were measured by the concentration decrease in an open 250 ml beaker. The concentration of the stirred solution (1,0 ppm initial concentration) was measured continously with a hollow fiber mass spectrometer. The evaporation rate at 25°C was for the first 2-5 half lives of first order kinetics.
Reliability : (3) invalid
Devaluated due to the test conditions
07.05.2002 (51)

Media : water - air
Method : other (measurement)
Year : 1988

Result : Henry`s Law constants

Temp (°C)	H(Pa x m3 / mol)	COV, %
10	119	7,49
15	132	1,23
20	149	1,91
25	143	1,93
30	176	2,42

Percent coefficient of variation COV=(S.D.x100)/mean
Test condition : According to the EPICS procedure (Equilibrium Partitioning in Closed Systems) dilute solutions (10 mg/l) were filled into 4 septum bottles. A second set was prepared and analyzed on a separate day. After 16 h equilibration time, haedspace samples were analyzed by GC.
Reliability : (2) valid with restrictions
Flag : Critical study for SIDS endpoint
13.06.2002 (10)

3.4 MODE OF DEGRADATION IN ACTUAL USE

3.5 BIODEGRADATION

Type : aerobic
Inoculum : other bacteria: Strain DE 2 (from soil)

Deg. product	:	
Method	:	other: According to Stucki et al. 1981
Year	:	1981
GLP	:	no data
Test substance	:	no data
Remark	:	1,2-Dichloroethane may serve as the sole carbon source. Substrate: 494.8 mg/l 1,2-dichloroethane which can be completely consumed (growth rate: 0.08/h). Degradation product: chloride. 1,2-Dichlorethane is enzymatically degraded by strain DE 2 as follows: oxidation to unstable 1,2-dichloroethanol, decomposes spontaneously to hydrochloric acid and 2-chloroacetaldehyde which in turn is being oxidized to chloroacetate which is dehalogenated to glycolic acid.
Source	:	Wacker - Chemie GmbH, Burghausen, Germany.
Test condition	:	Temperature: 37°C, pH: 7.5, dehalogenation
Reliability	:	(2) valid with restrictions Study well documented, meets generally accepted scientific principles
Flag	:	Critical study for SIDS endpoint
10.08.2001		(162) (163)
Type	:	aerobic
Inoculum	:	other bacteria: soil and ground water
Deg. product	:	
Method	:	other: Laboratory
Year	:	1988
GLP	:	no data
Test substance	:	no data
Remark	:	After induction gram-negative bacteria of the strain Pseudomonas fluorescens (strain PFL 12) isolated from soil and water samples of a landfill (contaminated with 1,2-dichloroethane) are capable of metabolising 1,2-dichloroethane. Degradation of 100 µg dichloroethane/ml by PFL to 10 µg/ml within 24 h.
Source	:	Wacker - Chemie GmbH, Burghausen, Germany.
Test condition	:	Incubation: 24 hours in a shaker in closed bottles with a minimum-salt-medium containing glucose and yeast at 25°C.
Reliability	:	(2) valid with restrictions Acceptable study
Flag	:	Critical study for SIDS endpoint
30.01.2002		(178)
Type	:	aerobic
Inoculum	:	other: mixture synthetic seawater: wastewater
Deg. product	:	
Method	:	other: Laboratory (BOD)
Year	:	1974
GLP	:	no data
Test substance	:	no data
Result	:	Biodegradability (% Bio-Oxidation) in synthetic salt water: After 5, 10 and 15 days based on theoretical oxygen demand of 0.97 mg/mg oxygen a bio-oxidation of 7 and after 20 days of 15 % was determined. Biodegradability (% Bio-Oxidation) in fresh water (BOD dilution water): Under non-acclimated conditions, degradation rates were 0 and 18% after five and ten days, respectively. No rates were given anymore for days 15 and 20. Under acclimated conditions no degradation rates were presented.
Source	:	Wacker - Chemie GmbH, Burghausen, Germany.

Test condition	:	20 days, inoculum from natural seawater and small amounts of settled raw waste water.
Reliability	:	(3) invalid methodological deficiencies, although stated that study was conducted according to a published BOD procedure

11.05.2002 (134)

Type	:	aerobic
Inoculum	:	other bacteria: groundwater, mixture of the strains GJ 10 and DE 1
Contact time	:	
Degradation	:	= 95 (±) % after 35 day(s)
Result	:	
Deg. product	:	
Method	:	other: Laboratory (Biodegradation)
Year	:	1992
GLP	:	no data
Test substance	:	no data
Remark	:	First analysis of bacterial 1,2-dichloroethane degradation in reactor 1 was conducted 3 weeks after inoculation. A deacrease of initially 25mg/l to a few mg/l 1,2-dichloroethane was observed during a period of about 140 days. Disappearance of 1,2-dichloroethane was paralleled by consumption of oxygen, a decrease of pH, an increase of conductivity in the effluent and formation of chloride ions. A complete mineralisation of 1,2-dichloroethane was observed. A stepwise reduction of the water-temperature to 20, 15 and 10°C, respectively, did not influence degradation. In reactor 2 1,2-dichloroethane disappearance was not pursued at the beginning of the experiment because it was expected that most of the substance was adsorbed to the carrier material leaving only small amounts available for degradation. An indication of the beginning of 1,2-dichloroethane mineralisation was obtained after five weeks. A mean degradation efficiency of about 95% was observed as demonstrated by the comparison of amounts fed and effluent amounts quantfied. It was additionally shown that carrier material influenced 1,2-dichloroethane disappearance and mineralisation. An equilibrium between adsorption onto and desorption from the carrier was observed. After a bioregeneration phase (e.g. beyond day 100) most of entered 1,2-dichloroethane was biodegraded before it was adsorbed. The capability of the microorganisms to degrade 1,2-dichloroethane was sustained even after a withdrawal of the substance for three weeks.
Source	:	Wacker - Chemie GmbH, Burghausen, Germany.
Test condition	:	Use of nutrient solution. Incubation under flow-through conditions, neutral pH, temperature between 10 and 30°C, oxygen supply by H2O2. Bioreactor 1: Containing a fixed bed of sintered glass beads; reactor was run in a once-through mode. Bioreactor 1 contained a 1,2-dichloroethane contaminated groundwater medium and the additional components in tap water: ammoniumsulphate, magnesiumsulphate, sodiumsulphate and potassiumdhydrogenphosphate. Bioreactor 2: filled with granular char coal as adsorption and carrier material. Reactor was run with a recycle. Bioreactor 2 contained a groundwater medium consisting of the components 1,2-dichloroethane, ammoniumhydrogenphosphate and a yeast extract.
Reliability	:	(2) valid with restrictions Study well documented, meets generally accepted scientific principles
Flag	:	Critical study for SIDS endpoint

13.08.2001 (164)

Type	:	aerobic
Inoculum	:	other bacteria: isolated from subsurface sediments
Deg. product	:	
Method	:	other: Laboratory (Biodegradation)
Year	:	
GLP	:	no data
Test substance	:	no data
Remark	:	Enrichment of two trichloroethene consuming bacterial mix-populations (strain PM-M, SM-1, isolated from surface-near, contaminated sediment); 73 % degradation of both strains.
Source	:	Wacker Chemie GmbH, Burghausen, Germany
Test condition	:	Incubation in propane-fed continous-recycle expanded bed bioreactors for 21 days at pH 7.2 and a temperature of 22°C. Mineral salt medium, phosphate/bicarbonate buffer, for propane and methane oxidising culture mix addition of methane (5 % v/v) and/or propane (3 % v/v). 1,2-Dichloroethane concentrations: 18-23 µg/l contained in contaminated groundwater (mixed organic wastes containing 14 different toxicants)
Reliability	:	(2) valid with restrictions Study well documented, meets generally accepted scientific principles
Flag	:	Critical study for SIDS endpoint

10.08.2001 (133)

Type	:	aerobic
Inoculum	:	other bacteria: methane utilizing mixed culture enriched from soil
Contact time	:	
Degradation	:	> 90 (±) % after 20 day(s)
Result	:	
Deg. product	:	
Method	:	other: Laboratory (Microbial Degradation)
Year	:	1989
GLP	:	no data
Test substance	:	
Remark	:	Degradation of 200-300 µg 1,2-dichloroethane/l by methanotrophic culture mix. Degree of degradation refers to 1,2-dichloroethane concentration and on soil sample controls not being previously enriched with methane.
Source	:	Wacker Chemie GmbH, Burghausen, Germany.
Test condition	:	Sterile salt medium, closed bottles; temperature: 25°C. for degradation studies enrichment with bacterial consortium which uses methane as carbon and energy source. Mixture of haloethanes used in degradation studies.
Test substance	:	Purity indicated with 99%.
Reliability	:	(2) valid with restrictions Study well documented, meets generally accepted scientific principles
Flag	:	Critical study for SIDS endpoint

10.08.2001 (74)

Type	:	aerobic
Inoculum	:	domestic sewage
Concentration	:	5 mg/l related to Test substance related to
Deg. product	:	
Method	:	other: flask-screening procedure according to Bunch and Chambers (modified)
Year	:	1967
GLP	:	no data

Test substance	:	no data
Remark	:	After stepwise adaptation degradation of 63 and 53 % was observed after 28 days with 1,2-dichloroethane concentrations of 5 and 10 mg/l, respectively. Because of unsatisfactory controls this investigation has to be evaluated critically.
Source	:	Wacker Chemie GmbH, Burghausen, Germany.
Test condition	:	BOD dilution water containing 5 mg yeast/l, 5-10 mg/l of the test compound and ethanal as the solubilizing agent; a seven day static incubation at 25°C in the dark followed by three weekly subcultures.
Reliability	:	(3) invalid Methodological deficiencies

10.08.2001 (166)

Type	:	aerobic
Inoculum	:	activated sludge
Contact time	:	
Degradation	:	(±) % after
Result	:	under test conditions no biodegradation observed
Deg. product	:	
Method	:	
Year	:	1982
GLP	:	no data
Test substance	:	as prescribed by 1.1 - 1.4
Remark	:	Biodegradability tests with 1,2-dichloroethane resulted in little or no biodegradation in aerobic systems using sewage seed or activated sludge. The one river die-away test reported no degradation. The percent BOD produced in 5-10 days was 0-7%. Another investigator reported slow to moderate biodegradation activity. The extent of biodegradation is difficult to assess due to compounds' susceptibility to volatilization. No degradation occurred in an acclimated anaerobic system after 4 months incubation.
Source	:	Wacker Chemie GmbH, Burghausen, Germany.
Reliability	:	(4) not assignable Secondary literature

25.01.2002 (83)

Type	:	anaerobic
Inoculum	:	other bacteria: methanogen
Concentration	:	174 µg/l related to Test substance related to
Contact time	:	
Degradation	:	= 63 (±) % after 175 day(s)
Result	:	
Deg. product	:	
Method	:	other: Batch Experiment
Year	:	1983
GLP	:	no data
Test substance	:	no data
Result	:	After 25 weeks 63 % of the initial amount were transformed. The primary transformation product was CO2, confirming a biological mechanism. In a further continous-flow experiment only small amounts were transformed. Either the acclimation period of 16 weeks or the detention time in the column (2days) were too short.
Source	:	Wacker - Chemie GmbH, Burghausen, Germany.
Test condition	:	A batch experiment (160 ml bottles) with a methanogenic mixed culture, containing 174 µg/l 1,2-DCE from a methanolic stock solution (1,6 mg/l) with carbon-14-labeled tracer (2µCi/ml), was conducted at 35°C.

After incubation, samples were extracted at low, neutral and high pH with either pentane or methylene chloride. Other samples were bubbled with nitrogen with changing pH. The production of CO2 was confirmed with barium nitrate. By use of a stripping apparatus, equipped with CO2-traps, an adsorber, a combustion chamber and a trap with organic scintillator solution, it was possible to differentiate the volatilized compounds in the stripping gases.

Reliability : (2) valid with restrictions
Study well documented
Flag : Critical study for SIDS endpoint
08.05.2002 (26)

Type : anaerobic
Inoculum :
Deg. product :
Method : other: Laboratory investigation
Year : 1989
GLP : no data
Test substance : no data
Remark : No degradation observed after 7 days.
Source : Wacker Chemie GmbH, Burghausen, Germany.
Reliability : (3) invalid
Methodological deficiencies
10.08.2001 (189) (190)

Remark : Some evidence exists for the occurrence of slow to moderate aerobic biodegradation of EDC, especially in the presence of substances such as methane. There is less information on the occurance of anaerobic degradation, although reports have stated that it is possible. The aerobic degradation of EDC in soil was studied by Henson et al (1989). The soil used contained a consortium of 3 bacterial types which were able to aerobically degrade chlorinated ethanes, but only in the presence of methane. At an initial level of 200-300 µg/l approximately 10% of theEDC remained in the soil after 20 days incubation. Methane was the sole carbon and energy source for the degradation.
Source : Wacker Chemie GmbH, Burhausen, Germany.
Reliability : (2) valid with restrictions
Flag : non confidential
25.01.2002 (176)

3.6 BOD5, COD OR BOD5/COD RATIO

Remark : Results of the determination of the chemical oxygen demand (COD) conducted according to standard procedures for water and waste water examination showed that 1,2-dichloroethane is only minimally oxidisable by chromium -VI (silver ion mediated catalytic effect) and not oxidisable by manganese-VII. Dichromate oxidati on in the presence and absence of silverions resulted in 10 and 6.5 % of the theoretical COD, respectively. With manganese 0 % of the theoretical value was found.
Source : Wacker - Chemie GmbH, Burghausen, Germany
Reliability : (2) valid with restrictions
Conducted according to national standard methods
Flag : non confidential
10.08.2001 (88)

3.7 BIOACCUMULATION

Species	:	Lepomis macrochirus (Fish, fresh water)
Exposure period	:	14 day(s) at 16 °C
Concentration	:	95.7 µg/l
BCF	:	= 2
Elimination	:	yes
Method	:	other: Tracer Study (14C-labeled solution)
Year	:	1980
GLP	:	no data
Test substance	:	no data
Remark	:	BCF related to whole fish; t1/2 (tissue) >1-<2 days. Measured and calculated BCFs of 2 and 3.4 (logBCF = 0.3 and 0.53, respectively) have been reported. The equation log BCF = 0.76 x logP - 0.23 is proposed for the estimation of the bioconcentration factor from the partition coefficient.
Source	:	Wacker - Chemie GmbH, Burghausen, Germany.
Test condition	:	Well water was used in this test (flow through system); pH: 6.3-7.9; total hardness: 35mg/l (as CaCO3); dissolved oxygen: 5.9-8.6 mg/l Glass aquaria measuring 40 by 20 by 25 (length by with by height); test aquaria were maintained in a water bath (ambient temperature, 16+/- 1°C); water temperature was measured daily; due to the high volatility of the chemicals aeration of the aquaria water was not used; dissolved oxygen concentration was measured periodically during the study. Three populations of bluegill sunfish were maintained in the holding facilities for a minimum of 30 days prior to initiation of the test. Mean wet weights of fish were 0.37 +/- 0.18 to 0.94 +/- 0.34 and mean standard lengths ranging from 25 +/- 3mm to 32 +/- 4mm. Fish mortality was less than 3% during the acclimation period.
Reliability	:	(2) valid with restrictions Study well documented, meets generally accepted scientific principles
Flag	:	Critical study for SIDS endpoint
11.05.2002		(16) (165) (179)

Species	:	other: calculated
Exposure period	:	at °C
Concentration	:	
BCF	:	ca. 2.75
Elimination	:	
Method	:	other: calculated
Year	:	
GLP	:	
Test substance	:	
Remark	:	Bioconcentration factor estimated according to BCFWIN v2.14
Source	:	Wacker Chemie GmbH, Burghausen, Germany.
Reliability	:	(2) valid with restrictions Generally accepted calculation method
Flag	:	Critical study for SIDS endpoint
10.08.2001		(19)

3.8 ADDITIONAL REMARKS

4.1 ACUTE/PROLONGED TOXICITY TO FISH

Type	:	flow through
Species	:	Limanda limanda (Fish, marine)
Exposure period	:	96 hour(s)
Unit	:	mg/l
LC50	:	= 115
Limit test	:	
Analytical monitoring	:	yes
Method	:	other: Acute Toxicity
Year	:	1975
GLP	:	no data
Test substance	:	no data
Source	:	Wacker Chemie GmbH, Burghausen, Germany.
Test condition	:	Due to the volatility of 1,2 -dichloroethane, no artificial aeration was provided. Only oxygen available was that in the influent sea water.
Reliability	:	(2) valid with restrictions Acceptable study
Flag	:	Critical study for SIDS endpoint

04.05.2002 (131)

Type	:	flow through
Species	:	Pimephales promelas (Fish, fresh water)
Exposure period	:	96 hour(s)
Unit	:	mg/l
LC50	:	= 116
conf. lmts.	:	= 110 - 123
Limit test	:	
Analytical monitoring	:	yes
Method	:	other: Acute Toxicity
Year	:	1983
GLP	:	no data
Test substance	:	no data
Remark	:	LC50-value for 72 h and 96 h identical. LC50-values after 24 h and 48 h comparable to 72 h value: 24 h 48 h LC50 141 mg/l 118 mg/l conf.lmts. 131-153 mg/l 111-125 mg/l
Result	:	Additional LC50-values for 1,2 -dichloroethane (mg/l) in this study were determined after 24, 48 and 72 hours (95 % C.I. in parenthesis), respectively: 24 hr LC50 48hr LC50 72hr LC50 141 (131-153) 118 (111-125) 116 (110-123)
Source	:	Wacker - Chemie GmbH, Burghausen, Germany.
Test condition	:	Temperature: 25°C; pH: 6.7 - 7.6; hardness: 45 - 45.5 mg/l (as CaCO3); 10-50 fish were randomly selected to 12 exposure tanks with 5 toxicant concentrations and a control, in duplicate; Chemical analysis was achieved by gas chromatography after extraction of test solutions with n-hexane;

Reliability : (1) valid without restriction
Comprehensive study with very acceptable documentation; conduction according to national standard method
Flag : Critical study for SIDS endpoint
04.05.2002 (3) (183)

Type : flow through
Species : Pimephales promelas (Fish, fresh water)
Exposure period : 96 hour(s)
Unit : mg/l
LC50 : = 118
Limit test :
Analytical monitoring : yes
Method : other: Acute Toxicity
Year : 1983
GLP : no data
Test substance : no data
Source : Wacker - Chemie GmbH, Burghausen, Germany.
Test condition : Temperature: 25°C; pH: 7.5; hardness: 45.5 mg/l (as CaCO3); animals not fed during the test;

Five different test substance concentrations (not specified) plus one control were included;

20-25 unfed 30 d old fish were used in the test; deaths were recorded after 1, 3, 6, 12, 24, 48, 72 and 96 h.

Substance concentrations in water were measured daily by gas chromatography;
Reliability : (2) valid with restrictions
Study meeting generally accepted principles
Flag : Critical study for SIDS endpoint
27.06.2002 (180)

Type : flow through
Species : Pimephales promelas (Fish, fresh water)
Exposure period : 96 hour(s)
Unit : mg/l
LC50 : = 136
conf. lmts. : = 129 - 144
Limit test :
Analytical monitoring : yes
Method :
Year : 1979
GLP : no data
Test substance : other TS: purity 99 %
Result : The number of dead fish was nored every 24 h after beginning of the test, at which time they were also removed.
The estimated LC 50 with corresponding 95 % confidence interval was calculated using the corrected average of the analyzed tank concentrations.
Mortalities (average of the duplicated tests)

	control	53	81	185	270	560 mg/l
3h	-	-	-	-	-	49
24h	-	-	-	30	45	50
48h	-	-	2	40	48	50
72h	-	-	2	41	48	50
96h	-	-	2	41	49	50

Source : Wacker Chemie GmbH, Burghausen, Germany.

Test condition	:	Temperature 25 °C; pH = 7.41; dissolved oxygen 7.8 mg/l; Hardness 44.8 mg/l (as CaCO3) Five different test concentrations (53; 81; 185; 270; 560 mg/l) and control group, duplicate tests with all concentrations, analytical control by GLC in 24 h intervals up to 72 h. In each test 50 species, 31 d old with a measured mean weight of 0,19 g were exposed in a test vessel of 41 l.
Reliability	:	(2) valid with restrictions Study well documented meeting generally accepted principles
Flag	:	Critical study for SIDS endpoint
10.06.2002		(39)
Type	:	semistatic
Species	:	Poecilia reticulata (Fish, fresh water)
Exposure period	:	7 day(s)
Unit	:	mg/l
LC50	:	= 106
Limit test	:	
Analytical monitoring	:	no data
Method	:	
Year	:	1981
GLP	:	no data
Test substance	:	no data
Remark	:	Closed system conditions were used (test vessels loosely covered with watch glasses).
Source	:	Wacker Chemie GmbH, Burghausen, Germany.
Test condition	:	8 guppies, 2-3 month old; tests were performed in 1.5 l vessels filled with 1 l; daily renewal of test solution; hardness: 25 mg/l as CaCO3; dissolved oxygen > 5 mg/l; temperature 22+/-1°C; pH: no data solubilizing agent: acetone; ratio between succeeding concentrations was 3.2
Reliability	:	(2) valid with restrictions Study well documented, conducted according to generally accepted scientific principles
Flag	:	Critical study for SIDS endpoint
18.05.2002		(98)
Type	:	static
Species	:	Cyprinodon variegatus (Fish, estuary, marine)
Exposure period	:	96 hour(s)
Unit	:	mg/l
NOEC	:	= 130
LC50	:	> 130 - 230
Limit test	:	
Analytical monitoring	:	no
Method	:	other: acc. to US EPA 660/3-75-009: Methods for acute toxicity tests with fish, macroinvertebrates and amphibians (1975)
Year	:	1981
GLP	:	no data
Test substance	:	other TS: > 80%
Remark	:	24 h, 48 h, 72 h and 96 h LC-50-values are virtually in the same range. Concentrations used in the definitive test based on range finding test; the cited values refer to nominal concentrations;

Result : Additional LC50-values for 1,2-dichloroethane (mg/l) in this study were determined after 24, 48 and 72 hours, respectively:

24 hr LC50	48hr LC50	72hr LC50
> 130 < 230	> 130 < 230	> 130 < 230

Source : Wacker - Chemie GmbH, Burghausen, Germany.
Test condition : Unfed animals used (10 fish);14-28 d old posthatch: length 8-15 mm;

no aeration during exposure;

natural sea water: 10-31 °/00 salinity; temperature 25-31°C

Dissolved oxygen concentration was measured at the beginning of the test and daily thereafter;

pH-measurements were performed in the control and low and high concentrations at the initiation and after 96 hr of testing;
Reliability : (3) invalid
Analytical data are not sufficient
30.01.2002 (71)

Type : static
Species : Cyprinodon variegatus (Fish, estuary, marine)
Exposure period : 96 hour(s)
Unit : mg/l
NOEC : = 126
LC50 : > 126 - 226
Limit test :
Analytical monitoring : no data
Method :
Year : 1978
GLP : no data
Test substance : no data
Source : Wacker Chemie GmbH, Burghausen, Germany.
Reliability : (3) invalid
Study documentation incomplete, only raw data available.
11.09.2001 (165)

Type : static
Species : Lepomis macrochirus (Fish, fresh water)
Exposure period : 96 hour(s)
Unit : mg/l
LC50 : = 550
Limit test :
Analytical monitoring : no data
Method : other: Acute Toxicity
Year : 1975
GLP : no data
Test substance : other TS
Result : Survival after 24, 48, 72 and 96 hr:

Concentration (ppm)	Survival rate (%) after			
	24hr	48hr	72hr	96hr
1,000	20 (2h)	20	0	--
560	57	43	43	39

		420	100	100	100	100
		320	100	100	100	90

With a concentration of 1,000 ppm, all animals were found dead after an exposure time of 2 hours.

Source : Wacker - Chemie GmbH, Burghausen, Germany.
Test condition : Temperature: 23 °C, pH: 7.6- 7.9; hardness: 55 mg/l (as CaCO3).

Fish were not fed for 48 hr prior to testing; no information regarding number of fish/concentrations used; fish length: 33-75 mm; aeration of test solution if necessary;

Dissolved oxygen was metered on a daily basis, pH was noted at the end of the assay time period;

Dichloroethane concentrations were 1,000 ppm, 560 ppm, 420 ppm and 320 ppm, respectively.

Reliability : (3) invalid
Study in general well documented, but analytical data are not sufficient

30.01.2002 (49)

Type : static
Species : Lepomis macrochirus (Fish, fresh water)
Exposure period : 96 hour(s)
Unit : mg/l
LC50 : = 430
conf. lmts. : = 230 - 710
Limit test :
Analytical monitoring : no
Method : other: US EPA 660/3-75-009: Methods for acute toxicity tests with fish, macroinvertebrates and amphibians
Year : 1975
GLP : no data
Test substance : other TS: > 80 %
Result : LC50 value for 1,2-dichloroethane after 24 hr of exposure was >600mg/l;
Source : Wacker - Chemie GmbH, Burghausen, Germany.
Test condition : Temperature: 21-23 Grad C; pH: 6.5 - 7.9; hardness: 32 – 48 mg/l (as CaCO3), total alkalinity: 28-34 mg/l CaCO3.
Dissolved oxygen 7.0 -8.8 mg/l;

pH and dissolved oxygen of test solutions were measured at 0, 24, 48 and 96 hr of exposure;

10 fish, wet weight 0.32-1.2g; fish were not fed during the test; closed system conditions applied;

Test substance : In this study 64 chemicals, inorganic and organic, were tested, which were procured from those commercial sources able to provide the purest grade available. It is assumed, that the 1,2 -dichloroethane had a much higher purity than 80 %.

Reliability : (2) valid with restrictions
Study conducted acc. to national standard methods

Flag : Critical study for SIDS endpoint

14.06.2002 (41)

Type : static
Species : Lepomis macrochirus (Fish, fresh water)
Exposure period : 96 hour(s)
Unit : mg/l
LC50 : = 94

C.I.	:	= 79.7 - 110.9
Limit test	:	
Analytical monitoring	:	yes
Method	:	
Year	:	1971
GLP	:	no data
Test substance	:	no data
Remark	:	A TL50 (tolerance limit), based on the survival, is given instead of a LC50 value.
Result	:	Mortalities: 0/10; 3/10; 6/10; 8/10; 10/10 In the 2nd highest dose group adverse effects (gyrating, inverted, on side swimming) were observed after 72 h, in the highest dose group after 1 h.
Source	:	Wacker Chemie GmbH, Burghausen, Germany.
Test condition	:	Temperature 18°C; pH=7 30 mg calcium sulfate, 30 mg magnesium sulfate, 48 mg sodium bicarbonate and 2 mg potassium chloride were added per liter deionized water. The test material was dispensed into the bioassay vessels in the form of a 10.0 percent (w/w) solution in ethanol. Dissolved oxygen after 96 h 6.1-6.7 ppm. Testruns with 56, 75, 100, 135 and 180 mg/l, determined by GC, the final concentrations are the mean values for each time period, 10 fishes per testrun
Reliability	:	(2) valid with restrictions Acceptable study
Flag	:	Critical study for SIDS endpoint

13.05.2002 (143)

Type	:	Static
Species	:	Leuciscus idus melanotus (Fish, fresh water)
Exposure period	:	48 hour(s)
Unit	:	mg/l
LC0	:	= 1.3
LC50	:	= 1.8
LC100	:	= 2.4
Limit test	:	
Analytical monitoring	:	no data
Method	:	other: DIN 38412, part 15
Year	:	1983
GLP	:	no data
Test substance	:	no data
Source	:	Wacker Chemie GmbH, Burghausen, Germany.
Reliability	:	(3) invalid Documentation insufficient
Flag	:	non confidential

12.08.2001 (97)

Type	:	Static
Species	:	Leuciscus idus melanotus (Fish, fresh water)
Exposure period	:	48 hour(s)
Unit	:	mg/l
LC0	:	= 250
LC50	:	= 406
LC100	:	= 500
Limit test	:	
Analytical monitoring	:	no data
Method	:	other: DIN 38412, part 15

Year : 1976
GLP : no data
Test substance : no data

Remark : Additional LC50 and LC100 values given are 356 mg/l and 438 mg/l, respectively.
Source : Wacker - Chemie GmbH, Burghausen, Germany.
Reliability : (3) invalid
Documentation insufficient
Flag : non confidential
12.08.2001 (91)

Type : Static
Species : Menidia beryllina (Fish, estuary, marine)
Exposure period : 96 hour(s)
Unit : mg/l
LC50 : = 480
Limit test :
Analytical monitoring : no data
Method : other
Year : 1975
GLP : no data
Test substance : other TS
Result : Similar procedure as for bluegill sunfish was applied to test the toxicity of 1,2-dichloroethane on the saltwater species tidewater silversides (Menidia beryllina):

Survival after 24, 48, 72 and 96 hr:

Concentration (ppm)	Survival rate (%) after			
	24hr	48hr	72hr	96hr
560	0	--	--	--
420	50	50	50	30
320	90	90	90	90
180	100	100	100	100

Estimated LC50 after 96hr: 480 ppm;
Source : Wacker - Chemie GmbH, Burghausen, Germany
Test condition : Temperature: 20 °C; synthetic seawater; open aquaria; continuous aeration;

Fish were not fed for 48 hr prior to testing; no information regarding number of fish/concentrations used; fish length: 40-100 mm;

Dissolved oxygen was metered on a daily basis, pH was noted at the end of the assay time period;

Dichloroethane concentrations were 560 ppm, 420 ppm, 320 ppm and 180 ppm, respectively.
Reliability : (3) invalid
Documentation insufficient/methodological deficiencies
30.01.2002 (49)

Type : Static
Species : Micropterus salmoides (Fish, fresh water)

Exposure period	:	96 hour(s)
Unit	:	mg/l
LC50	:	= 66
C.I.	:	= 48.9 - 89.1
Limit test	:	
Analytical monitoring	:	yes
Method	:	
Year	:	1971
GLP	:	no data
Test substance	:	no data
Remark	:	A TL50 (tolerance limit), based on the survival, is given instead of a LC50 value.
Result	:	Mortalities: 0/10; 0/10; 5/10; 8/10; 10/10 In the two highest dose group adverse effects (gyrating swimming) were observed after 24(48) h
Source	:	Wacker Chemie GmbH, Burghausen, Germany.
Test condition	:	30 mg calcium sulfate, 30 mg magnesium sulfate, 48 mg sodium bicarbonate and 2 mg potassium chloride were added per liter deionized water. The test material was dispensed into the bioassay vessels in the form of a 10.0 percent (w/w) solution in ethanol. Dissolved oxygen after 96 h 3.9-4.2 ppm. Temperature 13°C; pH=7 Testruns with 32, 42, 56, 100 and 180 mg/l, determined by GC, the final concentrations are the mean values for each time period, 10 fishes per testrun
Reliability	:	(2) valid with restrictions Acceptable study
Flag	:	Critical study for SIDS endpoint

14.06.2002 (143)

Type	:	static
Species	:	Oncorhynchus mykiss (Fish, fresh water)
Exposure period	:	96 hour(s)
Unit	:	mg/l
LC50	:	= 336
conf. lmts.	:	= 324 - 350
Limit test	:	
Analytical monitoring	:	no data
Method	:	other: US EPA 660/3-75-009: Methods for acute toxicity tests with fish, macroinvertebrates and amphibians
Year	:	1979
GLP	:	no data
Test substance	:	other TS: DOW Chemical, Canada
Remark	:	LC50-values after 24, 48, 72 and 96 h, respectively, are all in the same range: 24 h 48 h 72 h LC50 362 340 337 conf. lmts.: 353-387 314-362 325-352
Source	:	Wacker - Chemie GmbH, Burghausen, Germany.
Test condition	:	10 fish per aquaria and concentration tested; weight: 0.39 g, length: 32.5 mm; Temperature: 12°C; pH: 7.6 - 7.8; hardness 98 - 128 mg/l (as CaCO3); animals were not fed during exposure; experimental set up without aeration

Reliability : (3) invalid
Study according to national standard, but analytical data not sufficiently reported.
30.01.2002 (18)

Type : static
Species : Oncorhynchus mykiss (Fish, fresh water)
Exposure period : 96 hour(s)
Unit : mg/l
LC50 : = 225
Limit test :
Analytical monitoring : no data
Method :
Year : 1986
GLP : no data
Test substance : no data

Source : Wacker Chemie GmbH, Burghausen, Germany.
Reliability : (3) invalid
Flag : non confidential
12.08.2001 (90) (111)

4.2 ACUTE TOXICITY TO AQUATIC INVERTEBRATES

Type : static
Species : Artemia salina (Crustacea)
Exposure period : 24 hour(s)
Unit : mg/l
EC50 : = 36.4
C.I. : = 30.6 - 43
Analytical monitoring : no data
Method : other: immobilization test
Year : 1985
GLP : no data
Test substance : other TS: > 98%
Remark : Closed system conditions were employed and test vessel was equipped with headspace; IC50-values refer to nominal concentrations.

Two different artificial seawater (ASW) solutions were used with a reduced salinity of 25 and 50 %, to perform different osmotic stress; results presented above refer to 25% ASW

In the control groups no immobilisation occurred, indicating that the salinity stress was not a major contributor to mortality. But in 25% ASW 12% of the nauplii appeared to have difficulties moulting and the synchrony of instar moults was uncertain.

Immobilised nauplii on the bottom of the flask were counted for the calculated IC50.
Result : Artificial seawater (50%): IC50 = 80 mg/l (C.I.= 69.7-90.6 mg/l).
Source : Wacker Chemie GmbH, Burghausen, Germany.
Test condition : 25 nauplii (30 h after hatching);
temperature: 19°C;
pH 8.3-8.6; dissolved oxygen: 7.3-8.7mg/l;
test vessel: 150 ml filled with 144 ml
5 concentrations tested,bracketing the results of the preliminary rangefinding test, logarithmic intervals, measurements at each concentration were performed in triplicate; solubilizing agent:

acetone (< 0.2 ml/l)

Salinity, pH and dissolved oxygen were measured at the start and completion of each experiment. No variation during the experiments.

Only minor deviations from OECD 202.

Reliability : (2) valid with restrictions
Acceptable study
Flag : Critical study for SIDS endpoint
22.05.2002 (59)

Type :
Species : Artemia salina (Crustacea)
Exposure period : 24 hour(s)
Unit : mg/l
EC50 : = 94
Analytical monitoring : no
Method : other: immobilization test
Year : 1984
GLP : no data
Test substance : no data
Remark : Closed system conditions were employed, but the investigation showed that volatilization of the material was possible; the values given refer to nominal concentrations;
confidence interval: 77.0-113.6 mg/l
Source : Wacker Chemie GmbH, Burghausen, Germany.
Test condition : 25 nauplii (30 h after hatching); temperature 19°C; pH 8.5-8.7; dissolved oxygen: 6.5-8.1 mg/l; salinity 32°/oo; 5-8 concentrations tested;
Reliability : (3) invalid
Devaluated due to the test conditions.
Flag : non confidential
30.01.2002 (58)

Type : Static
Species : Artemia salina (Crustacea)
Exposure period : 24 hour(s)
Unit : mg/l
EC50 : = 320
Analytical monitoring : no data
Method :
Year : 1974
GLP : no data
Test substance : no data
Remark : Closed system conditions were employed (test vessels loosely capped); EC50-values refer to nominal concentrations.
Source : Wacker Chemie GmbH, Burghausen, Germany.
Test condition : temperature 24.5°C; test conducted in seawater;
Reliability : (2) valid with restrictions
Study well documented, meets generally accepted scientific principles
Flag : Critical study for SIDS endpoint
12.08.2001 (134)

Type : Static
Species : Artemia salina (Crustacea)
Exposure period : 24 hour(s)
Unit : mg/l
Analytical monitoring : no data
Method :
Year : 1983
GLP : no data

Test substance	:	no data
Remark	:	No EC50 but change in growth rate has been measured.
Result	:	20 % change of growth rate at 0.25 mg/l 1,2-dichloroethane.
Source	:	Wacker Chemie GmbH, Burghausen, Germany.
Reliability	:	(3) invalid Unsuitable test system
Flag	:	non confidential

12.08.2001 (94)

Type	:	Static
Species	:	Crangon crangon (Crustacea)
Exposure period	:	24 hour(s)
Unit	:	mg/l
EC50	:	= 170
Analytical monitoring	:	no data
Method	:	
Year	:	1975
GLP	:	no data
Test substance	:	no data
Source	:	Wacker Chemie GmbH, Burghausen, Germany.
Reliability	:	(3) invalid Unsuitable test system
Flag	:	non confidential

12.08.2001 (147)

Type	:	
Species	:	Daphnia magna (Crustacea)
Exposure period	:	24 hour(s)
Unit	:	mg/l
EC50	:	= 150
Analytical monitoring	:	yes
Method	:	OECD Guide-line 202
Year	:	1994
GLP	:	no data
Test substance	:	no data
Source	:	Wacker Chemie GmbH, Burghausen, Germany.
Test condition	:	Groups of 10 daphnia (age: 6 - 24 h) were exposed to each concentration, duplicate testing. Referring to the referenced OECD-Guideline no details of the test conditions are given.
Reliability	:	(1) valid without restriction Guideline study
Flag	:	Critical study for SIDS endpoint

04.05.2002 (61)

Type	:	static
Species	:	Daphnia magna (Crustacea)
Exposure period	:	48 hour(s)
Unit	:	mg/l
EC50	:	= 160
LC50	:	= 270
Analytical monitoring	:	yes
Method	:	other: ASTM-Standard practice for conducting acute toxicity tests with fish, macroinvertebrates, and amphibians (1980)
Year	:	1983
GLP	:	no data
Test substance	:	other TS: > 95%
Remark	:	Values given above refer to unfed animals; additional EC50- and LC50-values with fed animals were 180 mg/l and 320 mg/l, respectively, after an

exposure period of 48 h.
Source : Wacker - Chemie GmbH, Burghausen, Germany.
Test condition : 5 daphnids <24h old per concentration tested; temperature: 20°C; pH: 7.1 - 7.7 and 7.0 - 7.5 for unfed and fed acute tests, respectively; hardness: 44.7 mg/l (as CaCO3); alkalinity: 41.5 mg/l (as CaCO3); dissolved oxygen concentrations: 7.9 - 9.9 mg/l and 4.1 - 8.4 mg/l for unfed and fed tests, respectively.

closed system conditions used.
Reliability : (1) valid without restriction
Study conducted acc. to national standard methods
Flag : Critical study for SIDS endpoint
14.08.2001 (142)

Type :
Species : Daphnia magna (Crustacea)
Exposure period : 24 hour(s)
Unit : mg/l
EC0 : = 385
EC50 : = 540
EC100 : = 682
conf. lmts.: : 506 - 576
Analytical monitoring : no
Method : other: DIN 38412, part 11
Year : 1982
GLP : no data
Test substance : no data
Source : Wacker - Chemie GmbH, Burghausen, Germany.
Test condition : 10 daphnids (<24h old) per test vessel; temperature: 20°C;
pH: 8; oxygen concentration >= 2 mg/l;
open system; animals remained unfed.

nominal concentrations were given;
Reliability : (3) invalid
Unsuitable test system
Flag : non confidential
12.08.2001 (38)

Type :
Species : Daphnia magna (Crustacea)
Exposure period : 24 hour(s)
Unit : mg/l
EC0 : = 67
EC50 : = 600
EC100 : = 1075
Analytical monitoring : no data
Method : other: DIN 38412, part 11
Year : 1983
GLP : no data
Test substance : no data
Source : Wacker - Chemie GmbH, Burghausen, Germany.
Test condition : pH: 8; no further details; nominal concentrations
Reliability : (3) invalid
Documentation insufficient
Flag : non confidential
25.01.2002 (97)

Type :
Species : Daphnia magna (Crustacea)
Exposure period : 48 hour(s)

Unit	:	mg/l
EC0	:	= 186
EC50	:	= 324
EC100	:	= 714
Analytical monitoring	:	no
Method	:	other: DIN 38412, part 11
Year	:	1989
GLP	:	no data
Test substance	:	no data
Remark	:	95% -C.I.: 48h: 285-368 mg/l 24h: 340-431 mg/l; Closed system conditions were employed.
Source	:	Wacker - Chemie GmbH, Burghausen, Germany.
Test condition	:	20 daphnids 6-24h old per concentration step; animals not fed during test period; temperature: 20°C; pH: 8.0 +/- 0.2; hardness: 240 mg/l (as CaCO3); closed system (test vessels with headspace);
Reliability	:	(2) valid with restrictions Study conducted acc. to national standard methods
Flag	:	Critical study for SIDS endpoint

12.08.2001 (102)

Type	:	static
Species	:	Daphnia magna (Crustacea)
Exposure period	:	24 hour(s)
Unit	:	mg/l
LC50	:	= 250
C.I. (24 hr)	:	= 190 - 320
ECLo	:	< 68
Analytical monitoring	:	no data
Method	:	other: Static Laboratory Test according to US EPA-660/3-75-009 (1975)
Year	:	1975
GLP	:	no
Test substance	:	no data
Remark	:	The same study was performed in the same test conditions with an exposure period of 48 hours LC50 (24 hours) = 250 mg/l Confidence Intervals: 190 - 320 mg/l LC50 (48 hours) = 220 mg/l Confidence Intervals: 160 - 280 mg/l
Source	:	Wacker Chemie GmbH, Burghausen, Germany.
Test condition	:	Temperature: 22°C; pH: 7; hardness: 72 mg/l (as CaCO3); no details regarding feeding of animals,15 daphnids/test, closed system. The tests were performed in 2000 ml vessels, filled with 500 ml test solution. The loss of test substance into the gas phase reduces the concentration of 250 mg/l to 220 mg/l.
Reliability	:	(2) valid with restrictions Study conducted according to a national standard method. The study is devaluated, due to the ratio of gas/liquid phase and the missing test concentrations.
Flag	:	Critical study for SIDS endpoint

18.05.2002 (104)

Type	:	semistatic
Species	:	Daphnia magna (Crustacea)
Exposure period	:	48 hour(s)
Unit	:	mg/l

EC50	:	= 155
LC50	:	= 268
Analytical monitoring	:	yes
Method	:	other: acc. to Standard practice for conducting basic acute toxicity tests with fish, macroinvertebrates, and amphibians (1979)
Year	:	1979
GLP	:	no data
Test substance	:	other TS: > 95 %
Remark	:	Values given above refer to unfed animals; additional 48 h EC50- and LC50 values determined with fed Daphnia magna were 183 mg/l and 315 mg/l, respectively. Confidence intervals: LC50 (unfed): 246-293 mg/l LC50 (fed) : 265-414 mg/l EC50 (unfed): 137-188 mg/l EC50 (fed) : 154-225 mg/l
Source	:	Wacker - Chemie GmbH, Burghausen, Germany.
Test condition	:	25 daphnids < 24 hrs old; Temperature: 20°C; total hardness: 44.5 mg/l (as CaCO3); 16h light/8h dark; closed system conditions were used.
Reliability	:	(1) valid without restriction Study conducted acc. to national standard methods
Flag	:	Critical study for SIDS endpoint

25.01.2002 (3) (42)

Type	:	
Species	:	Daphnia magna (Crustacea)
Exposure period	:	24 hour(s)
Unit	:	mg/l
LC0	:	= 850
LC50	:	= 1350
LC100	:	= 1820
Analytical monitoring	:	no
Method	:	other: immobilization test acc. to Bringmann & Kühn
Year	:	1977
GLP	:	no data
Test substance	:	no data
Remark	:	Figures given express LC50-values. No EC50-values stated.
Source	:	Wacker - Chemie GmbH, Burghausen, Germany.
Test condition	:	10 daphnids =< 24h old per vessel; temperature: 21°C; pH: 7.6 - 7.7; hardness: 284 mg/l (as CaCO3); test system slightly covered; no details regarding feeding of animals
Reliability	:	(3) invalid Unsuitable test system
Flag	:	non confidential

25.01.2002 (31)

Type	:	static
Species	:	Gammarus fasciatus (Crustacea)
Exposure period	:	96 hour(s)
Unit	:	mg/l
EC50	:	> 100
Analytical monitoring	:	no data
Method	:	

Year : 1986
GLP : no data
Test substance : no data
Source : Wacker Chemie GmbH, Burghausen, Germany.
Reliability : (3) invalid
Insufficient documentation
Flag : non confidential
12.08.2001 (111)

Type :
Species : Mysidopsis bahia (Crustacea)
Exposure period : 96 hour(s)
Unit : mg/l
NOEC : = 75.1
EC50 : = 113
Analytical monitoring : no data
Method : other: no data
Year : 1978
GLP : no data
Test substance : no data
Remark : Following LC50-values are available:

LC50	1,2-dichloroethane (mg/l)	95 % confidence interval
24 h	108	102 - 112
48 h	110	105 - 113
72 h	112	108 - 115
96 h	113*	109 - 115

* In a static procedure identical 96 h LC50-values have been given by the US EPA (no further details).

Source : Wacker - Chemie GmbH, Burghausen, Germany.
Reliability : (3) invalid
Study documentation incomplete, only raw data available
25.01.2002 (165) (177)

Type : static
Species : other: Eliminius modestus
Exposure period : 48 hour(s)
Unit : mg/l
LC50 : = 186
Analytical monitoring : no data
Method :
Year : 1975
GLP : no data
Test substance : no data
Source : Wacker Chemie GmbH, Burghausen, Germany.
Test condition : 20 nauplii per 100 ml; glass stoppered bottles; clean seawater;
Reliability : (2) valid with restrictions
Acceptable study
Flag : Critical study for SIDS endpoint
12.08.2001 (131)

4.3 TOXICITY TO AQUATIC PLANTS E.G. ALGAE

Species	:	Haematococcus pluvialis (Algae)
Endpoint	:	other: change in photosynthetic oxygen production
Exposure period	:	24 hour(s)
Unit	:	mg/l
EC10	:	= 500
EC50	:	> 1000
Limit test	:	
Analytical monitoring	:	no data
Method	:	other: DIN 38412, part 12
Year	:	1982
GLP	:	no data
Test substance	:	no data
Remark	:	Incubation conditions: An algae culture tube is being entirely filled with solution under exclusion of air and algae were exposed for 24 h. Temperature: 20°C; pH: 7; tempered light and dark incubator, respectively.
Source	:	Wacker - Chemie GmbH, Burghausen, Germany.
Reliability	:	(2) valid with restrictions Acceptable study
Flag	:	non confidential

25.01.2002 (100)

Species	:	Haematococcus pluvialis (Algae)
Endpoint	:	other: inhibition of oxygen production
Exposure period	:	
Unit	:	mg/l
EC50	:	= 130
Limit test	:	
Analytical monitoring	:	no data
Method	:	other: acc. to von Tümpling (1972)
Year	:	1983
GLP	:	no data
Test substance	:	no data
Source	:	Wacker Chemie GmbH, Burghausen, Germany.
Reliability	:	(3) invalid Documentation insufficient
Flag	:	non confidential

12.08.2001 (97) (182)

Species	:	Microcystis aeruginosa (Algae, blue, cyanobacteria)
Endpoint	:	growth rate
Exposure period	:	8 day(s)
Unit	:	mg/l
LOEC	:	= 105
TT	:	= 105
Limit test	:	
Analytical monitoring	:	no
Method	:	other: Cell multiplication inhibition Test
Year	:	1975
GLP	:	no data
Test substance	:	no data
Remark	:	Endpoint measured: TT (Toxicity Threshold) = EC3; Closed system conditions were employed (test vessels with headspace).
Source	:	Wacker - Chemie GmbH, Burghausen, Germany.
Test condition	:	Temperature: 27°C; pH: 7; conducti on in closed system under permanent lighting conditions; substance dissolved in bidest. water.

Reliability : (3) invalid
It is not confirmed, that the test results are based on an exponential growth rate.
Flag : non confidential
23.06.2002 (28) (33) (34)

Species : Phaeodactylum tricornutum (Algae)
Endpoint : other: primary productivity
Exposure period :
Unit : mg/l
EC50 : = 340
Limit test :
Analytical monitoring : no data
Method :
Year : 1975
GLP : no data
Test substance : no data
Remark : Measured parameter were changes in the uptake of carbon, from atmospheric carbon dioxide, during photosynthesis.
Source : Wacker Chemie GmbH, Burghausen, Germany.
Reliability : (3) invalid
Insuffi cient analytical data.
Flag : non confidential
30.01.2002 (131)

Species : Scenedesmus subspicatus (Algae)
Endpoint : growth rate
Exposure period : 7 day(s)
Unit : mg/l
TT : = 412
Limit test :
Analytical monitoring : no data
Method : other: Cell Inhibition Test
Year : 1982
GLP : no data
Test substance : no data
Remark : Exposure set up: flask closed with metal caps.

TT (toxic threshold) measurement: 1,2-dichloroethane (3% inhibition with respect to weight in substance). Effective concentration in stock solution (nominal: 1005 mg/l) was 41% resulting in a corrected TT of 412 mg/l 1,2-dichloroethane.
Source : Wacker - Chemie GmbH, Burghausen, Germany.
Reliability : (4) not assignable
Secondary literature
Flag : non confidential
30.01.2002 (171)

Species : Scenedesmus subspicatus (Algae)
Endpoint : growth rate
Exposure period : 8 day(s)
Unit : mg/l
LOEC : = 710
TT : = 710
Limit test :
Analytical monitoring : no
Method : other: Cell Multiplication Inhibition Test acc. to Bringmann
Year : 1977
GLP : no data
Test substance : no data

Remark	:	TT = Toxicity Threshold (EC3) Closed system conditions were employed (test vessels with headspace).
Source	:	Wacker - Chemie GmbH, Burghausen, Germany.
Test condition	:	Temperature: 27°C, pH: 7; dissolution of substance in bidistilled water; exposure in a closed system. From the test substance a dilution series (15 samples) by factor 2 is prepared. To 40 ml of each dilution 5 ml standard suspension of algae and 5 ml of a salt solution (containing per litre 248 mg $NaNO_3$, 19,5 mg $KHPO_4$, 750 mg $MgSO_4$, 360 mg $CaCl_2$, 30 mg citric acid, 30 mg Fe(III)-citrate, 100 mg Disodium salt of ethylenediaminotetraacetic acid, traces of metal salts) are added. From each dilution 3 samples of 10 ml are exposed to artificial light for 8 days. Comparing the extinction (Hg 578 nm) with the controls the concentration having a decrease of 3 % extinction at the end of the test is interpolated.
Reliability	:	(3) invalid It is not confirmed, that the test results are based on an exponential growth rate.
Flag	:	non confidential
23.06.2002		(32) (33) (34) (35) (36)

Species	:	Scenedesmus subspicatus (Algae)
Endpoint	:	growth rate
Exposure period	:	72 hour(s)
Unit	:	mg/l
EC50	:	= 189
Limit test	:	
Analytical monitoring	:	yes
Method	:	other: OECD Guide-line 201, modified
Year	:	1981
GLP	:	no data
Test substance	:	no data
Remark	:	Aeration with CO_2 enriched air prior to the experiment and variation of the air-space of the closed test containers were optimized in such a way that growth of the algae in the closed containers was equal to the growth in the open test vials; Closed system conditions were employed.
Source	:	Wacker Chemie GmbH, Burghausen, Germany.
Reliability	:	(1) valid without restriction Similar to guideline study
Flag	:	Critical study for SIDS endpoint
12.08.2001		(61)

Species	:	Scenedesmus subspicatus (Algae)
Endpoint	:	growth rate
Exposure period	:	96 hour(s)
Unit	:	mg/l
EC50	:	= 213
Method	:	
Year	:	1995
GLP	:	no data
Test substance	:	other TS: >= 98%
Result	:	In all testruns no further growth was observed after 72 h. In the testruns, where the vessels had not to be opened for concentration measurements, the growth curves were better reproducible (six parallels) and the EC50-values (5 chemicals were tested) were 63%-94% lower. The EC50 for EDC was in these testruns 166 mg/l. The possibility of an additional inhibition effect due to decreasing CO_2-concentration is not discussed.

From the authors an EC 50 of 189 mg/l has been published previously (Freitag et al. 1994).

Test condition : The test was performed in 500 ml vessels according to OECD 201. Increasing concentrations of the test substance by factor 1,4 covered the range from 0 to 100 % survival of alga. Prior to test begin the flasks were aerated with air containing 3 % CO2. The flasks were closed with a screw cap.

The initial concentration of the EDC was measured by GC, the final concentration was not determined.

In a second testrun the srew caps were connected to cuvettes. Alga concentrations were measured by turning the whole test equipment upside down into the spectrophotometer.

Alga concentrations were measured in an interval of 24 h.

Test substance : Purity 98% or higher
Reliability : (2) valid with restrictions
Guideline study with modification
Flag : Critical study for SIDS endpoint
23.06.2002 (20)

Species : Skeletonema costatum (Algae)
Endpoint : growth rate
Exposure period : 96 hour(s)
Unit : mg/l
EC50 : > 433
Limit test :
Analytical monitoring : no data
Method : other: no data
Year :
GLP : no data
Test substance : no data
Remark : No different EC50 values are given for 24, 48, 72 and 96 h exposure, respectively.
Source : Wacker - Chemie GmbH, Burghaus en, Germany.
Reliability : (3) invalid
Study documentation incomplete, only raw data available
Flag : non confidential
25.01.2002 (165)

4.4 TOXICITY TO MICROORGANISMS E.G. BACTERIA

Type : aquatic
Species : Entosiphon sulcatum (Protozoa)
Exposure period : 72 hour(s)
Unit : mg/l
TT : = 1127
Analytical monitoring : no
Method : other: Cell Multiplication Inhibition Assay according to Bringmann & Kuehn
Year : 1977
GLP : no data
Test substance : no data
Remark : Growth parameter: cell number
TT (toxicity threshold) = EC5

Investigations by Bringmann et al. (Gas -Wasserfach, Wasser-Abwasser 122, 308 - 313) in Uronema parduczi Chatton-Lwoff und Chilomonas

paramaecium Ehrenberg under conditions as described above yielded toxicity threshold concentrations of 1,050 and 943 mg/l, respectively.

Source : Wacker - Chemie GmbH, Burghausen, Germany.
Test condition : Temperature: 25°C; pH: 6.9; use of bidistilled water; closed system conditions employed (test vessels with headspace);
Reliability : (2) valid with restrictions
Acceptable study
Flag : Critical study for SIDS endpoint
25.01.2002 (29) (36) (37)

Type : aquatic
Species : Photobacterium phosphoreum (Bacteria)
Exposure period : 5 minute(s)
Unit : mg/l
EC50 : = 158
Analytical monitoring : no
Method : other: Microtox-Test
Year : 1982
GLP : no data
Test substance : no data
Remark : Measurement of degree of toxicity: decrease in intensity of luminescence
Source : Wacker - Chemie GmbH, Burghausen, Germany.
Reliability : (3) invalid
Unsuitable test system
Flag : non confidential
12.08.2001 (136)

Type : aquatic
Species : Photobacterium phosphoreum (Bacteria)
Exposure period : 15 minute(s)
Unit : mg/l
EC50 : = 1000
Analytical monitoring : no data
Method : other: Microtox-Test
Year : 1985
GLP : no data
Test substance : no data
Remark : Measurement of reduction of luminescence;
Source : Wacker - Chemie GmbH, Burghausen, Germany.
Reliability : (3) invalid
Unsuitable test system
Flag : non confidential
12.08.2001 (79)

Type : aquatic
Species : Pseudomonas putida (Bacteria)
Exposure period : 16 hour(s)
Unit : mg/l
TT : = 135
Analytical monitoring : no
Method : other: Cell Multiplication Inhibition Assay acc. to Bringmann
Year : 1976
GLP : no data
Test substance : no data

Remark : TT = Toxicity threshold
(TT: 3% inhibition as compared to controls)
Growth parameter: turbidity of culture
Source : Wacker - Chemie GmbH, Burghausen, Germany.
Test condition : Temperature: 25°C, pH: 7; closed system; substance has been dissolved in

bidistilled water.

From the test substance a dilution series (15 samples, 100 ml) by factor 2 is prepared. Comparing the extinction (Hg 436 nm) with the controls the concentration having a decrease of 3 % extinction is interpolated.

Reliability : (2) valid with restrictions
Acceptable study
Flag : Critical study for SIDS endpoint
20.05.2002 (30) (32) (36)

Type : aquatic
Species : Pseudomonas putida (Bacteria)
Exposure period : 18 hour(s)
Unit : mg/l
EC10 : = 583
Analytical monitoring : no data
Method : other: Cell Multiplication Inhibition Assay according to Bringmann & Kuehn
Year : 1977
GLP : no data
Test substance : no data
Remark : Measured concentration in the stock solution was 7 % of originally weighed in substance. Concerning controls (no 1,2 -dichloroethane added) a EC10 value of about 60mg/l 1,2-dichloroethane was determined.
Source : Wacker - Chemie GmbH, Burghausen, Germany.
Test condition : Temperature: 25°C; air impermeable closed containers were used.
Reliability : (4) not assignable
Literature not available
Flag : non confidential
05.05.2002 (171)

Type : Aquatic
Species : Pseudomonas putida (Bacteria)
Exposure period : 30 minute(s)
Unit : mg/l
TT : = 5300
Analytical monitoring : no data
Method : other: O2-Consumption Test according to Robra
Year : 1976
GLP : no data
Test substance : no data
Remark : TT: Toxicity threshold; measured parameter: concentration leading to 10 % inhibition when compared to concurrent controls.

Incubation time was 30 min. and toxicity assessed by increase in cell denstity.
Source : Wacker Chemie GmbH, Burghausen, Germany.
Reliability : (4) not assignable
Literature partly not available
Flag : non confidential
10.09.2001 (128) (144)

Type : aquatic
Species : other bacteria: Laboratory activated sludge/synthetic sewage
Exposure period : 24 hour(s)
Unit : mg/l
IC50 : = 2780
Analytical monitoring : no data
Method : other: serum bottle test according to Blum (1989)
Year : 1989
GLP : no data

Test substance	:	no data
Remark	:	Measured parameter: cumulative oxygen demand over 24 h; IC50 defined as concentration leading to a consumption of 50 % oxygen as compared to controls. Value given is corrected for loss to vapor phase using Henry's law constant;
Source	:	Wacker Chemie GmbH, Burghausen, Germany.
Reliability	:	(2) valid with restrictions Study well documented, meets generally accepted scientific principles
Flag	:	Critical study for SIDS endpoint

12.08.2001 (168)

Type	:	Aquatic
Species	:	other bacteria: Microorganisms, laboratory sewage sludge
Exposure period	:	4 day(s)
Unit	:	mg/l
EC50	:	= 50
Method	:	other: Anaerobic Toxicity Assay
Year	:	1980
GLP	:	no data
Test substance	:	no data
Remark	:	Two procedures were employed: batch assay using the ATA (Anaerobic Toxicity Assay) and the semicontinuous operation. Tha ATA procedure delivers information within 5 to 10 days while the semicontinuous operation requires an equilibration period resulting in information gathering not until after 60 days. A comparison of the two methods was made to examine the suitability for the assessment of anaerobic toxicity. Reactors were operated for at least 7 days in the absence of substance to achieve stable and reproducible performance.
Result	:	Batch results: 2.5 and 5 mg 1,2-dichloroethane/l, respectively, cause a small inhibition; within 10 days acclimatisation of microorganisms occurs. It was shown that using this experimental set up substance mediated stress (i.e. anaerobic toxicity) to the organisms started with concentrations in a range of 20 - 100 mg/l. A 50% retardation of total gas production was observed after 3 ½ days with 50 mg/l (intrapolated). The same holds true after 11 1/2 days. Semicontinuous digester performance: 1,2-Dichloroethane caused a significant retardation in the performance of the microorganisms already at 8 mg/l with partial recovery of the digester after 30 days. Control performance was not achieved after recovery. Significant retardation of performance was demonstrated after 5 or 6 days at 32 mg/l. After 22 days practically no performance was evident at that concentration. After a 60 days operation period the EC50 value for semicontinuous digester performance can be extrapolated to be less than 8 mg/l. 1,2-Dichloroethane induced stress to the organisms starts with 5 to 7.5 mg/l.
Source	:	Wacker - Chemie GmbH, Burghausen, Germany.
Test condition	:	Incubation at 35°C; batch-trial, nutrient and buffer solution; substrate: ethanol
Reliability	:	(2) valid with restrictions Study well documented
Flag	:	Critical study for SIDS endpoint

25.01.2002 (161)

4.5.1 CHRONIC TOXICITY TO FISH

Species	:	Oncorhynchus kisutch (Fish, fresh water, marine)
Endpoint	:	other: hatching
Exposure period	:	21 day(s)
Unit	:	mg/l
LOEC	:	= 56
LC100	:	= 320
Analytical monitoring	:	yes
Method	:	
Year	:	1982
GLP	:	no data
Test substance	:	no data
Source	:	Wacker Chemie GmbH, Burghausen, Germany.
Test condition	:	50 eyed coho eggs; temperature: 3°C; pH not adjusted; solution unaerated; solution changed daily; actual concentrations measured over the first 24 h period; concentrations tested: 56, 150, 320 and 560 mg/l;
Reliability	:	(2) valid with restrictions Study well documented, meets generally accepted scientific principles
Flag	:	Critical study for SIDS endpoint

12.08.2001 (140)

Species	:	Oncorhynchus mykiss (Fish, fresh water)
Endpoint	:	other: survival and hatching
Exposure period	:	27 day(s)
Unit	:	mg/l
NOEC	:	= .2
LC50	:	= 34
Analytical monitoring	:	yes
Method	:	
Year	:	1982
GLP	:	no data
Test substance	:	no data
Remark	:	The effect values found by Black et al. for several substances are usually very low compared to effect values by other authors. No explanation for these large discrepancies could be found. A careful examination of the entire information provided by Black et al. gave no plausible reason for the inconsistency of the data. However, as it was not possible to reproduce the effect values found by Black and his co-workers, it is proposed not to use these data for a derivation of a PNECaqua if other valid fish early life stage tests are available.
Source	:	Wacker Chemie GmbH, Burghausen, Germany.
-Test condition	:	Tests were conducted using a flow through system, the toxicant level was regulated by adjusting the mixing ratios between the pumping units for toxicant solution and dilution water. Flow rate was 200 ml/h for the 500 ml test chamber. Exposure concentrations, 6 concentrations ranging from 0,002 to 34,1 mg/l, were confirmed by daily analyses directly from the test water, using gas - liquid chromatography. Temperature: 13°C; dissolved oxygen: 9,5 mg/l: hardness: 93,9 mg/l as CaCO3; pH = 7. Exposure was initiated within 30 min fertilization, average hatching time was 23 days. Eggs were examined daily to gauge extent uf development and to remove dead specimens. Sample size ranged from 50 to 125 eggs per exposure

chamber.

Percent survival was expressed as the frequency in experimental populations/controls and was determined at hatching and 4 days after.

Reliability : (2) valid
Flag : non confidential
27.06.2002 (23)

Species : Pimephales promelas (Fish, fresh water)
Endpoint : other: survival rate
Exposure period : 32 day(s)
Unit : mg/l
NOEC : = 29
LOEC : = 59
Analytical monitoring : yes
Method : other: Early Life Stage Test (ELS-Test)
Year : 1984
GLP : no data
Test substance : other TS: 98-99 %
Remark : Survivalrate after exposure towards 59 mg/l 1,2-dichloroethane under aerated conditions was 90 % (controls: 92 %) but not considered to be statistically significant.

Flow-through conditions were employed in this study.

Source : Wacker - Chemie GmbH, Burghausen, Germany.
Test condition : Eggs of 24 h age; use of unfiltered sea-water; temperature: 25 +/- 1°C; pH: 7.4; dissolved oxygen content: 7.0 mg/l, hardness: 45 mg/l (as CaCO3); alkalinity: 42 mg/l (as CaCO3); acidity: 3 mg/l (as CaCO3); flow through conditions.
Reliability : (1) valid without restriction
Guideline concurring study
Flag : Critical study for SIDS endpoint
30.01.2002 (3)

Species : Pimephales promelas (Fish, fresh water)
Endpoint : weight of young fish
Exposure period : 32 day(s)
Unit : mg/l
MATC : 29 - 59
Analytical monitoring : yes
Method : other: acc. to methods intended to be incorporated in test standards of US EPA and ASTM
Year : 1982
GLP : no data
Test substance : other TS: 98-99 %
Remark : MATC = maximum-acceptable-toxicant-concentration; refers to reduced larval weight since larval growth is considered the most sensitive parameter.

Average weight was significantly (p = 0.05) reduced as compared to controls. Related to wet-weight the estimated MATC-value was betwen 29 and 59 mg/l 1,2-dichloroethane, respectively.

Exposure periods differed and were 28 (Benoit et al.) and 32 days (Ahmad et al.), respectively.

Source : Wacker - Chemie GmbH, Burghausen, Germany.
Test condition : Early Life Stage-Test (ELS-Test) conducted with 30 embryos at the age of 2 to 8 hours after spawning. Tests were run with four replicates/test concentration.

Water temperature: 25 +/- 1°C;
Water hardness: 45 mg/l CaCO3;
Mean dissolved oxygen concentration: 7 mg/l;
Mean pH. 7.4;
Flow through conditions;

Test solution were measured for their respective chemical concentrations twice a week;

Test concentration range for 1,2-dichloroethane:
4, 7, 14, 29 and 59 mg/l

Reliability : (1) valid without restriction
Guideline concurring study
Flag : Critical study for SIDS endpoint
13.08.2001 (3) (21)

4.5.2 CHRONIC TOXICITY TO AQUATIC INVERTEBRATES

Species	:	Daphnia magna (Crustacea)
Endpoint	:	reproduction rate
Exposure period	:	28 day(s)
Unit	:	mg/l
NOEC	:	= 11
LOEC	:	= 21
Analytical monitoring	:	yes
Method	:	other: acc. to ASTM-Proposed standard practice for conducting static renewal life cycle toxicity tests with daphnid, Daphnia magna (1979)
Year	:	1983
GLP	:	no data
Test substance	:	other TS: 98-99%
Remark	:	NOEC for reproduction : 11 +/- 0.8 mg/l NOEC for growth : 42 +/- 2.4 mg/l LOEC for reproduction : 21 +/- 1.7 mg/l (p = 0.05) LOEC for growth : 72 +/- 4.8 mg/l (p = 0.01)
Source	:	Wacker - Chemie GmbH, Burghausen, Burghausen.
Test condition	:	Temperature: 20 +/- 1°C; pH: 7.1 - 7.5; hardness: 44mg/l (as CaCO3); conduction under closed, semistatic conditions; feeding of animals included. First instar daphnids (< 24 ours old) were collected from brood animals of approximately 3 weeks of age.
Reliability	:	(1) valid without restriction Study conducted acc. to. national standard methods
Flag	:	Critical study for SIDS endpoint

10.09.2001 (3) (42) (142)

4.6.1 TOXICITY TO SEDIMENT DWELLING ORGANISMS

4.6.2 TOXICITY TO TERRESTRIAL PLANTS

4.6.3 TOXICITY TO SOIL DWELLING ORGANISMS

Type	:	filter paper
Species	:	Eisenia fetida (Worm (Annelida), soil dwelling)

Endpoint	:	mortality
Exposure period	:	48 hour(s)
Unit	:	other: µg/cm2
LC50	:	= 60
Method	:	other: EEC79/831, Rev. 3: The contact and artificial soil test
Year	:	1982
GLP	:	no data
Test substance	:	other TS: Aldrich Chemical Co., USA
Remark	:	0.060 mg 1,2-dichloroethane/cm2 taken up via the skin proved to be toxic. No further details regarding skin changes given. 95 % Confidence Interval: 54 - 68 µg/cm2. The method applied is defined as the "contact test".
Source	:	Wacker - Chemie GmbH, Burghausen, Germany.
Test condition	:	Temperature: 20°C; weight of earth-worms: 300 - 500 mg; exposure of animals in the dark; exposure by means of filter paper
Reliability	:	(1) valid without restriction Guideline study
Flag	:	Critical study for SIDS endpoint

13.08.2001 (126) (127)

4.6.4 TOX. TO OTHER NON MAMM. TERR. SPECIES

4.7 BIOLOGICAL EFFECTS MONITORING

4.8 BIOTRANSFORMATION AND KINETICS

4.9 ADDITIONAL REMARKS

5.0 TOXICOKINETICS, METABOLISM AND DISTRIBUTION

5.1.1 ACUTE ORAL TOXICITY

Type	:	LD50
Value	:	= 967 mg/kg bw
Species	:	rat
Strain	:	other: Carworth-Wistar
Sex	:	male
Number of animals	:	5
Vehicle	:	
Doses	:	
Method	:	
Year	:	1969
GLP	:	no
Test substance	:	no data
Remark	:	LD50 = 0.77 ml/kg (= 967 mg/kg bw.): Study dated 1969. Confidence interval: 0.67-0.89 ml/kg (= 838-1113 mg/kg bw) Based upon mortalities during a 14-day observation period, the most probable LD50 value and its fiducial range were estimated by the method of Thompson using the tables of Weil (Experimental data from Smyth et al., 1962). Based upon mortalities during a 14-day observation period, the most probable LD50 value and its fiducial range are estimated by the method of Thompson using the tables of Weil (Experimental data from Smyth et al. 1962).
Source	:	Wacker Chemie GmbH, Burghausen, Germany.
Reliability	:	(2) valid with restrictions
Flag	:	Critical study for SIDS endpoint

24.06.2002 (153)

Type	:	other
Value	:	770 mg/kg bw
Species	:	rat
Strain	:	other: albino
Sex	:	male
Number of animals	:	10
Vehicle	:	other: corn oil
Doses	:	500, 630, 795, and 1000 mg/kg as 1-% solution (at 500 mg/kg) and 10-% solution (other doses)
Method	:	
Year	:	1948
GLP	:	no
Test substance	:	no data
Method	:	Gavage study, 10 animals per dose.
Result	:	Calculated LD50 by the method of Thompson is 770 mg/kg bw (667 - 889 mg/kg bw). Mortality observed: 0/10 animals at 500 mg/kg, 3/10 at 630 mg/kg bw after 1 to 5 days, 5/10 at 795 mg/kg after 1 day and 8/10 at 1000 mg/kg bw after 2 to 3 days. Note: Steep dose-response relationship! The gross pathology noted at autopsy included congestion of the lungs,

pale kidney and livers, and injection of blood vessels in the intestines. Deaths occurred within 24 h to 3d after dosing, in one case after 5 d.

Source : Wacker Chemie GmbH, Burghausen, Germany.
Reliability : (2) valid with restrictions
Comparative study, screening test, basic data given, based on scientific principles, results conclusive.
Flag : Critical study for SIDS endpoint
24.06.2002 (115)

Type : other
Value : = 625 mg/kg bw
Species : rat
Strain : Sprague-Dawley
Sex :
Number of animals :
Vehicle : petrolatum
Doses :
Method :
Year :
GLP : no data
Test substance : no data
Remark : Rats received 625 mg/kg bw as a single dose (maximal tolerated dose). Rats were killed 18 h after application. The investigation was focused on the hepatotoxic effects of 1,2-dichloroethane. Objective was not the determination of an oral LD50 value.

Decreased levels of hepatic aminolaevulinic acid dehydratase activity, porphyrin content, cytochrome P-450 and reduced glutathione 18 hrs after exposure were reported.
Reliability : (2) valid with restrictions
Flag : Critical study for SIDS endpoint
24.06.2002 (117)

Type : LD50
Value : = 413 - 489 mg/kg bw
Species : mouse
Strain : other: CD-1 (6 weeks old)
Sex : male/female
Number of animals :
Vehicle :
Doses :
Method :
Year : 1982
GLP : no data
Test substance : as prescribed by 1.1 - 1.4
Remark : Dosing by gavage
The mice died over a 48-h period. Those surviving 48 h recovered; and appeared normal at the end of the 14-days observation period. Post observation period 14 days.

LD50 (male) = 489 mg/kg bw; LD50 (female) = 413 mg/kg bw.
95 % confidence limit = 337 - 499 mg/kg bw for females and 424-552 mg/kg bw for males, respectively.
Target organs were reported to be liver and lungs.

Gross pathology: brain, liver, spleen, lungs, thymus, kidneys, testes (organ weight)
Source : Wacker Chemie GmbH, Burghausen, Germany.
Reliability : (2) valid with restrictions
Flag : Critical study for SIDS endpoint

24.06.2002 (119)

Type	:	LD50
Value	:	> 600 mg/kg bw
Species	:	mouse
Strain	:	other: strain not specified / data apply to only one particular strain ofmice";
Sex	:	no data
Number of animals	:	6
Vehicle	:	other: olive oil
Doses	:	500, 600, 700, 800, and 900 mg/kg as 10- and 5 -% solution
Method	:	other: Acute Oral Toxicity
Year	:	1945
GLP	:	no
Test substance	:	as prescribed by 1.1 - 1.4
Method	:	Comparative gavage study: Mice of various strains from the National Cancer Institute were used. Sections of liver, lung, heart, kidney, adrenal glands and spleen were taken for microscopic examination, but no data on histology quoted.
Result	:	Mortalities were 0/6 after 500 mg/kg bw, 2/10 after 600 mg/kg bw, 6/10 after 700 and 800 mg/kg bw, 10/10 after 900 mg/kg.
Source	:	Wacker - Chemie GmbH, Burghausen, Germany.
Reliability	:	(2) valid with restrictions Comparative study, screening test, basic data given, based on scientific principles, results conclusive.
Flag	:	Critical study for SIDS endpoint

24.06.2002 (75)

Type	:	LD50
Value	:	= 911 mg/kg bw
Species	:	mouse
Strain	:	other: albino
Sex	:	male/female
Number of animals	:	10
Vehicle	:	other: corn oil
Doses	:	630, 795, 1000, and 1260 mg/k bw as 1 - or 5 -% solution
Method	:	
Year	:	1948
GLP	:	no
Test substance	:	no data
Method	:	Gavage study, 10 animals per dose. Male: 1000 mg/kg bw; 1260 mg/kg bw. Female 630 mg/kg bw; 795 mg/kg bw. Male: 1000 mg/kg bw; 1260 mg/kg bw. Female 630 mg/kg bw; 795 mg/kg bw.
Result	:	Calculated LD50 by the method of Thompson is 911 mg/kg bw (870 - 953 mg/kg bw). Mortality observed: The majority of deaths occurred within 24 h after dosing: 0/10 at 630 mg/kg bw, 0/10 at 795 mg/kg within 14 days, 9/10 at 1000 mg/kg bw after 1 to 2 days, and 10/10 within 1 day. Note: Steep dose-response relationship! The gross pathology noted at autopsy included congestion of the lungs, pale kidney and livers, and injection of blood vessels in the intestines.
Reliability	:	(2) valid with restrictions Comparative study, screening test, basic data given, based on scientific principles, results conclusive.
Flag	:	Critical study for SIDS endpoint

24.06.2002 (115)

Type	:	LD50
Value	:	= 910 mg/kg bw
Species	:	rabbit
Strain	:	other: albino
Sex	:	male
Number of animals	:	29
Vehicle	:	other: 1 % "Tergitol 7" (dispersion)
Doses	:	795, 890, 1000, and 1260 mg/kg as 10-% dispersion
Method	:	other: Acute Oral Toxicity
Year	:	1948
GLP	:	no
Test substance	:	no data
Method	:	Gavage study, 3, 5 and 10 animals used per dose.
Result	:	Calculated LD50 (method of probits) was 910 mg/kg bw (857 - 966 mg/kg bw). Mortality observed in 14 days: 0/6 animals at 795 mg/kg, 6/10 at 890 mg/kg bw after 1 to 3 days, 7/10 at 1000 mg/kg, and 3/3 at 1260 mg/kg bw after 1 day. Note: Steep dose-response relationship! Lung congestion, pale kidneys and livers, congestion of the blood vessels of the intestine, congestion of stomach and intestine and increased amount of blood in peritoneal fluid.
Source	:	Wacker Chemie GmbH, Burghausen, Germany.
Reliability	:	(2) valid with restrictions Comparative study, screening test, basic data given, based on scientific principles, results conclusive.
Flag	:	Critical study for SIDS endpoint

24.06.2002 (115)

Type	:	LD50
Value	:	> 2500 mg/kg bw
Species	:	dog
Strain	:	other: no information
Sex	:	no data
Number of animals	:	5
Vehicle	:	other: mucilage of acacia
Doses	:	1500, 1750, 2000, 2250, and 2500 mg/kg as about 33-% dispersion
Method	:	other: Acute Oral Toxicity
Year	:	1934
GLP	:	no
Test substance	:	as prescribed by 1.1 - 1.4
Method	:	Comparative gavage study including various chlorinated solvents. One dog per dose used. Observation for 7 days.
Remark	:	Acc. to authors: The solvent is like the others tested a cardiac depressant, but death occurred through respiratory arrest prior to cardiac failure.
Result	:	Mortality: Animals given 1500 and 1750 mg/kg survived, the other 3 died after 4, 2, and 1 d, respectively. The calculated "M.L.D within 24 hrs" (no further explanation) is 2,5 g. Signs of toxicity were manifested as fatty degeneration of the liver in those dogs that died two days or more after giving the substance; on electric stimulation of different nerves normal qualitative contraction reactions were observable.
Source	:	Wacker - Chemie GmbH, Burghausen, Germany.
Reliability	:	(2) valid with restrictions Screening study, basic data given, based on scientific principles, results conclusive.
Flag	:	Critical study for SIDS endpoint

24.06.2002 (17)

5.1.2 ACUTE INHALATION TOXICITY

Type	:	LC0
Value	:	ca. 1500 ppm
Species	:	rat
Strain	:	Wistar
Sex	:	male/female
Number of animals	:	13
Vehicle	:	
Doses	:	1500 and 3000 ppm
Exposure time	:	4 hour(s)
Method	:	other: Acute Toxicity study
Year	:	1945
GLP	:	No
Test substance	:	As prescribed by 1.1 - 1.4
Method	:	Whole-body exposure design. No air analysis performed, concentrations calculated from dosing and air flow.
Result	:	At 3000 ppm (approx. 12400 mg/m3): 19/20 deaths in 1 d, 1/20 within 2 d after 7-hr exposure. 15/16 deaths in 5 days after 3.5-hr exposure, 5/16 within 3d, 8/16 on day 4. 0/15 deaths after a 1.5-hr exposure period. At 1500 ppm (approx. 6200 mg/m3): 4/20 deaths within 4 d after 7-h exposure. No death (0/13) after 4-h exposure. Pathological findings were: narcosis to loss of consciousness, dyspnoea and weakness observed during exposure. at necropsy: occasional peritoneal and pleural fluid, moderate pulmonary congestion or haemorrhage, visceral congestion (particular liver and spleen), slight to moderate cellular necrosis and fatty degeneration of the liver (most prominent focal areas), degeneration of the tubular epithelium of the kidney, and congestion of the adrenal cortex. No lesions found in sections of brain, cord, and sciatic nerve.
Source	:	Wacker Chemie GmbH, Burghausen, Germany.
Test substance	:	commercial grade of high purity
Reliability	:	(2) valid with restrictions Comparative study based on scientific principles, results conclusive in the context of the whole test programme.
Flag	:	Critical study for SIDS endpoint

09.05.2002 (75)

Type	:	LC50
Value	:	= 3290 mg/m³
Species	:	Rat
Strain	:	other: young albino rats
Sex	:	male
Number of animals	:	20
Vehicle	:	
Doses	:	
Exposure time	:	10 hour(s)
Method	:	other: Acute Inhalation Toxicity
Year	:	1956
GLP	:	No
Test substance	:	other TS

Remark : Rats were exposed to a vapor consisting of a 70%/30% mixture of 1,2-dichloroethane and carbontetrachloride.
1-hour LC50-value derived in this study was 28790 mg/m3.
(The data were extracted from a graph).

Examination of selected animals on days one and four post-exposure showed severe organic damage to the livers and kidneys as well as slight changes in the lungs, respectively.

Liver damage was characterized by fatty degeneration with varying degrees of hemorrhagic necrosis. In the kidneys severe degeneration of the tubular epithelium was observable while in the lungs of a few animals slight hemorrhage and congestion was detectable. Increases in the absolute and relative liver and kidney weights were found.

(compare also Spencer et al., 1951, Dow Chem.)
Source : Wacker - Chemie GmbH, Burghausen, Germany.
Reliability : (3) invalid
Study based on scientific principles, but relating to a mixture.
Flag : non confidential
07.05.2002 (112)

Type : LC50
Value : = 6770 mg/m³
Species : Rat
Strain : Sprague-Dawley
Sex : male
Number of animals : 12
Vehicle :
Doses : from approx. 1300 - approx. 1700 ppm (10 concentrations) (see Fig. 1)
Exposure time : 6 hour(s)
Method : other: Acute Inhalation Toxicity
Year : 1980
GLP : No
Test substance : As prescribed by 1.1 - 1.4
Method : Comparative study on various chlorinated solvents:
12 animals were used per test concentration.
Post-exposure observation period was 14 days. Autopsy performed.

Air concentrations of TS controlled and regulated via GC analysis.
Result : Mean LC50 was 1646 ppm (1577 - 1768 ppm, 95-% conf. limits).

At 1300 - 1700 ppm: mortality from about 17 to 75 % (Fig. 1): Very steep dose-response!!

Acute signs of intoxication: excitation, somnolence. On autopsy, no pathological findings in liver, lung, and kidney, and other organs (not further specified).
Source : Wacker - Chemie GmbH, Burghausen, Germany.
Test substance : purity 99%
Reliability : (2) valid with restrictions
Comprehensive and comparative study, basic data given, based on scientific principles apparently meeting current standards.
Flag : Critical study for SIDS endpoint
09.05.2002 (25)

Type : LC50
Value : ca. 1900 ppm
Species : rat

Strain	:	other: albino rats
Sex	:	female
Number of animals	:	31
Vehicle	:	other: none
Doses	:	200, 300, 600, 800, 1000, 1500, 3000, 12000, 20000 ppm (at various exposure times)
Exposure time	:	4 hour(s)
Method	:	other: Acute Inhalation Toxicity
Year	:	1951
GLP	:	no
Test substance	:	as prescribed by 1.1 - 1.4
Method	:	Whole-body exposure design. Analysis of air concentration: By means of combustion analysis, it was repeatedly shown that in every case the vapour was uniformly held within 10 % of the desired concentration of the TS. Evidence of organ pathology: Special, additional groups of animals were killed at various intervals within the time-frame of 0.2-h to 20-h exposure to determine b.w., liver and kidney weight, blood parameters (urea nitrogen, plasma prothrommbin clotting time, serum phosphatase), liver lipids, and histopathological changes (liver, kidney, adrenals).
Remark	:	Acc. to authors, deaths tended to occur at 3 different time intervals and in such a manner as to suggest 3 separate toxic actions of fatal degree (p. 486): 1. At very high concentrations (e.g. 20000 ppm), deaths occurred due to depression and paralysis of CNS functions. 2. At all vapour concentrations causing death, a large proportion died rather suddenly and quietly a few hours after termination of exposure, showing marked cyanosis, reduced body temperature, stupor or coma and failing respiration. The character and sudden development of this response suggest "shock" or cardiovascular collapse. 3. All other deaths occurred delayed over a period of 2 to 7 d with progressive loss of weight and other evidence of toxic effects, suggesting organ failure, probably due to kidney lesions.
Result	:	The 4-h LC50 corresponds to approx. 8000 mg/m3 and is derived from a dose-response graph (Chart 1). Further LC50-values measured in this study: Exposure time LC50 0.53 hours 49360 mg/m³ 2.75 hours 12330 mg/m³ 5.5 hours 6150 mg/m³ 7.2 hours 4110 mg/m³ With 22000 ppm (ca. 90420 mg/m3), death occurred within 24 min after deep anaesthesia by depression of the central nervous system. At 12000 ppm and lower concentrations this depressant action resulted in varying degrees of "drunkenness". In special groups of animals (exposure causing 99.9%, 50% or 0.01% death), reported signs of exposure mediated toxicity were decreased body weights, increased liver and kidney weights and slight parenchymatous degeneration to severe haemorrhagic necrosis (kidney, liver, adrenals), congestion (kidney, liver, adrenals, lungs) and oedema (kidney, lungs),

increase in blood urea nitrogen, plasma prothrombin clotting time, liver lipids, decrease in serum phospatase.

The following concentrations and exposure times were not lethal:
300 ppm (approx. 1200 mg/m3) after 7 h (20 animals)
600 ppm (" 2400 mg/m3) after 5 h (20 animals)
1500 ppm (approx. 6100 mg/m3) after 2 h (10 animals)
3000 ppm (" 12100 mg/m3) after 0.5 h (22 animals)
22000 ppm (" 81000 mg/m3) after 0.1 h (10 animals).

The following concentrations were void of adverse effects:
200 ppm (approx. 800 mg/m3) for 7 h;
300 ppm (" 1200 mg/m3) for 3 h (but effects at 5.5h)
1000 ppm (" 4000 mg/m3) for 1.5 h (but effects at 3h).

Source : Wacker - Chemie GmbH, Burghausen, Germany.
Test substance : Purity 99.7 %, Dow Chem.
Reliability : (2) valid with restrictions
Comprehensive and comparative study, basic data given, based on scientific principles apparently meeting current standards.
Flag : Critical study for SIDS endpoint
24.06.2002 (155)

Type : LC50
Value : = 1080 mg/m³
Species : mouse
Strain : other: OF1
Sex : female
Number of animals : 20
Vehicle : other: none
Doses :
Exposure time : 6 hour(s)
Method : other: Acute Inhalation Toxicity
Year : 1978
GLP : no
Test substance : no data
Method : Comparative study on various chlorinated solvents:
Post-exposure observation period was 14 days.
Air concentrations of TS controlled and regulated via GC analysis.
(compare also: Bonnet et al., 1980)

No gross pathology or histology data stated.
Result : Mean LC50 corresponds to 262 ppm: 95 % confidence limit = 1030 - 1120 mg/m3 (= 251 - 273 ppm). But mortality rate was from approx. 10 - >=95 % in the range of 200 - 400 ppm:
steep dose- response (see Fig. 3)!!

Signs of toxicity and time to death not reported.
Source : Wacker - Chemie GmbH, Burghausen, Germany.
Reliability : (2) valid with restrictions
Comparative study, basic data given, based on scientific principles acc. to current standards.
Flag : Critical study for SIDS endpoint
24.06.2002 (65)

Type : other: Acute intoxication
Value :
Species : mouse
Strain : other: no information, various strains from NCI
Sex : no data
Number of animals : 41

Vehicle	:	
Doses	:	1500 and 3000 ppm
Exposure time	:	hour(s)
Method	:	
Year	:	1945
GLP	:	no
Test substance	:	as prescribed by 1.1 - 1.4
Method	:	Whole-body exposure design. Daily chamber air analysis performed by chemical analysis.
Result	:	After 3000 ppm (approx. 12400 mg/m3): All mice died within 7hr exposure period. All mice died within 2 days following 2-hr exposure. After exposure to 1500 ppm (approx. 6200 mg/m3): All animals exposed for 7 hrs died, 4/20 immediately by the end of exposure, 16/20 within 24 h. 1/23 animals exposed for 2 hrs died after 3 days. Pulmonary and generalised visceral congestion and slight fatty degeneration of the liver.
Source	:	Wacker Chemie GmbH, Burghausen, Germany.
Test substance	:	commercial grade of high purity
Reliability	:	(2) valid with restrictions Comparative study based on scientific principles, results conclusive in the context of the whole test programme.
Flag	:	non confidential, Critical study for SIDS endpoint

24.06.2002 (75)

Type	:	other: metabolism-dependent toxicity
Value	:	
Species	:	Mouse
Strain	:	CD-1
Sex	:	Male
Number of animals	:	10
Vehicle	:	
Doses	:	1000, 1250, and 1500 ppm
Exposure time	:	4 hour(s)
Method	:	
Year	:	1986
GLP	:	no data
Test substance	:	as prescribed by 1.1 - 1.4
Method	:	Nose-only exposure, chamber air concentration was monitored by GC of air samples. Concentrations were within 10 % of the theoretical values. 10 animals per test concentration used; post-exposure observation was 48 h, histopathology done on liver and kidneys. Study was performed to investigate the effects of pretreatment of mice with typical cytochrome P450 inducers (phenobarbital [PB], 3-methylcholanthrene [MC]) and inhibitor (SK525A) on the mortality of the animals after acute inhalation.
Result	:	At 1000 ppm (approx. 4100 mg/m3) [4-h exposure], 17 % and 44 % of all DCE-treated mice died within 24 and 48 h, respectively (see Discussion of report). Concentration-related increase in mortality, reported to be due to respiratory failure. Ataxia, tremor, seizures, laboured breathing and cyanosis reported in some animals. Significant increases in relative kidney weight at all concentrations, and in relative liver weight at 1500 ppm.

Liver and kidney damage observed, the incidence and degree of damage being greater in the kidney.

Mortality as well as degree of renal tubular lesions were modified by pretreatment with the agents employed: increase by PB and 3-MC, decrease by SKF.

The result supports cytochrome-P450-dependent toxicity.

Source : Wacker Chemie GmbH, Burghausen, Germany.
Test substance : Purity >99 %
Reliability : (2) valid with restrictions
Study based on scientific principles, test design and conduct according to current standards, extent limited to the special issue.
Flag : non confidential, Critical study for SIDS endpoint
24.06.2002 (60)

Type : LC50
Value : < 12400 mg/m³
Species : rabbit
Strain : other: no information
Sex : no data
Number of animals : 16
Vehicle :
Doses : 3000 ppm
Exposure time : 7 hour(s)
Method :
Year : 1945
GLP : no data
Test substance : no data
Method : Whole-body exposure design. Daily chamber air analysis performed by chemical analysis.
Result : At 3000 ppm (approx. 12400 mg/m3):
12/16 deaths within 3 days. Varying degrees of narcosis, dyspnoea and weakness/prostration observed during exposure. After termination of exposure, apparent recovery to normal for a while, but then break down with increasing dyspnea. Necropsy: small amounts of peritoneal and pleural fluid, mild pulmonary congestion or scattered haemorrhage, visceral congestions (liver and spleen), slight-moderate hepatic necrosis and fatty degeneration of the renal tubular epithelium observed.
Source : Wacker Chemie GmbH, Burghausen, Germany.
Test substance : commercial grade of high purity
Reliability : (2) valid with restrictions
Comparative study based on scientific principles, results conclusive in the context of the whole test programme.
Flag : Critical study for SIDS endpoint
24.06.2002 (75)

Type : LC50
Value : ca. 6400 mg/m³
Species : guinea pig
Strain : other: no information
Sex : no data
Number of animals : 12
Vehicle :
Doses : 1500 and 3000 ppm
Exposure time : 7 hour(s)
Method : other: Acute Inhalation Toxicity
Year : 1945
GLP : no data
Test substance : no data

Method	:	Whole-body exposure design. Daily chamber air analysis performed by chemical analysis.
Result	:	At 3000 ppm (approx. 12400 mg/m3): 14/14 animals died within 3 days. Signs of toxicity were evident as inactivity, and laboured breathing, uncertain gait, considerable lacrimation and moisture around the mouth. On gross autopsy va rying degrees of congestion in the lungs, occurrence of clear pleural fluid and visceral congestions could be observed in all of them. Liver, lungs and adrenals were particularly affected. Focal necrosis of the adrenal cortex in 5 pigs with hemorrhage in 3 of them. Slight to moderate degeneration or renal tubular epithelium was noted in eight animals. At 1500 ppm (approx. 6200 mg/m3) [approximate LD50]: 6/12 deaths within 4 days. No signs of toxicity described after exposure for 7 hr.
Source	:	Wacker - Chemie GmbH, Burghausen, Germany.
Test substance	:	commercial grade of high purity
Reliability	:	(2) valid with restrictions Comparative study based on scientific principles, results conclusive in the context of the whole test programme.
Flag	:	Critical study for SIDS endpoint

24.06.2002 (75)

5.1.3 ACUTE DERMAL TOXICITY

Type	:	LD50
Value	:	= 4890 mg/kg bw
Species	:	rabbit
Strain	:	
Sex	:	male
Number of animals	:	
Vehicle	:	
Doses	:	Occluded applications : 3.16, 3.98, 4.45 and 5.0 ml/kg for 24 h (= 3972 mg/kg bw; 5000 mg/kg bw; 5594 mg/kg bw and 6285 mg/kg bw).
Method	:	
Year	:	1948
GLP	:	no
Test substance	:	no data
Result	:	Calculated LD50 (method of probits) 3.89 ml/kg bw (3.40 - 4.46 ml/kg bw) or 4890 mg/kg bw (4270 - 5600 mg/kg bw). Weight loss reported in most survivors. Gross necropsy evaluation revealed no adverse effects. Mortality observed within 14 days in 2/6 at 3972 mg/kg bw within 5 to 10 days, 3/11 within 1 to 5 days at 5000 mg/kg bw, 8/9 within 1 to 11 days at 5594 mg/kg bw, and 5/6 within 1 day at 6285 mg/kg bw.
Source	:	Wacker Chemie GmbH, Burghausen, Germany.
Reliability	:	(2) valid with restrictions
Flag	:	Critical study for SIDS endpoint

24.06.2002 (115) (153)

5.1.4 ACUTE TOXICITY, OTHER ROUTES

5.2.1 SKIN IRRITATION

Species	:	rabbit

Concentration	:	undiluted
Exposure	:	Occlusive
Exposure time	:	4 hour(s)
Number of animals	:	6
Vehicle	:	
PDII	:	
Result	:	not irritating
Classification	:	
Method	:	other: FDA revision, Fed. Reg. USA, 37, No. 244, 19 Dec. 1972
Year	:	1973
GLP	:	no
Test substance	:	as prescribed by 1.1 - 1.4
Result	:	The test on the intact skin revealed no signs of irritation (scores for all symptoms 0).
Source	:	Wacker - Chemie GmbH, Burghausen, Germany.
Test condition	:	0.5 ml of substance was applied under occluded conditions to the intact skin (contact time 4 h, observation time 4 h, 24 and 48 h). Abraded skin was not included. Animals are to be retained for observation 96 hour after initial application.
Test substance	:	TS was EDC (not further specified), not to be confused with "EDC/DMMP Condensation" product which also was tested.
Reliability	:	(2) valid with restrictions Comparable to guideline study, limited documentation of test design and performance.
Flag	:	Critical study for SIDS endpoint

25.06.2002 (158)

Species	:	Rabbit
Concentration	:	Undiluted
Exposure	:	Occlusive
Exposure time	:	24 hour(s)
Number of animals	:	30
Vehicle	:	
PDII	:	4.7
Result	:	moderately irritating
Classification	:	
Method	:	other: acc. to Draize (described in: Duprat et al., 1974)
Year	:	1976
GLP	:	No
Test substance	:	as prescribed by 1.1 - 1.4
Method	:	Comparative study including various chlorinated solvents: Dermal application of 0.5 ml under occluded conditions on the scarified and intact skin. Skin was histologically examined on day 3 post-exposure.
Remark	:	Only overall rating is given (by primary irritation index), but effects specified cannot be exactly allocated to the individual test substance. An appraisal is not possible but through comparison relative to the findings on the other substances involved. For example, chloroforme and perchloroethylene were graded as "severe" irritants (PI = 5.6 and 6.1, resp., of max. 8 scores), tetrachloromethane was assigned "moderate" (PI =4.2).
Source	:	Wacker - Chemie GmbH, Burghausen, Germany.
Test substance	:	commercial, from Merck
Reliability	:	(2) valid with restrictions Early standard study, very limited documentation, exposure regimen fails to allow interpretation on the basis current standards (4-h exposure).
Flag	:	Critical study for SIDS endpoint

27.06.2002 (54) (55)

Species	:	guinea pig
Concentration	:	undiluted

Exposure	:	Occlusive
Exposure time	:	
Number of animals	:	
Vehicle	:	
PDII	:	
Result	:	slightly irritating
Classification	:	
Method	:	other
Year	:	1981
GLP	:	no data
Test substance	:	as prescribed by 1.1 - 1.4
Method	:	Comparative study including various chlorinated solvents: Number of anim als used unclear. One to four glass rings were glued onto the clipped back skin of guinea pigs. To exclude other routes of adsorption a cover glass with a central hole was attached to the upper surface of the glass ring. One ml of the neat substance was ap plied with a syringe through the hole of the cover glass (occluded conditions, application area 3.1 cm2.). Note: The area-specific dose was about 4x higher than would have been under current standard conditions (0.5 ml/6 cm2). Glass rings were removed at different times (15 min, 1, 4 and 16 hours) and specimen of whole skin from exposed sites cut out and subsequently fixed in 10% formalin.
Result	:	No microscopic changes in the skin after 15 or 60 mins; after 4hrs and 16hrs slight degenerative changes seen in the epidermis - slight focal karyopyknosis, slight perinuclear oedema in the region of cells with pyknotic nuclei, spongiosis and junctional separation.
Source	:	Wacker Chemie GmbH, Burghausen, Germany.
Test substance	:	commercial from Merck (for spectroscopy)
Reliability	:	(2) valid with restrictions No standard study, based on scientific principles, not in compliance with current standards: Results cannot be correlated to the classical, macroscopic indicators for irritation and thus not evaluated under the current classification system.
Flag	:	Critical study for SIDS endpoint

27.06.2002 (101)

5.2.2 EYE IRRITATION

Species	:	Rabbit
Concentration	:	undiluted
Dose	:	.1 ml
Exposure time	:	
Comment	:	not rinsed
Number of animals	:	6
Vehicle	:	
Result	:	slightly irritating
Classification	:	
Method	:	Draize Test
Year	:	1976
GLP	:	No
Test substance	:	as prescribed by 1.1 - 1.4
Method	:	Comparative study including various chlorinated solvents, 6 animals used per test. For evaluation of irritating effects, a primary irritation index is derived by

means of the "Draize Score" on a scale from 0 - 110 scores. The range of categorisation for "mild" irritant is given as 4 <score <15 (= class 3). Observation regimen not specified (referred to another publication).

Result : After instillation of 0.1 ml of 1,2 -dichloroethane into the conjunctival sac, moderate lacrimation, mild-moderate catarrhal conjunctivitis and corneal epithelium abrasion visible in the slit lamp using fluorescein. On day 7 after instillation, keratitis was still evident, but regenerating, and fully disappeared after another 7 days.

The effects were graded as "mild" with an overall irritation index of 7 (of max. 110 scores).

[note: Chloroform reached an index of 41 (of 110 scores).]

Source : Wacker - Chemie GmbH, Burghausen, Germany.
Test substance : "pure" (for spectroscopy)
Reliability : (2) valid with restrictions
Comparable to guideline study, limited documentation.
Flag : Critical study for SIDS endpoint
24.06.2002 (54)

Species : Rabbit
Concentration : Undiluted
Dose : .1 ml
Exposure time :
Comment : not rinsed
Number of animals : 6
Vehicle :
Result : slightly irritating
Classification :
Method : other: Draize Test (Code of Federal Regulations Part 191.12)
Year : 1973
GLP : No
Test substance : as prescribed by 1.1 - 1.4
Result : After application of 0.1 ml 1,2-dichloroethane into the conjunctival sac slight reddening in 2/6 animals and annular conjunctival swelling in one animal. All symptoms disappeared completely within three days.

No rankings for findings given. However, the minor effects suggest no irritation potential based on current criteria for classification.
Source : Wacker - Chemie GmbH, Burghausen, Germany.
Reliability : (2) valid with restrictions
Comparable to guideline study, insufficient documentation, but result in line with findings of others.
Flag : Critical study for SIDS endpoint
24.06.2002 (158)

Species : Dog
Concentration :
Dose :
Exposure time : 7 hour(s)
Comment :
Number of animals : 17
Vehicle :
Result : irritating
Classification :
Method : other: inhalation exposure
Year : 1944
GLP : no
Test substance : as prescribed by 1.1 - 1.4
Method : Whole-body inhalation exposure design. Dogs were exposed once or

intermittently to 1500 or 1000 ppm. Repeated exposures were generally administered in series of 5, separated by a rest period of two days. Histological examinations of the corneas were carried out.

Result : At 1500 ppm:
1. After single exposure, 1/6 dogs showed no corneal damage;

one developed faint turbidity; 4/6 developed intense clouding of both corneas which cleared within 1 week in 1 animal and returned when the exposure was repeated.

2. After repeated exposure (three dogs), in all the animals bilateral corneal opacity developed, which became intense 48 h after the first exposure. One animal died after 5 and another after 6 exposures. The third animal was killed after 30 exposures. The turbidity remained at maximal intensity.

3. Histologic examination: The eyes which were turbid at the time of death showed the following changes: (1) corneal edema, with swelling, separation and distortion of the fibres of the substantia propria; (2) degeneration and sloughing of the corneal epithelium, and (3) infiltration of polymorpho-nuclear leukocytes into the substantia propria, especially at the corneoscleral junction, and occasionally into the anterior chamber and the filtration angle. The eyes which had cleared before death were histologically normal.

At 1000 ppm:
1. A single exposure of seven hours to 1000 ppm led to symmetric turbidity of the corneas on 8 of 10 dogs. The process tended to clear from the periphery inward. It sometimes took as long as three weeks for partial regression.

2. After repeated exposures, the turbidity became increasingly intense during the 5 exposure days and tended to clear during the rest periods.

3. In successive weeks the series of 5 exposures had less and less effect on the cornea. Finally, the cornea became almost completely resistant to the chemical. If exposures were resumed after an interval of rest of 2 to 4 weeks, the cornea still showed this resistant state.

Note: A fox showed similar symptoms, while cats, monkeys, chickens and various rodents exposed to dichloroethane in a concentration of 1000 ppm showed no changes in the eyes.

Source : Wacker Chemie GmbH, Burghausen, Germany.
Test substance : commercial grade
Reliability : (2) valid with restrictions
Comparative study using various species, based on scientific principles, results conclusive in the context of the whole test programme.
Flag : Critical study for SIDS endpoint
24.06.2002 (76)

Species : guinea pig
Concentration : undiluted
Dose :
Exposure time :
Comment :
Number of animals :
Vehicle :
Result : slightly irritating
Classification :
Method : other: Inhalation exposure
Year : 1930

GLP	:	no
Test substance	:	as prescribed by 1.1 - 1.4
Remark	:	Atmospheric exposure, including eye and nasal effects as well as clinical symptoms. Evaluation was based on clinical rather than clear pathological signs relevant for classification.
Result	:	At 4000 to 4500 ppm (0.4 - 0.45 vol%): Eye (squinting and lacrimation) and nose irritation (rubbing of the nose) reported within 3 - 10 mins of exposure. Signs of systemic intoxication reported as vertigo and unsteadiness under this condition after 8 - 18 min, semi- to unconsciousness after 30 - 60 min, and dyspnea after 4 h. No other clinical signs evident within maximum exposure time of 6 h. At 2000 ppm (0.2 vol%): Eye (squinting and lacrimation) and nose irritation (rubbing of the nose) reported within 6 mins of exposure. Signs of systemic intoxication reported as vertigo and unsteadiness under this condition after 20-45 h. At 1200 ppm (0.12 vol%), no irritation and signs of intoxication even after 8 h, except occasional retching in 1/18 animals. At 600 ppm (0.06 vol%), not any adverse effects were noted .
Source	:	Wacker Chemie GmbH, Burghausen, Germany.
Test substance	:	commercial grade, physical specification quoted
Reliability	:	(2) valid with restrictions Screening study based on scientific principles, results conclusive, but not appropriate for classification on current criteria.
Flag	:	Critical study for SIDS endpoint

27.06.2002 (149)

5.3 SENSITIZATION

5.4 REPEATED DOSE TOXICITY

Type	:	Chronic
Species	:	rat
Sex	:	male/female
Strain	:	other: no data, locally bred
Route of admin.	:	oral feed
Exposure period	:	2 yr
Frequency of treatm.	:	daily
Post exposure period	:	none
Doses	:	250, 500 ppm in feed, about 12.5 and 25 mg/kg bw/d
Control group	:	yes, concurrent no treatment
NOAEL	:	= 500 ppm
Method	:	other: Repeated Dose Toxicity/Fertility study
Year	:	1976
GLP	:	no
Test substance	:	no data
Method	:	Study was conducted to test the effects of 1,2 -dichloroethane fumigated mash on rats (strain of rats not specified). Eighteen animals per sex and group were used in this experiment which started at about 2 wk after weaning. The test design included a reproduction test over 2 years with all treated females mated with untreated males (female fertility) [6x/2y]. Each mating period interrupted feeding of DCE-fumigated diet to females for about 10 d each.

A special fumigation technique over 48 h and feeding regimen were employed to minimise loss of DCE from the diet. The mean loss was found to be 5 to 10 % only following 7 to 10 days of appropriately sealed storage.

The study included no histopathology, while essential blood biochemical parameters as well as liver fat content were determined.

Remark : Study was conducted to test the effects of 1,2 -dichloroethane fumigated mash on rats (strain of rats not specified). Eighteen animals per sex and group were used in this experiment.

Result : No effects on food consumption, body weight development or on liver and kidney function reported. The following serum level remained unaffected at the end of the experiment (2y):

Glucose, protein, albumin, globulin, urea, uric acid, cholesterol, ASAT, ALAT and chloride, sodium and potassium. Results of biochemical tests show no effects on liver (transaminases, cholesterol values) and kidney function (urea and uric acid levels), respectively. No increase in hepatic fatty content was found.

By 14th month, all animals including controls began to suffer from chronic respiratory disease causing the mortality rate to increase.

Source : Wacker - Chemie GmbH, Burghausen, Germany.

Reliability : (2) valid with restrictions
Study based on scientific principles, focussed upon liver/kidney effects, basic data given, results conclusive in light of findings by others.

Flag : Critical study for SIDS endpoint

24.06.2002 (4)

Type : Sub-acute
Species : rat
Sex : male/female
Strain : other: no data, locally bred
Route of admin. : oral feed
Exposure period : 5 or 7 weeks
Frequency of treatm. : daily
Post exposure period : none
Doses : 0, 300, 600 ppm (5 weeks), 1600 ppm (7 weeks) in feed
Control group : yes, concurrent no treatment
NOAEL : = 1600 ppm
NOEL : = 600 ppm
Method : other: Repeated Dose Toxicity
Year : 1976
GLP : no data
Test substance : no data

Remark : Prestudy of a long-term study (see other entry): 6 animals (4 weeks old) in each dose group.

Result : No influence on relative weight or relative total fat content of the liver at 300 (15 mg/kg bw/d) and 600 ppm (30 mg/kg bw/d), respectively.

Slight fat accumulation of about 15% (total fat and triglycerides) was noted at 1600 ppm (80 mg/kg bw/d) without concomitant increase in liver weight: The relative level of triglycerides was significantly increased (controls 16 mg/g wet liver,1600 ppm 28 mg/g wet liver ($P<0.05$).

[Note: In comparison, CCl4 simulataneously studied produced a strong effect on hepatic fat content.]

Source : Wacker Chemie GmbH, Burghausen, Germany.

Reliability : (2) valid with restrictions
Study based on scientific principles, focussed upon liver/kidney effects,

basic data given, results conclusive in light of findings by others.

Flag : Critical study for SIDS endpoint
24.06.2002 (4)

Type	:	Sub-chronic
Species	:	rat
Sex	:	male/female
Strain	:	other: a) Fischer 344; b) Sprague-Dawley; c) Osborne-Mendel
Route of admin.	:	drinking water
Exposure period	:	13 wk
Frequency of treatm.	:	continuous
Post exposure period	:	none
Doses	:	500, 1000, 2000, 4000 or 8000 ppm (see: Method for specific doses)
Control group	:	yes, concurrent no treatment
NOAEL	:	ca. 320 mg/kg bw
LOEL	:	ca. 50 mg/kg bw
Method	:	other: Repeated Dose Toxicity (NTP/USA)
Year	:	1990
GLP	:	yes
Test substance	:	as prescribed by 1.1 - 1.4
Method	:	10 animals/sex/group were used. Drinking water served as the vehicle. Hematologic and serum chemical analyses were performed on satellite groups of 10 males from each strain at interim intervals of d 3, 7, 14, and 45 and at terminal sacrifice in order to prevent any unknown effects of bleeding on core groups. Doses administered were (obtained by dividing the mean water consumption by the mean of the initial and final body weigts): Fischer 344 rats: 49, 86, 147, 259 and 515 mg/kg bw/d (m); 58, 102, 182, 320 and 601 mg/kg bw/d (f). Osborne-Mendel rats: 54, 88, 146, 266 and 492 mg/kg bw/d (m); 82, 126, 213, 428 and 727 mg/kg bw/d (f). Sprague-Dawley rats: 60, 99, 165, 276 and 518 mg/kg bw/d (m); 76, 106, 172, 311 and 531 mg/kg bw/d (f). Stability of the test substance was examined: at least 3 wk stable in the dark at 5 °C in sealed bottles.
Remark	:	The decrease in water intake (shown below), which was as muchas 60% at the highest dose in male and female Osborne-Mendel rats, indicates that the dose received by all exposed animals was less than the target dose. The decrease in water intake (shown below), which were as much as 60% at the highest dose in male and female Osborne-Mendel rats, indicates that the dose received by all exposed animals was less than the target dose. The estimated doses were obtained by dividing the mean water consumption over the 13-week studies by the mean of the initial and final body weigts. Water consumption Fisher 344 rats: Control 25 g/animal per d ay, dose group 500 ppm 24 g/animal per day (males); Control 19 g/animal per day, dose group 500 ppm 18 g/animal per day (females). Water consumption Osnorne-Mendel rats: Control 42 g/animal per day, dose group 500 ppm 35 g/animal per day (males); Control 43 g/animal per day, dose group 500 ppm 34 g/animal per day (females).

Water consumption Sprague-Dawley rats: Control 43 g/animal per day, dose group 500 ppm 37 g/animal per day (males); Control 44 g/animal per day, dose group 500 ppm 33 g/animal per day (females).

A NOAEL is not given by the authors of the study.
The authors remark, that because of limitations in the solubility and palatability of 1,2-dichloroethane, it was not possible to obtain a high enough dose in drinking water to see biologically significant toxic effects in rats.

Result : The test substance caused minimal toxicity in all three rat strains (Morgan et al., 1990).

None of the F344, Sprague-Dawley and Osborne-Mendel rats died during the study.

No clinical signs of toxicity observable in survivors of all three strain of rats. Body weight development was inhibited in dose-related fashion, statistically significant at the top dose and at 4000 ppm in F344 and Osborne males.

Increases in mean absolute and relative weights of kidneys and liver were observable, distinct at 1000 ppm and above for the kidney, and less frequent at 500 ppm ($p<0.05$ or 0.01).

Apart from dehydration related changes in blood count, no further influences on hematological or biochemical blood parameters (a total of 17 parameters have been considered). No substance-related macroscopical or histopathological organ changes have been found (more than 30 organs and tissues have been subjected to examination), but in female F344 female rats (see above: renal tubules). This lesion was minimal in severity in all affected F344 rats.

Source : Wacker - Chemie GmbH, Burghausen, Germany.
Test substance : purity >99 %
Reliability : (1) valid without restriction
In compliance with guideline study, OECD 408, National Toxicology Program.
Flag : Critical study for SIDS endpoint
24.06.2002 (118) (129)

Type : Sub-chronic
Species : rat
Sex : male/female
Strain : Fischer 344
Route of admin. : gavage
Exposure period : 13 wk
Frequency of treatm. : 5 d/wk
Post exposure period : none
Doses : m: 30, 60, 120, 240 or 480 mg/kg bw/d ; f: 18, 37, 75, 150 or 300 mg/kg bw/d
Control group : yes, concurrent vehicle
NOAEL : = 120 - 150 mg/kg bw
LOAEL : = 240 - 300 mg/kg bw
LOEL : = 18 - 30 mg/kg bw
Method : other: Repeated Dose Toxicity (NTP/USA)
Year : 1990
GLP : yes
Test substance : as prescribed by 1.1 - 1.4
Remark : 10 animals/sex/group were used. Corn oil was used as the vehicle. Hematologic and serum chemical analyses were performed on satellite groups of 10 males at interim intervals of d 3, 7, 14, and 45 and at terminal

sacrifice in order to prevent any unknown effects from bleeding on core groups.

Stability of DCE determined by GC was at least 3 weeks when stored in the dark at room temperature.

Result : The test substance caused low toxicity, even though more pronounced after oral bolus application (this study) than after administration in drinking water (see other entry).

The NOAEL was derived to be 120 to 150 mg/kg/d, based on treatment-related histopathological changes in the forestomach and clinical symptoms.
Corresponding LOAELs for male and female animals were 240 and 300 mg/kg bw/d, respectively, which were based on clinical signs of intoxication and mortality.
No NOEL is assumed: A LOEL is at 18 - 30 mg/kg/d, based on significant increases in liver and kidney weight in females and males, resp., which is considered as biologically relevant, but not pathological.

Mortality F344 rats: 10/10 males exposed to 240 mg/kg/d died within 1 to 11 wk and 10/10 males exposed to 480 mg/kg/d died within one week. 9/10 females exposed to 300 mg/kg bw/d died within 1 to 13 wk.

Signs of toxicity were evident as reduced body weight development in the highest dose group of both sexes, tremor, hypersalivation, ruffled fur as well as dyspnea in the second highest dose group of males and in the highest dose group of females.

Serum chemistry data were not indicative of liver and kidney injury. Hematology revealed no abnormal findings.

Statistically significant increases in the absolute and relative kidney and liver weights were observable in all dose groups to a different extent: $p<0.05$ at 30 mg/kg/d for abs. kidney weight; $p<0.01$ at 60 mg/kg/d for abs. and rel. kidney weights (males); $p<0.01$ at 18 mg/kg/d for rel. liver weight (females).

Despite increases of 10 to 20%, no substance-related macroscopical or histopathological changes of liver and kidneys detectable, including renal tubular regeneration without significant difference from the controls (not documented).

On necropsy, significant histopathological findings were minimal to mild hyperplasia and inflammation of the mucosa of the forestomach in males at 240 mg/kg/d and above ($P<0.05$) as well as necrosis of the thymus and cerebellum in the second highest dose group of males and in the highest dose group of females, respectively ($P<0.05$).

Source : Wacker - Chemie GmbH, Burghausen, Germany.
Test substance : Purity >99%
Reliability : (1) valid without restriction
In compliance with guideline study, National Toxicology Program
Flag : Critical study for SIDS endpoint
24.06.2002 (118) (129)

Type : Chronic
Species : Rat
Sex : male/female
Strain : Wistar
Route of admin. : inhalation: vapour

Exposure period	:	100 ppm: 151 exposures in 211 d (m), 142 exposures in 198 d (f); 200 ppm: 151 exposures in 212 d (m+f);
Frequency of treatm.	:	7 h/d, 5d/wk
Post exposure period	:	None
Doses	:	411 mg/m3 (100 ppm), 822 mg/m3 (200 ppm), 1644 mg/m3 (400 ppm)
Control group	:	yes, concurrent no treatment
NOAEL	:	= 200 ppm
Method	:	other: Repeated Dose Toxicity
Year	:	1951
GLP	:	No
Test substance	:	as prescribed by 1.1 - 1.4
Method	:	Whole-body exposure design with 15 or 20 male and 15 or 20 female per dosis group. Analysis: By means of continuously recording analyser (combustion analysis), it was shown that in every case the vapour was uniformly held within 10 % of the desired concentration of the TS. Surviving animals were killed and examined for significant changes as compared with groups of unexposed controls. Lungs, heart, liver, kidneys, spleen and testes were weighed. Tissues from these organs were saved for sections and in many instances sections of the following were prepared also: adrenal gland, pancreas, stomaches, intestine, bone marrow, urinary bladder, ureter, lymph nodes, muscle, brain and optic nerve.
Remark	:	In a first set of the experiment where 15 male and female rats were exposed to 400 ppm, no female rat survived more than 10 exposures in 14 days and no male rat survived more than 40 exposures in 56 days (for analogues effects at similar concentrations compare also: Hofmann et al., 1971, and Heppel et al., 1946, other entries). In additional groups of 20 male and 20 female rats each, subjected to exposure towards 1,620 mg/m3 (394 ppm) to 20 male and female Wistar rats for 2-3 days, 7 h/d, the following substance related effects were reported: High mortality of 60 %; rapid loss of body weight; slightly increased kidney and liver weight; slightly turbid swelling of liver with single gross fatty (predominantly centrilobular) vacuoles; small increase in the total lipid content of the liver (mainly due to increased neutral lipid level); no further substance-related macroscopical or histopathological changes of the kidneys or other inner organs including lung; blood findings without any significance (urea nitrogen level, content of non-protein bound nitrogen, serum phosphatase activity, plasma prothrombin time). [For intoxication effects, see also Chapter 5.1.2, this report, single exposure and discussion, p. 486/492): concentration- and time-dependent events: CNS depression/ paralysis, cardiovascular collapse/shock, organ failure.]
Result	:	1. In a first set of the experiment where 15 male and female rats were exposed to 400 ppm, no female rat survived more than 10 exposures in 14 days and no male rat survived more than 40 exposures in 56 days (for analogues effects at similar concentrations compare also: Hofmann et al., 1971, and Heppel et al., 1946, other entries). 2. In additional groups of 20 male and 20 female rats each, subjected to exposure towards 1,620 mg/m3 (394 ppm) to 20 male and female Wistar rats for 2-3 days, 7 h/d, the following substance related effects were reported: High mortality of 60 %; rapid loss of body weight; slightly increased kidney

and liver weight; slightly turbid swelling of liver with single gross fatty (predominantly centrilobular) vacuoles; small increase in the total lipid content of the liver (mainly due to increased neutral lipid level); no further substance-related macroscopical or histopathological changes of the kidneys or other inner organs including lung; blood findings without any significance (urea nitrogen level, content of non-protein bound nitrogen, serum phosphatase activity, plasma prothrombin time).

[For intoxication effects, see also Chapter 5.1.2, this report, single exposure and discussion, p. 486/492): concentration- and time-dependent events: CNS depression/paralysis, cardiovascular collapse/shock, organ failure.]

3. After exposure towards 98 and 197 ppm actual concentrations (corresponding to 100 and 200 ppm nominal concentrations), respectively, the following observations were made:

No symptoms of toxicity observable; no influence on body weight and weight of inner organs; no substance related macroscopical or histopathological changes of organs; blood findings without any significance (content of non-protein bound nitrogen, urea nitrogen level, serum phosphatase activity, plasma prothrombin time); no influence on total lipid content, neutral lipid and phospholipid levels and on free and esterified hepatic cholesterol content.

4. Conclusion: Based on findings made in the rat inhalation study, the NOAEL was defined to be 200 ppm (= 822 mg/m3). Because of the high mortality, the dose of 400 ppm cannot be described as a LOAEL.

(for analogues effects at 100 ppm in rats compare also:
Hofmann et al., 1971. 200 ppm (7 h/d) were clearly toxic and lethal in another study, but to varying extent depending on the rat strain: compare Heppel et al., 1946.)

Source : Wacker - Chemie GmbH, Burghausen, Germany.
Test substance : Purity >=99.7%
Reliability : (2) valid with restrictions
Comprehensive and comparative study, basic data given, based on scientific principles meeting today standards.
Flag : Critical study for SIDS endpoint
24.06.2002 (155)

Type : Sub-chronic
Species : Rat
Sex : male/female
Strain : Sprague-Dawley
Route of admin. : inhalation: vapour
Exposure period : up to 17 wk (at 100 ppm)
Frequency of treatm. : 6 h/d, 5d/wk
Post exposure period : None
Doses : 100 ppm (411 mg/m3), 500 ppm (2055 mg/m3)
Control group : yes, concurrent vehicle
NOAEL : = 100 ppm
LOAEL : = 500 ppm
Method : other: Repeated Dose Toxicity
Year : 1970
GLP : No
Test substance : as prescribed by 1.1 - 1.4
Method : 5 male and 5 female rats were used per test concentration.
Based on the vapour pressure, DCE must be assumed to have been available as gas/vapour.

At the end of the study all animals were necropsied and livers, kidneys, lungs and, if necessary, other selected organs examined.

Analyses of TS concentration in the inhalation chamber: colorimetric (Fujiwara-Reaktion)

Result : After a 6h/d exposure to 500 ppm nominal concentration (490 ppm analytical concentration) signs of dyspnea were observable in the rats exposed. Rats died after one to five inhalations without other clinical signs of intoxication.

Substance related effects were evident as hyperemia and slight edema of lungs, fatty degeneration and necrosis of the myocardium and livers, lipoid nephrosis and lipoid degradation of the adrenals.

After a 6h/d expsoure to 100 ppm nominal concentration (99.7 ppm analytical concentration) no clinical signs of intoxication were evident in the rats exposed. No influence on body weight development, relative kidney and liver weight, ALAT-ASAT activity as well as serum urea and serum creatinin levels. No substance related macroscopical or histopathological organ changes.

Source : Wacker - Chemie GmbH, Burghausen, Germany.
Test substance : purity > 99 %
Reliability : (2) valid with restrictions
Study based on scientific principles, screening test, results conclusive in the context of the whole test programme.
Flag : Critical study for SIDS endpoint
24.06.2002 (81)

Type : Sub-chronic
Species : Rat
Sex : male/female
Strain : no data
Route of admin. : inhalation: vapour
Exposure period : 74 exposures (about 15 wk)
Frequency of treatm. : 7 h/d, 5 d/wk
Post exposure period : None
Doses : 420 mg/m3 (102 ppm)
Control group : yes, concurrent no treatment
NOAEL : ca. 100 ppm
Method : other: Repeated Dose Toxicity
Year : 1946
GLP : no data
Test substance : as prescribed by 1.1 - 1.4
Method : Comprehensive test programme including various species (see other entries): 16 female and 23 male rats were used.
Gross examination of liver, heart, lungs, kidney, adrenal glands and spleen was undertaken on all animals at the end of the study.

Based on the vapour pressure, it must be assumed that DCE was available as gas/vapour.

Result : Sublethal concentration; no impairment of body weight development; no substance-related macroscopical or histopathological organ changes.
Source : Wacker - Chemie GmbH, Burghausen, Germany.
Test substance : commercial grade
Reliability : (2) valid with restrictions
Study based on scientific principles, screening test, results conclusive in the context of the whole test programme.
Flag : Critical study for SIDS endpoint
24.06.2002 (77)

Type	:	Sub-chronic
Species	:	rat
Sex	:	male/female
Strain	:	other: Wistar and Osborne-Mendel
Route of admin.	:	inhalation: vapour
Exposure period	:	up to 86 exposures
Frequency of treatm.	:	7 h/d, 5 d/wk
Post exposure period	:	none
Doses	:	730 mg/m3 (178 ppm)
Control group	:	yes, concurrent no treatment
Method	:	other: Repeated Dose Toxicity
Year	:	1946
GLP	:	no
Test substance	:	as prescribed by 1.1 - 1.4
Method	:	Comprehensive test programme including various species (see other entries): 12 animals per test group were used. Gross examination of liver, heart, lungs, kidney, adrenal glands and spleen was undertaken on all animals at the end of the study. Based on the vapour pressure, it must be assumed that DCE was available as gas/vapour.
Result	:	In this investigation with 28 exposures to 730 mg/m3 (200 ppm nominal) results obtained in male Osborne-Mendel rats were qualitatively comparable to those seen after 86 exposures in female Wistar rats exposed to the same concentration: Results obtained in male Osborne-Mendel rats: Mortality: 8/12; 5/12 after 1, and 3/12 after 6 exposures; signs of toxicity manifested in reduced body weight, irritation of eyes, apathy, ruffled fur and in some cases congestion of the lungs; no further substance related macroscopical or histopathological organ changes; no influence on blood status. Results obtained in female Wistar rats: Mortality: 7/12; 3/12 within 9, 3/12 from 27 to 44, and 1/12 after 73 exposure; signs of toxicity were characterised by reduced body weight, eye-irritation, apathy, ruffled fur and congestion of the lungs in some cases. Fatty degeneration of the renal convoluted tubules in one animal only after 86 exposures; no further substance-related macroscopical or histopathological organ changes evident; no influence on blood status.
Source	:	Wacker Chemie GmbH, Burghausen, Germany.
Test substance	:	commercial grade
Reliability	:	(2) valid with restrictions Study based on scientific principles, screening test, results conclusive in the context of the whole test programme.
Flag	:	Critical study for SIDS endpoint

12.05.2002 (77)

Type	:	Sub-chronic
Species	:	rat
Sex	:	male/female
Strain	:	no data
Route of admin.	:	inhalation: vapour
Exposure period	:	up to 69 exposures
Frequency of treatm.	:	7 h/d, 5 d/wk
Post exposure period	:	none
Doses	:	1540 mg/m3 (375 ppm)
Control group	:	yes, concurrent no treatment
Method	:	other: Repeated Dose Toxicity

Year	:	1946
GLP	:	no
Test substance	:	as prescribed by 1.1 - 1.4
Method	:	Comprehensive test programme including various species (see other entries): 15 male and one female rats were exposed to 1540 mg/m³ (400 ppm nominal) concentration of 1,2-dichloroethane. Based on the vapour pressure, it must be assumed that DCE was available as gas/vapour. Gross examination of liver, heart, lungs, kidney, adrenal glands and spleen was undertaken on all animals at the end of the study.
Result	:	Mortality: 9/16 after 2 (1/16), 4 (6/16), 13 (1/16), and 13 exposures (1/16 animals); signs of toxicity indicated by loss of body weight, general weakness, rough fur, congestion of the lungs; no further macroscopic organ changes in dead animals; diffuse myocarditis and slight to moderate fatty degeneration of liver, kidneys and heart in one animal only which survived 69 exposures.
Source	:	Wacker - Chemie GmbH, Burghausen, Germany.
Test substance	:	commercial grade
Reliability	:	(2) valid with restrictions Study based on scientific principles, screening test, results conclusive in the context of the whole test programme.
Flag	:	Critical study for SIDS endpoint

12.05.2002 (77)

Type	:	Sub-acute
Species	:	Rat
Sex	:	no data
Strain	:	no data
Route of admin.	:	inhalation: vapour
Exposure period	:	up to 15 exposures
Frequency of treatm.	:	7 h/d, 5 d/wk
Post exposure period	:	None
Doses	:	3900 mg/m3 (949 ppm)
Control group	:	yes, concurrent no treatment
Method	:	other: Repeated Dose Toxicity
Year	:	1946
GLP	:	no data
Test substance	:	as prescribed by 1.1 - 1.4
Method	:	Comprehensive test programme including various species (see other entries): 26 male rats were exposed to 1,000 ppm nominal (948 ppm actual) concentration of 1,2-dichloroethane. Based on the vapour pressure, it must be assumed that DCE was available as gas/vapour. Gross examination of liver, heart, lungs, kidney, adrenal glands and spleen was undertaken on all animals at the end of the study.
Result	:	Mortality after 15 exposures: 20/26; signs of toxicity characterised by ruffled fur, irritation nasal mucous membrane and side position; degenerative and proliferative changes of the renal tubular epithelium and chronic splenitis; congestion as well as focal blood extravasation in the lungs; no further substance related macroscopic organ changes.
Source	:	Wacker - Chemie GmbH, Burghausen, Germany.
Test substance	:	commercial grade
Reliability	:	(2) valid with restrictions Study based on scientific principles, screening test, results conclusive in the context of the whole test programme.
Flag	:	Critical study for SIDS endpoint

12.05.2002 (77)

Type	:	Chronic
Species	:	Rat
Sex	:	male/female
Strain	:	Sprague-Dawley
Route of admin.	:	inhalation: vapour
Exposure period	:	18 months
Frequency of treatm.	:	7h/d, 5 d/wk
Post exposure period	:	
Doses	:	5, 10, 50, and 150-250 ppm [ca. 20, 40, 202 and 1012 mg/m3 (reduced to 607 mg/m3 after "a few weeks")]
Control group	:	yes, concurrent no treatment
NOAEL	:	ca. 150 ppm
LOAEL	:	> 150 ppm
NOEL	:	= 50 ppm
Method	:	other: see Maltoni et al., 1980
Year	:	1980
GLP	:	no data
Test substance	:	as prescribed by 1.1 - 1.4
Method	:	Clinico-chemical/biochemical and hematological as well as pharmacokinetic part within the scope of a comprehensive test programme (see also Maltoni et al., 1980), comprised the following measurements: from blood (by heart puncture) at 3, 6, 12, and 18 months: BUN, bili., chol., uric acid, glucose, albumin, total protein, SGOT (asp transaminase), SGPT (ala transaminase), alk. phosphatase, LDH, CPK, g-GT; Hb, hematocrit, RBC volume, total RBC, WBC count, platelet count. Animals used for 3, 6, and 18 months were 3 months of age, while those for 12 months were 14 months at the onset of the study.
Result	:	Overall, no consistent treatment-related effects that could provide evidence of liver or kidney lesions through DCE exposure were observed (see also IARC, 1999, p. 523). The inhalation exposure to 150 ppm for 18 months was not associated with marked and generalised toxicity in all rats and are in general agreement with previous studies. No clear indications of DCE-dependent abnormalities in the SGOT, SGPT, and g-GT levels and other blood parameters could be detected, for GPT and g-GT without significant differences from the controls at all doses and time intervals. For GOT, there was a non-significant, not dose-related increase in treated males at the 3rd month 8all doses); a significant increase was present in females exposed to 5 and 250-150 ppm at the 3rd month. No changes were seen after either 6 and 18 months (Tab. 4). Alk. phosphatase was decreased after 3 months, significantly in all females, not significantly in males, without dose-response relationship in either sex (all doses). At 6 and 18 months, the values of treated and control animals were not significantly different. As for CPK, slightly higher, but not statistically significant levels were seen only in males exposed to 50 and 150 ppm at 18 months. LDH levels were significantly higher after 3 months in both males and females of all treated groups, but unrelated to the doses. No dose-related changes were discernible in both sexes after 18 months (Tab. 4). For bilirubin and cholesterol, only slightly and non-significantly increased (6 months) and decreased (18 months) levels could be measured without treatment-related evidence.

Source	:	Wacker Chemie GmbH, Burghausen, Germany.
Test substance	:	Purity 99.6 %
Reliability	:	(1) valid without restriction Part of a comprehensive testing programme: compararable to guideline, sufficiently documented
Flag	:	Critical study for SIDS endpoint
12.05.2002		(85) (109) (156)
Type	:	Sub-acute
Species	:	rat
Sex	:	male/female
Strain	:	Wistar
Route of admin.	:	inhalation: vapour
Exposure period	:	7 h/d
Frequency of treatm.	:	5x
Post exposure period	:	none
Doses	:	1500 ppm
Control group	:	
Method	:	
Year	:	1945
GLP	:	no
Test substance	:	as prescribed by 1.1 - 1.4
Method	:	Whole-body exposure design. No air analysis performed, concentrations calculated from dosing and air flow. Based on the vapour pressure, it must be assumed that DCE was available as gas/vapour.
Result	:	29/29 deaths within 5 d including 21 females. Pathological findings were: Roughened fur, uncertain gait, inappetence, bloody crusts around the nose, occasional transient tremor, narcosis to loss of consciousness, dyspnoea and weakness observed during exposure. At necropsy: occasional peritoneal and pleural fluid, moderate pulmonary congestion or haemorrhage, visceral congestion, occasional necrosis and fatty degeneration of the liver and of the myocardium, in all rats degeneration and necrosis of the tubular epithelium of the kidney, and frequently congestion of the adrenal cortex.
Test substance	:	commercial grade of high purity
Reliability	:	(2) valid with restrictions Comparative study based on scientific principles, results conclusive in the context of the whole test programme.
Flag	:	Critical study for SIDS endpoint
12.05.2002		(77)
Type	:	Chronic
Species	:	Rat
Sex	:	male/female
Strain	:	Sprague-Dawley
Route of admin.	:	inhalation: vapour
Exposure period	:	2 years
Frequency of treatm.	:	7 h/d, 5 d/wk
Post exposure period	:	
Doses	:	50 ppm
Control group	:	yes, concurrent no treatment
NOAEL	:	= 50 ppm
NOEL	:	ca. 50 ppm
Method	:	other: inhalation study
Year	:	1990
GLP	:	no data

Test substance	:	as prescribed by 1.1 - 1.4
Method	:	Comparative study testing DCE alone and in coadministration of disulfiram (in the diet) or ethanol (in drinking water) at a sublethal/subtoxic EDC dose. The distribution of EDC within exposure chambers was analysed on hourly basis and varied by less than 6 %. Gross and histopathology was comprehensive and corresponded to guidelines. The study comprised blood analysis for DCE concentration and kinetics (0.25 and 2 h post-exposure).
Result	:	No exposure-related effect on survival, no significant inhibitory effects on food and water consumption, no histological changes found in the liver, bile duct, kidney, or any other tissue. Blood levels of unaltered 1,2-dichloroethane 15 minutes after the end of a 7-h exposure to 50 ppm were 0.26 to 0.28 µg/mL in male and females.
Test substance	:	Purity >99%
Reliability	:	(2) valid with restrictions Study based on scientific principles and current standard, no full guideline study with respect to dose groups, focussed upon mechanistic aspects, results conclusive
Flag	:	Critical study for SIDS endpoint

25.06.2002 (43)

Type	:	Sub-chronic
Species	:	mouse
Sex	:	male/female
Strain	:	CD-1
Route of admin.	:	drinking water
Exposure period	:	90 d
Frequency of treatm.	:	daily
Post exposure period	:	none
Doses	:	20, 200 or 2000 mg/l (calculated time weighted average doses: 3, 24 or 189 mg/kg bw /d)
Control group	:	yes, concurrent no treatment
NOAEL	:	ca. 190 mg/kg bw
NOEL	:	= 24 mg/kg bw
Method	:	other: Repeated Dose Toxicity
Year	:	1982
GLP	:	no
Test substance	:	as prescribed by 1.1 - 1.4
Remark	:	Study was undertaken with special emphasis on the effects on organs of the lymphoreticular system. Substance was administered in drinking water. Four-week-old mice were used with exposures beginning at 5 weeks of age.48 animals (random -bred) were used as deionised-water control, 32 animals used per test groups and the Dexamethasone group (as positive control) (legend fig 3 and 4). Humoral and cell-mediated immune status were evaluated by the ability of spleen cells to produce IgM antibody forming cells (AFC) against sheep erythrocytes (sRBC) and the delayed-type-hypersensitivity (DTH) response to sRBC, respectively.
Result	:	The NOAEL refers only to the endpoints (immune responsiveness) considered in this study. The NOEL relates to depression of body weight gain seen at 189 mg/kg/d. Dose-dependent inhibition of body weight development and reduction of water consumption (low dose: 5.5 ml/animal/day; mid dose: 4.2 ml/animal/day; high dose: 2.8 ml/animal/day; control: 5.0 ml/animal/day). No influence on absolute or relative weight of

liver, spleen, lungs, kidneys and thymus as well as erythrocyte and leukocyte count, haemoglobin content, hematocrit and prothrombin time.

A positive trend towards a suppression of the immune system was indicated by a decline in the dose-dependent haemagglutination titer, but awhich was not considered statistically significant.

In conclusion, in the 90 day study no adverse effects were observable on both humoral and cell-mediated immunity.

Source : Wacker - Chemie GmbH, Burghausen, Germany.
Test substance : from Aldrich Chemical Co.
Reliability : (2) valid with restrictions
Study based on scientific principles, focussed upon immune responsiveness, largely meeting current standards, basic data given.
Flag : Critical study for SIDS endpoint
24.06.2002 (119)

Type : Sub-chronic
Species : Mouse
Sex : male/female
Strain : B6C3F1
Route of admin. : drinking water
Exposure period : 13 wk
Frequency of treatm. : Continuous
Post exposure period : None
Doses : 500, 1000, 2000, 4000 or 8000 mg/l (m: 249, 448, 781, 2710 or 4207 mg/kg bw/d; f: 244, 647, 1182, 2478 or 4926 mg/kg bw/d) [Tab. 15]
Control group : yes, concurrent no treatment
NOAEL : ca. 780 mg/kg bw
LOEL : ca. 250 mg/kg bw
Method : other: Repeated Dose Toxicity (NTP/USA)
Year : 1991
GLP : Yes
Test substance : as prescribed by 1.1 - 1.4
Remark : 10 animals/sex/dose group were used.
Result : The test substance caused minimal toxicity.
A NOAEL of 2000 ppm has been established by the authors, corresponding to corresponding to about 780 mg/kg bw/d and relating to a dose-dependent increase in renal tubular regeneration in male mice only, disregarding isolated cases at 500 to 2000 ppm as biologically relevant: 0/10 (contr.), 1/10 (500 ppm), 2/10 (1000 ppm), 2/10 (2000 ppm), 8/10 (4000 ppm), and 9/10 (8000 ppm) (Tab. 14, p. 30; Discussion, p. 34). The NOAEL for females (approx. 2500 mg/kg bw) is based on mortality at the upper dose.

No NOEL was established: The LOEL of about 240 - 250 mg/kg/d is based on abs. and rel. increases in kidney weights already evident in 500-ppm groups and considered as substance-related, but not yet pathological (Tab. 13, p.30).

Clinical signs: none.
Mortality: 9/10 females in the highest dose group.
Mean body weight development: inhibition at 500 ppm and higher (males) and at 1000 ppm and higher (females), more pronounced in males.
Average water consumption remained unaffected in all dose groups.
Statistically significant increases in absolute and relative kidney weights in all dose groups of females ($P<0.01$) and at 1000 ppm and higher in males ($P<0.05$ and <0.01); statistically significant increases of absolute liver weights in males and females exposed to 4000 ppm and above ($P<0.05$), and of relative liver weights in all dose groups of males ($P<0.01$) and in

females exposed to 1000 ppm and above (P<0.05 and <0.01).

Pathological findings were minimal to moderate and only observed in the kidneys of male animals (NTP, 1991, p. 28, and Tab. 14):
At 8000 ppm, 5/10 to 10/10 animals showed tubular regeneration, hyaline urinary cylinders, dilatation of the tubules and focal mineralisation in the renal papilla of all dose groups.
At 4000 ppm, only tubular regeneration was prominent in 8/10 animals.
At all lower doses, only tubular regeneration was seen in 1/10 (500 ppm) and 2/10 animals (each at 1000 and 2000 ppm).

No such effects occurred in the male control group. A historical control range of tubular regeneration is not presented.

Hematology and blood biochemistry: no data.

Source : Wacker - Chemie GmbH, Burghausen, Germany.
Test substance : Purity >99%
Reliability : (2) valid with restrictions
Largely in compliance with guideline study, National Toxicology Program, but hematology and blood biochemistry not performed [s. Tab. 4, p. 17]; very limited documentation.
Flag : Critical study for SIDS endpoint
24.06.2002 (129)

Type : Sub-acute
Species : mouse
Sex : male
Strain : CD-1
Route of admin. : gavage
Exposure period : 14 d
Frequency of treatm. : daily
Post exposure period : none
Doses : 4.89 or 48.9 mg/kg bw/ d
Control group : yes, concurrent vehicle
Method : other: Repeated Dose Toxicity
Year : 1982
GLP : no
Test substance : as prescribed by 1.1 - 1.4
Remark : Study was undertaken with special emphasis on the effects on organs of the lymphoreticular system. Substance was administered in drinking water. No information available concerning number of animals used per sex and dose group. Four-week-old mice were used with exposures beginning at 5 weeks of age.

Humoral and cell-mediated immune status were evaluated by the ability of spleen cells to produce IgM antibody forming cells (AFC) against sheep erythrocytes (sRBC) and the delayed-type-hypersensitivity (DTH) response to sRBC, respectively.
Result : No influence on body weight and the weight of liver, spleen, lungs, kidneys, thymus and brain; significant reduction in the number of leucocytes by 30 % in the highest dose group; no influence on hematocrit, hemoglobin-, fibrinogen- and urea nitrogen levels of the blood; no influence on prothrombin time and on the activity of lactate dehydrogenase and alanine-aminotransferase.

1,2-Dichloroethane caused an apparent dose-dependent suppression of humoral immune response with about 25 and 40% suppression at 4.9 and 49 mg/kg bw /d, respectively. In contrast cell-mediated immune response was only slight and not dose-dependent.

No NOAEL can be defined because of the unclear biological relevance (compare also other entry: 90-d drinking water study).

Source : Wacker - Chemie GmbH, Burghausen, Germany.
Test substance : from Aldrich Chemical Co.
Reliability : (3) invalid
Study based on scientific principles, focussed upon immune responsiveness, largely meeting current standards, basic data given. However, note: In light of the considerable fluctuations observed in mean values of the vehicle controls, the biological relevance of the findings appears to be poor.
Flag : non confidential
06.05.2002 (119)

Type : Sub-chronic
Species : Rabbit
Sex : male/female
Strain : no data
Route of admin. : inhalation: vapour
Exposure period : up to 125 exposures (see Results)
Frequency of treatm. : 7 h/d, 5 d/wk
Post exposure period : None
Doses : 200 ppm (730 mg/m3), 400 ppm (1540 mg/m3), and 1000 ppm (3900 mg/m3)
Control group : yes, concurrent no treatment
NOAEL : ca. 200 ppm
Method : other: Repeated-Dose study
Year : 1946
GLP : No
Test substance : as prescribed by 1.1 - 1.4
Remark : Comparative study including rats, mice, rabbits, guinea pigs dogs, cats, and monkeys: 5 - 6 rabbits were used per test group.
Based on the vapour pressure, it must be assumed that DCE was available as gas/vapour.
Result : At 200 ppm (125 exposures), normal behaviour, normal weight development as well as generally good condition were observed. No remarkable findings upon gross and microscopic tissue examination.

At 400 ppm, 5/5 animals died, 1/5 after 1 exposure (no reason specified), 4/5 after 89 to 97 exposures. The rabbits showed no remarkable behavioral signs of intoxication before death. No data on histopathology documented.

At 1000 ppm, 1/6 animals survived 64 exposures. 5/6 animals died, 2/5 after 2, 2/5 after 15 and 20, respectively, 1/5 after 43 exposures. Autopsy and histopathology revealed no obvious effects from exposure.
Test substance : Commercial grade
Reliability : (2) valid with restrictions
Study based on scientific principles, screening test, results conclusive in the context of the whole test programme.
Flag : Critical study for SIDS endpoint
12.05.2002 (77)

Type : Chronic
Species : rabbit
Sex : male/female
Strain : other: Albino
Route of admin. : inhalation: vapour
Exposure period : up to 165 exposures (<= 46 wk) (see Results)
Frequency of treatm. : 7 h/d; 5d/wk
Post exposure period : none
Doses : 100 ppm (405 mg/m3), and 400 ppm (1620 mg/m3)

Control group	:	no data specified
NOAEL	:	= 400 ppm
Method	:	other: Repeated-Dose study
Year	:	1951
GLP	:	no
Test substance	:	as prescribed by 1.1 - 1.4
Method	:	Comparative study including rats, rabbits, guinea pigs, and monkeys: 3 rabbits (2 male/1 female) per test group were used. Whole-body exposure design. Based on the vapour pressure, it must be assumed that DCE was available as gas/vapour. Analysis: By means of continuously recording analyser (combustion analysis), it was shown that in every case the vapour was uniformly held within 10 % of the desired concentration of the TS.
Result	:	At 100 ppm (178 exposures within 248 d; approx. 35 wk), no evidence of adverse effects as judged by general appearance and behaviour, growth, final body and organ weights, and gross and microscopic examination of the tissues. Also blood (bio)chemical parameters were in normal range. At 400 ppm (165 exposures within 232 d), no evidence of adverse effects as judged by general appearance and behaviour, mortality, and growth, final body and organ weights, and gross and microscopic examination of the tissues. Also blood (bio)chemical parameters were in normal range.
Test substance	:	Purity 99.7 %
Reliability	:	(2) valid with restrictions Study based on scientific principles, screening test, results conclusive in the context of the whole test programme.
Flag	:	Critical study for SIDS endpoint

24.06.2002 (155)

Type	:	Sub-chronic
Species	:	Rabbit
Sex	:	male/female
Strain	:	other: "Bunte"
Route of admin.	:	inhalation: vapour
Exposure period	:	up to 17 wk
Frequency of treatm.	:	6 h/d, 5 d/wk
Post exposure period	:	None
Doses	:	100 and 500 ppm
Control group	:	yes, concurrent no treatment
NOAEL	:	ca. 400 mg/kg bw
Method	:	other: Repeated Toxicity
Year	:	1970
GLP	:	no
Test substance	:	as prescribed by 1.1 - 1.4
Method	:	2 male and 2 female rabbits were used per test concentration. At the end of the study all animals were necropsied and livers, kidneys, lungs and, if necessary, other selected organs examined. Analyses of TS concentration in the inhalation chamber: colorimetric (Fujiwara-Reaktion) Based on the vapour pressure, it must be assumed that DCE was available as gas/vapour.
Result	:	After a 6h/d exposure to 500 ppm nominal concentration (490 ppm analytical concentration) no clear signs of intoxication were observable. 3/4 rabbits died after 10 - 17 inhalations without distinct clinical signs of intoxication. Substance-related effects (based upon blood parameters, organ weights, and histopathology) were not evident for liver and kidney, only heart

dilatation was noted.

After a 6h/d expsoure to 100 ppm nominal concentration (99.7 ppm analytical concentration), no clinical signs of intoxication were evident. No substance-related, pathological macroscopical or histopathological organ changes. 1/4 rabbits showed some increase in serum urea, but not considered as relevant.

Test substance : Purity >99 %
Reliability : (2) valid with restrictions
Comparative study based on scientific principles, screening test, results conclusive in the context of the whole test programme.
Flag : Critical study for SIDS endpoint
12.05.2002 (81)

Type : Sub-chronic
Species : Dog
Sex : Female
Strain : no data
Route of admin. : inhalation: vapour
Exposure period : 173 - 177 exposures (24 - 25 weeks)
Frequency of treatm. : 7 h/d, 5 d/wk
Post exposure period : None
Doses : 1540 mg/m3 (375 ppm)
Control group : yes, concurrent no treatment
NOAEL : ca. 400 ppm
Method : other: Repeated Dose Toxicity
Year : 1946
GLP : no data
Test substance : other TS: commercial grade
Method : Comparative study including rats, rabbits, guinea pigs, dogs, and monkeys: Whole-body exposure design. Six female dogs of unknown strain were used. Based on the vapour pressure, it must be assumed that DCE was available as gas/vapour.
Result : Concentration corresponds to sublethal concentration; no mortalities; no impairment of food uptake, body weight gain, nerve system and eye background and cornea; no influence on arterial blood pressure, on bromosulphaleine excretion rate, hematological and biochemical parameters (erythrocyte and leukocyte count, hemoglobin levels, differential blood count, icterus index, prothrombin time as well as protein-, albumin-, globulin- and non-protein bound serum nitrogen levels) and urinary status (pH, urobilin- and urobilinogen-level); no substance related macroscopical organ changes, slight fatty degeneration of the liver in 5/6 animals and the kidneys in 1/6 animals.
Source : Wacker - Chemie GmbH, Burghausen, Germany.
Reliability : (2) valid with restrictions
Study based on scientific principles, screening because of the low number of animals; results conclusive in the context of the whole test programme.
Flag : Critical study for SIDS endpoint
12.05.2002 (77)

Type : Sub-chronic
Species : Dog
Sex : Female
Strain : no data
Route of admin. : inhalation: vapour
Exposure period : 23 - 66 exposures (4 - 13 weeks)
Frequency of treatm. : 7 h/d, 5 d/wk
Post exposure period : None
Doses : 3900 mg/m3 (949 ppm)
Control group : yes, concurrent no treatment

Method	:	other: Repeated Dose Toxicity
Year	:	1946
GLP	:	no data
Test substance	:	other TS: commercial grade
Method	:	Comparative study including rats, rabbits, guinea pigs, dogs, and monkeys: Whole-body exposure design. Six female dogs of unknown strain were used. Based on the vapour pressure, it must be assumed that DCE was available as gas/vapour.
Result	:	Mortality: 2/6 (30th and 43th exposure); substance related effects were corneal turbidity, apathy, coma; no influence on hematological parameters such as erythrocyte and leucocyte count, hemoglobin level, differential blood count as well as urinary status (pH, specific weight, albumin-, glucose-, acetone urobilin- and urobilinogen levels); pathologically fatty degeneration of the liver and slight focal myocarditis was evident in one animal.
Source	:	Wacker - Chemie GmbH, Burghausen, Germany.
Reliability	:	(2) valid with restrictions Study based on scientific principles, screening because of the low number of animals; results conclusive in the context of the whole test programme.
Flag	:	Critical study for SIDS endpoint

12.05.2002 (77)

Type	:	Chronic
Species	:	guinea pig
Sex	:	male/female
Strain	:	no data
Route of admin.	:	inhalation: vapour
Exposure period	:	up to 180 exposures (<= approx. 45 wk) (see Results)
Frequency of treatm.	:	7 h/d; 5d/wk
Post exposure period	:	None
Doses	:	100 (405 mg/m3), 200 ppm (810 mg/m3), and 400 ppm (1620 mg/m3)
Control group	:	yes, concurrent no treatment
NOAEL	:	ca. 200 ppm
NOEL	:	ca. 100 ppm
Method	:	other: Repeated-Dose study
Year	:	1951
GLP	:	No
Test substance	:	as prescribed by 1.1 - 1.4
Method	:	Comparative study including rats, rabbits, guinea pigs, and monkeys: 8 guinea pigs per sex and test group were used. Whole-body exposure design. Analysis: By means of continuously recording analyser (combustion analysis), it was shown that in every case the vapour was uniformly held within 10 % of the desired concentration of the TS. Based on the vapour pressure, it must be assumed that DCE was available as gas/vapour.
Result	:	At 100 ppm, the male animals tolerated 121 exposures (170 d), the female animals 162 exposures (226 d) and exhibited no evidence of adverse effects as judged by mortality, growth and hematological and blood chemical examinations, final body and organ weights, and gross and microscopic examination of the tissues. At 200 ppm, animals tolerated 180 exposures (246 d), but body weight gain was slightly to moderately retarded, more pronounced in males. Organ weights showed no deviations. Blood parameters were in normal range. Microscopic examination of tissues were without pathological findings, but half of the animals exhibited slight parenchymatous degeneration of the liver, with a few fat vacuoles diffusely distributed. A slight increase over controls was found in total lipid, phospholipid, neutral fat, and free and

esterified cholesterol.

At 400 ppm, animals experienced severe intoxication: no male survived more than 10 exposures (14 d), and no female animal 24 exposures (32 d). Signs of intoxication: rapid loss in body weight and increase in weights of liver and kidneys. Histopathology revealed slight to moderate central fatty degeneration of the liver and slight to moderate cloudy swelling of the tubular epithelium of the kidneys. No alterations in other tissues noted. The average blood nonprotein nitrogen was 91.6 ml vs. 61.6 mg/100 ml in the control; average BUN was 42.8 vs. 20.2 mg/100 ml.

No significant difference in serum phosphatase and plasma prothrombin clotting time.

Test substance : Purity >=99.7%
Reliability : (2) valid with restrictions
Comprehensive and comparative study, basic data given, based on scientific principles largely meeting current standards.
Flag : Critical study for SIDS endpoint
24.06.2002 (155)

Type : Sub-chronic
Species : guinea pig
Sex : male/female
Strain : no data
Route of admin. : inhalation: vapour
Exposure period : up to 124 exposures (<= approx. 25 wk) (see Results)
Frequency of treatm. : 7 h/d, 5 d/wk
Post exposure period : None
Doses : 100 ppm (420 mg/m3); 200 ppm (730 mg/m3); 400 ppm (1540 mg/m3)
Control group : yes, concurrent no treatment
NOAEL : ca. 100 ppm
LOAEL : ca. 200 ppm
Method : other: Repeated-Dose study
Year : 1946
GLP : No
Test substance : as prescribed by 1.1 - 1.4
Method : Comparative study including rats, mice, rabbits, guinea pigs dogs, cats, and monkeys: variable numbers of guinea pigs from 14 to 20 animals were used per sex and test group. Based on the vapour pressure, it must be assumed that DCE was available as gas/vapour.
Result : At 100 ppm, gross autopsy as well as histopathology of 10 treated animals (>69 exposures) were negative vs. controls. (note: The test was impaired by a disease characterized by enlarged caseous glands in the neck, associated by depression of growth and a mortality of about 10 % in treated as well as control animals.)

At 200 ppm, 5/14 animals died vs. 1/18 in the control (1/14 after 5 exposures, 4/14 from 73 to 115 exposures). Microscopic examination of the 9 surviving animals (after 124 exposures) gave no findings in 5, pulmonary congestion in 4, additionally necrosis and hemorrhage of the liver in one, and necrosis and hemorrhage of the adrenal cortex in one other animal. Of 5 control animals, 2 showed slight fatty infiltration of liver and myocardium, while 3 were negative.

At 400 ppm, 14/20 animals died vs. 3/30 control animals, (9/20 from 8 to 14 exposures, 2/20 at 28 exposures, 3/20 from 42 to 65 exposures). Deceased animals showed moderate fatty degeneration of the livers and kidneys or slight fatty degeneration of the heart. No effects on lung reported. Surviving animals (70 exposures) were normal except one with slight fatty degeneration of the liver.

Test substance	:	commercial grade
Reliability	:	(2) valid with restrictions Study based on scientific principles, results conclusive in the context of the whole test programme.
Flag	:	Critical study for SIDS endpoint
24.06.2002		(77)

Type	:	Sub-chronic
Species	:	guinea pig
Sex	:	male/female
Strain	:	other: Pirbright-white
Route of admin.	:	inhalation: vapour
Exposure period	:	up to 17 wk
Frequency of treatm.	:	6 h/d, 5d/wk
Post exposure period	:	none
Doses	:	100 and 500 ppm
Control group	:	yes, concurrent no treatment
NOAEL	:	ca. 400 mg/m³
Method	:	other: Repeated Dose Toxicity
Year	:	1970
GLP	:	no
Test substance	:	as prescribed by 1.1 - 1.4
Method	:	5 male and 5 female guinea pigs were used per test concentration. At the end of the study all animals were necropsied and livers, kidneys, lungs and, if necessary, other selected organs examined. Analyses of TS concentration in the inhalation chamber: colorimetric (Fujiwara-Reaktion) Based on the vapour pressure, it must be assumed that DCE was available as gas/vapour.
Result	:	After a 6h/d exposure to 500 ppm nominal concentration (490 ppm analytical concentration) signs of apathy and weight loss were observable. 9/10 guinea pigs died after 4 to 14 inhalations without other clinical signs of intoxication. Substance related effects were evident as fatty degeneration and necrosis of the myocardium and livers, lipoid nephrosis and lipoid depletion of the adrenals. After a 6h/d expsoure to 100 ppm nominal concentration (99.7 ppm analytical concentration) no clinical signs of intoxication were evident. No substance-related, pathological macroscopical or histopathological organ changes.
Test substance	:	Purity >99 %
Reliability	:	(2) valid with restrictions Comparative study based on scientific principles, screening test, results conclusive in the context of the whole test programme.
Flag	:	Critical study for SIDS endpoint
13.05.2002		(81)

Type	:	Sub-chronic
Species	:	Monkey
Sex	:	Male
Strain	:	other: Rhesus
Route of admin.	:	Inhalation
Exposure period	:	see Results
Frequency of treatm.	:	7 h/d; 5 d/wk
Post exposure period	:	up to 148 exposures (<= approx. 30 wk)

Doses	:	100 ppm (405 mg/m3) and 400 ppm (1620 mg/m3)
Control group	:	Yes
NOAEL	:	= 100 ppm
Method	:	other: Repeated-Dose study
Year	:	1951
GLP	:	No
Test substance	:	as prescribed by 1.1 - 1.4
Method	:	Comparative study including rats, rabbits, guinea pigs, and monkeys: 2 monkeys were used per test concentration. Whole-body exposure design. Analysis: By means of continuously recording analyser (combustion analysis), it was shown that in every case the vapour was uniformly held within 10 % of the desired concentration of the TS.
Result	:	At 100 ppm, two animals subjected to 148 exposures in 212 days exhibited no evidence of adverse effects as judged by general appearance and behaviour, periodic haematological examination, growth, final body and organ weights, and gross and microscopic examination of the tissues. At 400 ppm, the two animals experienced rapid and severe intoxication: one monkey was killed in moribund state after 8 exposures and showed enlargement of the liver with increases in neutral fat and esterified cholesterol content, marked degeneration and vacuolation of liver cells, moderate degeneration of the epithelium of the renal tubules with cast formation and distention of the lumens and prolonged plasma prothrombin clotting time. The second monkey, killed after 12 exposures, showed similar changes, but of considerably milder degree. Hematological values obtained on these monkeys, either midway in the experiment or terminally, showed no significant changes as compared with values obtained in one to three pre-exposure examinations.
Test substance	:	Purity >=99.7%
Reliability	:	(2) valid with restrictions Study based on scientific principles, screening because of the low number of animals, results conclusive in the context of the whole test programme.
Flag	:	Critical study for SIDS endpoint

24.06.2002 (155)

Type	:	Sub-chronic
Species	:	monkey
Sex	:	no data
Strain	:	other: Rhesus
Route of admin.	:	inhalation: vapour
Exposure period	:	up to 125 exposures (<= 25 wk)
Frequency of treatm.	:	7 h/d
Post exposure period	:	none
Doses	:	200 ppm (av. 730 mg/m3); 1000 ppm (av. 3900 mg/m3)
Control group	:	no data specified
NOAEL	:	ca. 200 ppm
Method	:	other: Repeated-Dose study
Year	:	1946
GLP	:	no
Test substance	:	as prescribed by 1.1 - 1.4
Method	:	Comparative study including rats, mice, rabbits, guinea pigs dogs, cats, and monkeys. Based on the vapour pressure, it must be assumed that DCE was available as gas/vapour.
Remark	:	Comparative study including rats, mice, rabbits, guinea pigs dogs, cats, and monkeys: 2 monkeys were used per test concentration. Reduced test

programme without examination of blood parameters.

Result : At 1000 ppm, one animal died already after 2 exposures while the second survived 32 exposures.

The first showed necrosis, hemorrhage and fatty degeneration of the liver, and very slight fatty changes in the renal tubular epithelium. The second - towards the end – refused to eat, lost weight and finally became comatose. Microscopic sections showed fatty degeneration of the liver, focal myocarditis and slight fatty changes in the kidney.

200-ppm exposure was well tolerated without signs of inappetence and developed normal. At autopsy, one of them showed focal calcification of the adrenal medulla and both showed fine fat droplets in liver and myocardium.

Reliability : (2) valid with restrictions
Study based on scientific principles, screening because of the low number of anuimals, results conclusive in the context of the whole test programme.

Flag : Critical study for SIDS endpoint
24.06.2002 (77)

5.5 GENETIC TOXICITY 'IN VITRO'

Type : Ames test
System of testing : Salmonella typhimurium TA 1530, TA 1535, 1538
Test concentration : <= 2573 ug/plate
Cycotoxic concentr. :
Metabolic activation : without
Result : positive
Method : other: Spot Test
Year : 1974
GLP : no
Test substance : no data
Result : With a dose of 990 µg/plate no mutagenic effects were observable in the absence of metabolic activation in Salmonella typhimurium strain TA 1538, while mutation rate was doubled in TA 1530 and TA 1535 compared with the water control. There was evidence of a dose-related increase in mutation rate.

Results principally in line with those by Barber et al., 1981 (see other entry).

Source : Wacker - Chemie GmbH, Burghausen, Germany.
Reliability : (2) valid with res trictions
Comparative non-standard study, limited documentation, based on scientific principles: dose selection apparently insufficient (compare Barber et al., 1981).

Flag : Critical study for SIDS endpoint
24.06.2002 (27)

Type : Ames test
System of testing : Salmonella typhimurium TA 98, TA 100, TA 1535, TA 1537, TA 1538
Test concentration : <= 3563 ug/plate
Cycotoxic concentr. :
Metabolic activation : with and without
Result : Negative
Method : other: Plate Incorporation Assay
Year : 1979
GLP : No
Test substance : as prescribed by 1.1 - 1.4

Remark	:	S9 mix was prepared from livers of male Sprague-Dawley rats pretreated with five subsequent i.p. injections of 500 mg/kg Aroclor 1254. Positive controls were included and performed with MNNG, benzo[a]pyrene, 2-amino-anthracene and N-nitrosomorpholine.
Source	:	Wacker - Chemie GmbH, Burghausen, Germany.
Test substance	:	commercial, from Merck
Reliability	:	(2) valid with restrictions Comparable to guideline study, limited documentation.
Flag	:	non confidential

15.05.2002 (95)

Type	:	Ames test
System of testing	:	Salmonella typhimurium TA 1535
Test concentration	:	1.98 mg/plate; 3.96 mg/plate
Cycotoxic concentr.	:	
Metabolic activation	:	with and without
Result	:	positive
Method	:	other: Preincubation Assay
Year	:	1980
GLP	:	no data
Test substance	:	as prescribed by 1.1 - 1.4
Method	:	S9 mix was prepared from livers of Sprague-Dawley rats pretreated with three subsequent i.p. injections of 80 mg/kg phenobarbital prior to sacrifice. Positive controls comprised N-methyl-N´-nitro-N-nitroso-guanidine (MNNG) and 2-anthramine.
Result	:	weakly positive effects were reported. Reduced glutathione was included in the incubation system.
Source	:	Wacker - Chemie GmbH, Burghausen, Germany.
Test substance	:	Purity 99.3 %
Reliability	:	(2) valid with restrictions No standard study, based on scientific principles, test system modified for scientific purposes. Result in line with findings by others.
Flag	:	Critical study for SIDS endpoint

17.05.2002 (68)

Type	:	Ames test
System of testing	:	Salmonella typhimurium TA 98, TA 100, TA 1535, TA 1537, TA 1538
Test concentration	:	3.6 and 9 mg/plate
Cycotoxic concentr.	:	
Metabolic activation	:	with and without
Result	:	Ambiguous
Method	:	other: Standard Plate Incorporation Assay - Closed System
Year	:	1980
GLP	:	No
Test substance	:	no data
Method	:	S9 mix was prepared from livers of rats pretreated with Aroclor 1254. Positive controls comprised N-methyl-N´-nitro-N-nitrosoguanidine MNNG), 2-amino-anthracene (ANTH), 2-nitrofluorene (NF), 9-aminoacridine (9-AA) and 2-aminofluorene (2-AF)
Result	:	A weak but dose-related response was observable with strains TA1535 and TA100 in the absence and presence of a metabolic activation system when plates were incubated with 1,2-dichloroethane inside a desiccator. The response for TA100 was only slightly above background with plus 20 revertants (data not shown; background for TA100 in two other experiments were 144 or 114 revertants/plate without metabolic activation and 177 or 124 revertants with metabolic activation). The maximal response in strain TA1535 is given with a doubling of mutant colonies.

Source : Wacker - Chemie GmbH, Burghausen, Germany.
Test substance : from ChemService, not further specified
Reliability : (2) valid with restrictions
Comparable to guideline study, limited documentation; result in line with findings by others.
Flag : Critical study for SIDS endpoint
25.06.2002 (125)

Type : Ames test
System of testing : Salmonella typhimurium TA 98, TA 100, TA 1535 (standard plate assay)
Test concentration : 6.25/12.5/31.25/62.5/125 mg/plate
Cycotoxic concentr. :
Metabolic activation : with and without
Result : Negative
Method :
Year : 1981
GLP : no data
Test substance : as prescribed by 1.1 - 1.4
Method : S9 mix was prepared from livers of Sprague-Dawley rats pretreated with Arochlor 1254.

Positive controls were:
ethyl methanesulphonate for TA 1535;
9-aminoacridine for TA 1537;
4-nitro-o-phenylenediamine for TA 1538 and TA 98;
methyl methanesulphonate for TA 100;
2-aminoanthrancene for all strains with S9 mix.

Result : 100 µl (125 mg) is given as the highest non-toxic concentration. With S. typhimurium strains TA98, TA100 and TA1535, no mutagenic effects were observed both in the presence and absence of metabolic activation (Fig. 2).
Source : Wacker - Chemie GmbH, Burghausen, Germany.
Test substance : analytical grade
Reliability : (2) valid with restrictions
Comparative non-standard test design, limited documentation, based on scientific principles; result in line with findings by others.
Flag : Critical study for SIDS endpoint
25.06.2002 (135)

Type : Escherichia coli reverse mutation assay
System of testing : Escherichia coli WP2 uvrA
Test concentration : <= 990 ug/ml
Cycotoxic concentr. :
Metabolic activation : Without
Result : Ambiguous
Method : other: Liquid Incubation
Year : 1980
GLP : no data
Test substance : as prescribed by 1.1 - 1.4
Method : Comparative study including a broad spectrum of chemicals, seeking to correlate DNA-alkylation and mutagenicity.
Remark : 1,2-Dichloroethane was found to reveal no DNA-alkylating properties in the test without metabolic activation. Furthermore, the compound was shown to have only a weak mutagenic potential under the conditions of the study: 2 % of epichlorohydrin, less than 3 % of dibromoethane, and identical to that of acrolein.
Source : Wacker - Chemie GmbH, Burghausen, Germany.
Test substance : analytical grade
Reliability : (2) valid with restrictions
Screening study based on scientific principles, results conclusive in relation to findings with other compounds.

Flag : Critical study for SIDS endpoint
15.05.2002 (72)

Type : HGPRT assay
System of testing : Chinese hamster ovary (CHO) cells
Test concentration : 98.9 µg/ml, 148.4 µg/ml, 197.9 µg/ml, 247.4 µg/ml, 494.5 µg/ml, 989 µg/ml, 1979 µg/ml, 2474 µg/ml, 3958.4 µg/ml, 4948 µg/ml;
Cycotoxic concentr. : 50 mM (4950 µg/ml)) (Cell survival reduced to 50%)
Metabolic activation : with and without
Result : Positive
Method : other: 6-Thioguanine resistance test
Year : 1981
GLP : no data
Test substance : as prescribed by 1.1 - 1.4
Method : Cells were subcultured on days 1, 3 and 6 after mutagen treatment and selected for 6-TG resistance on day 8. All experiments were performed under gold light to minimise mutagenic effects mediated by cool white light.

EMS (ethyl methanesulphonate) and DMN (Dimethylnitroso amine) were enclosed in these experiments as positive controls in the absence and presence of metabolic activation, respectively. Metabolic activation was achieved by S9 mix from rat livers pretreated with Aroclor 1254.

In parenthesis the relative cloning efficiency of CHO-cells are given:
With metabolic activation: 98.9 µg/ml (103), 148.4 µg/ml (94), 197.9 µg/ml,(70) 247.4 µg/ml (75), 296.9 µg/ml (29) Without metabolic activation: 494.5 µg/ml (113), 989 µg/ml (96), 1979 µg/ml (96), 2474 µg/ml (90), 3958 µg/ml (93), 4948 µg/ml (81).
Result : Increases in mutant frequency were concentration-dependent in both the presence and absence of S9.

Positive results with metabolic activation were found in the mM-range (100 - 300 µg/ml), while without activation about 10- to 20-fold higher concentrations were needed (Fig 3).
Source : Wacker - Chemie GmbH, Burghausen, Germany.
Test substance : Commercial, reagent grade, from Matheson Coleman and Bell
Reliability : (2) valid with restrictions
Comparable to guideline study, sufficient documentation
Flag : Critical study for SIDS endpoint
25.06.2002 (167)

Type : Chromosomal aberration test
System of testing : Chinese hamster lung (CHL) fibroblasts
Test concentration : 0, 500, 1000, 2000, 4000, 6000 µg/ml (see: Method)
Cycotoxic concentr. :
Metabolic activation : with and without
Result : positive
Method : other: no data
Year : 1985
GLP : no data
Test substance : no data
Method : Comparative study including a broad spectrum of chemicals:
S9-mix was prepared from PCB (KC400)-induced rat livers.

Without metabolic activation: 0, 500, 1000, 2000, 4000, and 6000 µg/ml in DMSO; 24, 48 h treatment time; and 0, 250, 500, 1000 µg/ml in Saline, 24, 48 h treatment time.

With metabolic activation: 0, 500, 1000, 2000, 4000 µg/ml in DMSO; probably 6-h treatm ent time (p. 64; Gregg et al., 1993).

Result	:	Without S9-mix, no increases in chromosomal aberrations up to 4 mg/ml following 24- and 48-h exposure, ambiguously positive at 6000 µg/ml. With S9-mix, a dose-related increase in chromosomal effects was noted at 1000 and 2000 µg/ml. No effect at 500 µg/ml. 4000 µg/l was cytotoxic (no mitosis). The structural abnormalities comprised primarily significant increases in chromatid breaks and chromatid exchanges, but no chromosomal breaks or exchanges.
Source	:	Wacker - Chemie GmbH, Burghausen, Germany.
Reliability	:	(2) valid with restrictions Comparable to guideline study, linguistic limitations.
Flag	:	Critical study for SIDS endpoint
25.06.2002		(66) (154)

Type	:	Unscheduled DNA synthesis
System of testing	:	rat primary hepatocytes
Test concentration	:	>= 13 ug/ml
Cycotoxic concentr.	:	
Metabolic activation	:	without
Result	:	positive
Method	:	other: Autoradiographic procedure
Year	:	1983
GLP	:	no data
Test substance	:	no data
Method	:	Comprehensive testing programme including 312 chemicals: Rat hepatocytes were derived from Osborne-Mendel rats. Exposure time: 18 - 20 h. 2-Aminofluorene was used as positive control in this experiment on the 1,2-dichloroethane induced DNA-repair.
Result	:	DCE positive, based on the following evaluation criteria: positive net grain number (>5), dose-response relationship and two concentrations significant above solvent control.
Source	:	Wacker - Chemie GmbH, Burghausen, Germany.
Reliability	:	(2) valid with restrictions Comparable to guideline study, but limited documentation
Flag	:	Critical study for SIDS endpoint
27.06.2002		(188)

Type	:	Unscheduled DNA synthesis
System of testing	:	human lymphocytes
Test concentration	:	2.5, 5, and 19 ul/ml (ca. 3.1, 6.2, and 12.5 mg/ml)
Cycotoxic concentr.	:	
Metabolic activation	:	with and without
Result	:	ambiguous
Method	:	other: 3H-TdR incorporation
Year	:	1981
GLP	:	no data
Test substance	:	as prescribed by 1.1 - 1.4
Method	:	For metabolic activation, S9 was derived from phenobarbital-induced rat liver. DMSO served as solvent, with a final concentration of 0.5 % in the incubation. Treatment 4 h. The toxic effects of the TS were measured by inhibition of [3H]-TdR uptake for the scheduled (replicative) DNA synthesis (SDS). For UDS measurement, 10 mM hydroxyurea was added to suppress TdR uptake due to SDS. No positive control included.

Source : Wacker - Chemie GmbH, Burghausen, Germany.
Test substance : purity 97 - 99 %
Reliability : (3) invalid
Insufficient test method and design, insufficient documentation: thymidine incorporation in relation to hydroxyurea-suppressed DNA synthesis not appropriate and reliable; pos. control missing; misleading calculation of result.
Flag : non confidential
25.06.2002 (132)

Type : Ames test
System of testing : Salmonella TA98, TA100, TA1535, TA, 1537, TA1538
Test concentration : 3.15, 6.24, 12.7, 22.9 mg/plate
Cycotoxic concentr. :
Metabolic activation : with and without
Result : positive
Method : other: modified Ames test (closed incubation)
Year : 1981
GLP : no data
Test substance : as prescribed by 1.1 - 1.4
Method : Comparative study including various halogenated compounds, test design modified such as to prevent escape of volatiles from the test system with analytical gas-phase control.

S9 mix was prepared from livers rats pretreated with Aroclor 1254.

Positive controls were:

TA 1535:
N-methyl-N´-nitro-N-nitrosoguanidine (- S9 mix)
2-aminoanthracene (+ S9 mix)

TA 1537:
9-aminoacridine (- S9 mix)
2-aminoanthracene (+ S9 mix)

TA 1538:
Picrolonic acid (- S9 mix)
2-aminoanthracene (+ S9 mix)

TA 98:
ICR-191, 3 (- S9 mix)
2-aminoanthracene (+ S9 mix)

Result : Test substance was shown to respond negative in S. typhimurium strains TA 98, 100, 1537 and 1538 and positive in S. typhimurium strain TA 1535 only, in dose-related manner, likewise, in the absence and presence of metabolic activation.

Result principally in line with that of Brem et al., 1974 and principe et al., 1981) (see other entries).
Source : Wacker Chemie GmbH, Burghausen, Germany.
Reliability : (2) valid with restrictions
Comprehensive and comparative study, well documented, based on scientific principles, meeting current standards.
Flag : Critical study for SIDS endpoint
08.05.2002 (15)

Type : Mammalian cell gene mutation assay
System of testing : AHH-1 and TK6 human lymphoblastoid cell lines
Test concentration : 100 - 1000 µg/ml

Cycotoxic concentr. : 1000 µg/ml
Metabolic activation : without
Result : positive
Method :
Year : 1985
GLP : no data
Test substance : as prescribed by 1.1 - 1.4
Remark : Test system uses the resistance against the purine analogue 6-thioguanine due to mutations at the HGPRT locus.

Negative control was dimethylsulfoxide, positive controls were for TK6 and AHH-1 cells without activation were 4-nitroquinoline-N-oxide and benzo[a]pyrene, respectively.

TK6 and AHH-1 cells were exposed 20 and 28 hours, respectively, to at least 4 concentrations of test substance with the highest dose causing cytotoxicity. In AHH-1 cells 0,100, 250, 500 and 1000 µg/ml were tested, in TK6 cells 0, 200, 500 and 1000 µg/ml.

The period of phenotypic expression of the mutant fraction was 3 and 6 days for the tk locus in TK6 cells and for the hgprt locus in the AHH-1 cells, respectively.
Result : There was a reproducible, dose-related increase in mutant colonies, distinctly more pronounced in AHH-1 cells (about 25x: based least squares linear regression analysis).

In AHH-1 cells, mutagenic responses were at or above 100 µg/ml; mutagenic responses in TK6 cells occurred at or above concentrations of 500 µg/ml.

This differential sensitivity correlates with the levels of glutathione-S-transferase which is about 5-fold higher in AHH-1 than in TK6-cells.
Source : Wacker Chemie GmbH, Burghausen, Germany.
Test substance : Commercial, from Mallinckrodt
Reliability : (2) valid with restrictions
Comparable to guideline study, sufficient documentation
Flag : Critical study for SIDS endpoint
25.06.2002 (48)

Type : other: mammalian cell transformation test
System of testing : BALB/C-3T3 cells
Test concentration : 5, 10, 25, 50 µg/ml
Cycotoxic concentr. :
Metabolic activation : without
Result : negative
Method :
Year : 1985
GLP : no data
Test substance : as prescribed by 1.1 - 1.4
Method : Comparative study including various chlorinated chemicals:
3-Methylcholanthrene served as positive control, showing high responsiveness.
Selection of concentrations based on cytotoxicity, but not well documented.

Type-III foci (= aggregation of stainable, dense multilayers) were scored as indicator for transformation.
Remark : Type: Cell transformation
Source : Wacker Chemie GmbH, Burghausen, Germany.
Test substance : purity 97- 99 %, from Aldrich
Reliability : (4) not assignable

Comparable to guideline study, insufficient documentation with respect to cytotoxicity: Concentrations selected appear to be low.

Flag : non confidential
15.05.2002 (175)

Type : Escherichia coli reverse mutation assay
System of testing : E. coli K12/343/113
Test concentration : <= 10 mM
Cycotoxic concentr. :
Metabolic activation : with and without
Result : negative
Method : other: Mohn and Ellenberger, Handbook of Mutagenicity Test Procedures, 1977
Year : 1979
GLP : no
Test substance : as prescribed by 1.1 - 1.4
Method : Mutations to 5-methyltryptophan resistance, galactose utilisation, and arginine independence were tested.
Test substance : commercial, from Merck
Reliability : (4) not assignable
Non validated test procedure, limited documentation.
Flag : non confidential
15.05.2002 (95)

Type : Ames test
System of testing : Salmonella typhimurium TA 98, TA 100, TA 1535, TA 1537, 1538 (spot test)
Test concentration : 100 ul (125 ug/ml)
Cycotoxic concentr. :
Metabolic activation : with and without
Result : positive
Method :
Year : 1981
GLP : no data
Test substance : as prescribed by 1.1 - 1.4
Method : S9 mix was prepared from livers of male Sprague-Dawley rats pretreated with Aroclor 1254.

Positive controls were:
ethyl methanesulphonate for TA 1535;
9-aminoacridine for TA 1537;
4-nitro-o-phenylenediamine for TA 1538 and TA 98;
methyl methanesulphonate for TA 100;
2-aminoanthrancene for all strains with S9 mix.

Result : Positive in Salmonella typhimurium TA1535: 100 µl (125 mg) is given as the highest non-toxic concentration. Test substance revealed a slight positive effect in the spot test with Salmonella typhimurium strain TA 1535 in the presence and of a metabolic activation system.
Test substance : Analytical grade
Reliability : (2) valid with restrictions
Comparative non-standard test design, limited documentation, based on scientific principles; result in line with findings by others.
Flag : Critical study for SIDS endpoint
25.06.2002 (135)

5.6 GENETIC TOXICITY 'IN VIVO'

Type : Dominant lethal assay

Species : mouse
Sex : male
Strain : Swiss
Route of admin. : drinking water
Exposure period : unclear
Doses : 0.03, 0.09, 0.29 mg/ml
Result : negative
Method : other: in combination with reproduction study
Year : 1982
GLP : no data
Test substance : as prescribed by 1.1 - 1.4
Remark : The possible dominant lethal effects of 1,2-dichloroethane were studied in the course of a modified multigeneration study where dominant lethal and teratogenic effects were investigated, too.

10 treated male mice per test group of the F1C and F2B were used for the examination of dominant lethal effects.

Treated males were housed 1:3 with 9-week old naive, nulliparous females for 7 days, resulting in 15 to 27 pregnancies per group. Gravid females were evaluated for the number of fetal implants, early and late resorptions as well as viable fetuses.

Fertility index, number of implants, resorptions, live fetuses, ratio of dead vs. life fetuses, frequency of dominant lethal factors, FL, (determined as FL%=[1-(mean live fetuses, treatment/mean live fetuses, naive ctrl)]x100) were determined.
Result : After mating of treated F1C and F2B males with untreated females no adverse effects on fertility index, number of implants, resorptions and live fetuses were observable when compared to untreated controls.
Source : Wacker Chemie GmbH, Burghausen, Germany.
Test substance : commercial, >99%
Reliability : (2) valid with restrictions
Screening study: Study protocol unclear with respect to duration of treatment for males; MTD dose not reached.
Flag : Critical study for SIDS endpoint
25.06.2002 (103)

Type : Drosophila SLRL test
Species : Drosophila melanogaster
Sex : male
Strain : other: Berlin K
Route of admin. : oral feed
Exposure period : 3 d
Doses : 4948 ug/ml
Result :
Method : other: Sex-Linked Recessive Lethal Test
Year : 1979
GLP : no data
Test substance : no data
Remark : Test substance was fed 3 days to 1-2 day old Berlin K males.
Treated Berlin K males were mated individually to 3 Basc virgin females.

A minimum of one thousand F1 females were handled in each brood.
SLRLs were scored in the F2 generation and confirmed in the F3 generation.
Result : Test substance produced increases in the frequency of sex-linked-recessive-lethal mutations in all treated broods when compared to untreated controls.
Source : Wacker - Chemie GmbH, Burghausen, Germany.

Reliability : (2) valid with restrictions
Flag : Critical study for SIDS endpoint
15.05.2001 (95)

Type : Drosophila SLRL test
Species : Drosophila melanogaster
Sex : male
Strain : other: Berlin K
Route of admin. : inhalation
Exposure period : 1 or 2 wk and 96hr
Doses : 7 mg/m3 (1 and 2 weeks) and 8, 125 mg/m3 (96 hr) and 800 mg/m3 (6 hr)
Result :
Method : other: Sex-Linked Recessive Lethal Test
Year : 1991
GLP : no data
Test substance : as prescribed by 1.1 - 1.4
Remark : Impairment of fertility after two weeks of exposure.
Result : Test substance produced positive effects in Drosophila melanogaster. A clear effect was observable already at 8 mg/m3 (4-5 times control rates) for the 96 hr exposure and a near linear relationship between exposure concentrations for 6 hr and 96 hr exposure. Impairment of fertility after two weeks of exposure.
Source : Wacker - Chemie GmbH, Burghausen, Germany.
Test substance : commercial, from Fluka
Reliability : (2) valid with restrictions
Comparable to guideline study, limited documentation.
Flag : Critical study for SIDS endpoint
15.05.2002 (99)

Type : Micronucleus assay
Species : mouse
Sex : male/female
Strain : NMRI
Route of admin. : i.p.
Exposure period : in total 30 h, 6 h after 2nd treatment
Doses : 0, 98.7, 197.4 and 3986 mg/kg bw (2x each)
Result : negative
Method : other:
Year : 1979
GLP : no
Test substance : as prescribed by 1.1 - 1.4
Method : Four mice were used for each of three doses and controls.
Doses were selected on the basis of previous toxicity experiments ranging from non-toxic to approximate lethal doses.

Test substance was given twice i.p. with a 24 hour interval in between. Animals were killed 6 hours after the second dose and bone-marrow smears were prepared. A total of 1000 polychromatic erythrocytes was analysed for the formation of micronuclei.
Result : As compared to controls injected olive oil alone, no increases in the frequency of micronucleated PCEs could be detected.
Source : Wacker - Chemie GmbH, Burghausen, Germany.
Test substance : commercial, from Merck
Reliability : (2) valid with restrictions
Comparable to guideline study, limited documentation, part of a comprehensive test programme.
Flag : Critical study for SIDS endpoint
25.06.2002 (95)

Type : Micronucleus assay

Species	:	mouse
Sex	:	male
Strain	:	CBA
Route of admin.	:	i.p.
Exposure period	:	30 h
Doses	:	100 mg/kg bw
Result	:	negative
Method	:	other: Micronucleus Test in Bone Marrow Cells
Year	:	1980
GLP	:	no
Test substance	:	as prescribed by 1.1 - 1.4
Remark	:	Comprehensive test programme including 143 chemicals: Treatment group and control had three male mice, samples were taken 30 h after treatment. No dose- and time-response conducted.
Test substance	:	commercial, from BDH Chemicals
Reliability	:	(3) invalid Screening study based on scientific principles, results conclusive in relation to findings with other compounds. But time between treatment and sampling may have been too long.
Flag	:	non confidential

25.06.2002 (89)

Type	:	Micronucleus assay
Species	:	mouse
Sex	:	male/female
Strain	:	other: Eμ-PIM-1 transgenic mice, lymphona prone
Route of admin.	:	gavage
Exposure period	:	14 and 40 weeks, once daily
Doses	:	100+200 mg/kg (males); 150+300 mg/kg (females)
Result	:	negative
Method	:	other: procedures in compliance with OECD Guide-line 474
Year	:	1993
GLP	:	yes
Test substance	:	as prescribed by 1.1 - 1.4
Method	:	Repeated dosing of up to toxic dose; TS was given in corn oil (5 ml/kg). 10 mice per dose were analysed after 14 and 42 week (1 week after termination of exposure): peripheral erys were selected. At study termination, only normochrome erythrocytes could be scored because of the short residence time of polychromatics. Due to failing, treatment-related weight gain in week 6, the top doses of 200 mg/kg in males and 300 mg/kg in females were reduced to 100 and 150 mg/kg bw, respectively. Dosing was discontinued 1 week prior to study termination at week 41. 2-AAF and benzene were also tested.
Result	:	No micronucleus induction or polychromatic erythrocyte suppression detected in the blood after 14 (documented) or 41 weeks (not documented). Note: Benzene and 2-aminofluorene induced significant increases in MN rates.
Source	:	Wacker Chemie GmbH, Burghausen, Germany.
Test substance	:	commercial, from Sigma
Reliability	:	(1) valid without restriction Comparative non-standard test design and uncommon test strain, but following guideline procedure, based on scientific principles, sufficient documentation
Flag	:	Critical study for SIDS endpoint

25.06.2002 (9)

Type	:	Sister chromatid exchange assay
Species	:	mouse
Sex	:	male
Strain	:	Swiss
Route of admin.	:	i.p.
Exposure period	:	single dose: 24 h
Doses	:	0, 0.5, 1, 2, 4, 8, 16 mg/kg
Result	:	positive
Method	:	other: SCE Test in Bone Marrow Cells
Year	:	1988
GLP	:	no data
Test substance	:	as prescribed by 1.1 - 1.4
Remark	:	Vehicle: groundnut oil Seven male mice were administered test substance by the i.p. route at each concentration. No pos. control was enclosed. 24 hours after a single i.p. injection animals were killed by cervical dislocation. Exposure time was 22 hours followed by a single injection of colchicine. Two hours later animals were sacrificed. 20 metaphases per animal x 7 animals per dose = 140 metaphases per dose and control were sored. Differential staining of the sister chromatids was performed by a modification of the fluorescence-plus-Giemsa technique.
Result	:	Dose-dependent increase in SCEs at 1 mg/kg and above ($p<0.01$ at 2 mg/kg and above). At a dose of 4 mg/kg, the SCE rate was doubled. No significant increase in SCEs at 0.5 mg/kg.
Source	:	Wacker Chemie GmbH, Burghausen, Germany.
Test substance	:	commercial, from Sigma
Reliability	:	(2) valid with restrictions Comparable to guideline study, sufficient documentation
Flag	:	Critical study for SIDS endpoint

25.06.2002 (63)

Type	:	Somatic mutation assay
Species	:	Drosophila melanogaster
Sex	:	male/female
Strain	:	other: flr:mwh
Route of admin.	:	oral feed
Exposure period	:	no data
Doses	:	50 - 1000 ppm (mg/kg nutrient medium)
Result	:	Positive
Method	:	other: Somatic Mutation and Recombination Test (SMART)
Year	:	1990
GLP	:	no data
Test substance	:	as prescribed by 1.1 - 1.4
Result	:	Dose-related increase in the frequency of spots in larvae, 10-fold above background at the highest concentration (1000 ppm). Mutation rate was significantly reduced or enhanced after pretreatment of larvae with L-ButhionineS,R-sulfoximine (GSH inhibitor) or phenobarbital CYP450 inducer), respectively.
Source	:	Wacker - Chemie GmbH, Burghausen, Germany.
Test substance	:	commercial, BDH Chemicals
Reliability	:	(2) valid with restrictions Comparable to guideline study, limited documentation.
Flag	:	Critical study for SIDS endpoint

15.05.2002 (137) (146)

Type	:	other: in-vivo/in-vitro alkaline DNA unwinding test / single strand breaks
Species	:	Mouse
Sex	:	Male
Strain	:	B6C3F1
Route of admin.	:	other: gavage, i.p. (inhalation: see other entry)
Exposure period	:	single application: 4 h
Doses	:	100 - 400 mg/kg bw
Result	:	positive
Method	:	other: Alkaline Elution Test
Year	:	1984
GLP	:	no data
Test substance	:	other TS: purity >= 99.9 %
Result	:	Single-strand breaks and/or alkali-labile lesions were demonstrated by alkaline DNA-unwinding/hydoxyapatite chromatography in hepatic DNA at subtoxic/sublethal doses: 1. Gavage administration: Doses: 100, 200, 300, 400 mg/kg bw in corn oil 4 male animals/group Positive effects were observed in all groups: dose-response at 100 and 200 mg/kg, thereafter levelling off at about a decrease in the double-strand DNA fraction of -20 to -25 %. In another study mortality resulted at 400 (2/5), 500 (4/5) and 600 (4/5) mg/kg bw. Sub-toxic liver effects were demonstrated at 300 mg/kg and above by significant increases in liver enzymes in serum (IDH = sorbitol dehydrogenase; and AAT = alanine aminotransferase). 2. i.p. administration: Doses: 100, 150, 200, 300 mg/kg bw in corn oil 6 male animals/group Positive effects were assessed at 150 mg/kg bw and above, similar to oral dosage: apparent trend to levelling off at about a decrease in double-stranded DNA of -20 to -27 %. After i.p. admistration no mortality up to 600 mg/kg bw occurred. Sub-toxic liver effects were demonstrated at 500 mg/kg and above by significant increases in liver enzymes in serum (IDH = sorbitol dehydrogenase; and AAT = alanine aminotransferase). 3. Inhalation (see other entry)
Source	:	Wacker - Chemie GmbH, Burghausen, Germany.
Reliability	:	(2) valid with restrictions Comprehensive screening study based on scientific principles
Flag	:	Critical study for SIDS endpoint

25.06.2002 (160)

Type	:	other: in-vivo/in-vitro alkaline DNA unwinding test / single strand breaks
Species	:	mouse
Sex	:	male
Strain	:	B6C3F1
Route of admin.	:	inhalation
Exposure period	:	4 h
Doses	:	150 and 500 ppm; (1000 and 2000 ppm)
Result	:	negative
Method	:	other: Alkaline Elution Test
Year	:	1984
GLP	:	no data

Test substance : other TS: purity >= 99.9 %
Result : Single-strand breaks and/or alkali-labile lesions were not demonstrated by alkaline DNA-unwinding/hydoxyapatite chromatography in hepatic DNA, but at toxic/lethal concentrations:

5 male animals/group:
No effects were detectable up to 500 ppm. A sub-toxic, but significant liver effect was demonstrated at 500 ppm by significant increases in liver enzymes in serum (IDH = sorbitol dehydrogenase; and AAT = alanine aminotransferase).

At the higher, lethal exposure concentrations, significant DNA damage resulted: decrease in double-strand fraction -20 % (1000 ppm) and -43 % (2000 ppm).

2. Gavage administration (see other entry)

3. i.p. admistration (see other entry)

Reliability : (2) valid with restrictions
Comprehensive screening study based on scientific principles
Flag : Critical study for SIDS endpoint
25.06.2002 (160)

5.7 CARCINOGENICITY

Species : rat
Sex : male/female
Strain : Osborne-Mendel
Route of admin. : gavage
Exposure period : 78 wk
Frequency of treatm. : 5 d/wk
Post exposure period : 15 - 32 wk
Doses : 47 and 95 mg/kg bw/d
Result : positive
Control group : other: yes, concurrent vehicle and concurrent no treatment
Method : other: Carcinogenicity
Year : 1978
GLP : no data
Test substance : other TS: purity >90 %; impurities: unspecified (11 different substances)
Method : Carcinogenicity bioassay. Similar to OECD 451, major deficiencies outlined under Remark.
Remark : Experimental design differs largely from current test procedure and requirements: Limitations include questionable, unclear TS purity with contaminants not being characterized, potential of influence from other chemicals being tested in the same room (1,1-dichloroethane, dibromopropane, trichloroethylene, and carbon disulfide), only 2 dose levels tested, poor survival at the high dose (top dose was distinctly too high contrary to requirements), lack of a third non-toxic lower dose, adjusted and intermittent dosage including prolonged higher doses than the average makes believe, low number of controls, application mode (gavage) with poor practical relevance.

Technical grade TS was used in this study. Data on degree of purity given in this study and in the publication of Ward (1980) are conflicting. According to Maltoni et al. (1980; page 4), technical product was found to contain up to 7% of bis(2-chloroethyl)ether amongst other impurities.

However, this study has been regarded as valid key study and the results were used by EPA to derive carcinogenicity potency factors (e.g. unit risk values).

Result : Clinical observation
From week 6 several treated rats showed hunched appearance and transient labored respiration. The incidence of signs was higher in treated animals during the first year. Respiratory signs (labored respiration, wheezing, nasal discharge) were observed in all groups in the second year, and were predominant observations in all survivors at termination of the study. Chronic murine pneumonia was identified in 60-95% of all control and test group rats. Body weight development was not influenced.

Mortality
Mortality was early and severe especially in high dose animals. In high-dose groups, 50% of males were dead by week 55 and 50% of females by week 57; by week 75, 84% of males and 80% of females were dead. The last high-dose male rat died during week 23 and the last high-dose female rat died during week 15 of the observation period. In low-dose group, 52% of males survived over 82 week, and 50% of females survived over 85 week. Thus at the low dose survival was similar to the matched vehicle controls.

Mean survival was approx. 90, 74, 75, and 55 weeks for male animals (untreated, low dose, vehicle control, high dose, resp.). Mean survival of females was approx. 90, 76, 55 weeks (vehicle control, low dose, high dose, resp.). Animals dying early had a variety of lesions, including bronchopneumonia and endocardial thrombosis, but no tumors (cf. Ward 1980). According to Ward (1980) the early deaths were usually not due to cancer. Susceptibility to pneumonia may have been aggravated by toxicity of the TS.

Tumor formation
Tumors seen in male rats (low and high dose, resp.)
Subcutaneous fibroma: 5/50 (p=0.017) and 6/50 (p=0.007)
Forestomach; squamous-cell carcinomas: 3/50 (NS) and 9/50 (p=0.001)
Hemangiosarcomas(spleen and other sites): 9/50 (p=0.003) and 7/50 (p=0.016)
Vehicle controls: 0/20 for each of the listed tumors.

Tumors seen in female rats (low and high dose, resp.)
Mammary gland, adenocarcinomas 1/50 (NS) and 18/50 (p<0.001)
Hemangiosarcomas (spleen and other sites): 4/50 (p=0.041) and 4/50 (p=0.041)
Vehicle controls: 0/20 for each of the listed tumors.

Subcutaneous fibroma: 1/50 and 2/50. Vehicle control 1/20
Mammary gland, fibroadenomas 14/50 (p=0.007) and 8/50 (NS).
Untreated controls 2/20

Note: P-values give the level of probability for the Fisher exact test for the comparison with the pooled vehicle control group. NS=not significant.

Additionally, 7 other cases of unusual tumors were seen in kidney, stomach and small intestine. 9 Rats developed metastatic tumors, predom inantly in the high dose groups.

Source : Wacker Chemie GmbH, Burghausen, Germany.

Test condition : TEST ANIMALS
Osborne Mendel rats, 9 wk old, were used. Animals were singly housed.
EXPOSURE

Groups of 50 male & 50 female Osborne Mendel rats, 9 wk old, were administered technical-grade 1,2-dichloroethane in corn oil (concentration 5-7.5%) by gavage on 5 consecutive days/wk for a total of 78 wk. The time-weighted average doses were 195 and 47 mg/kg body wt/day for high- and low-dose males and females. The experimental design of the low and high dose groups was as follows:

weeks	dose (mg/kg bw/d)
7	50 and 100
10	75 and 150
18	50 and 100
34 (+ 9)	50 and 100 (intermittent)
32	0 (observation period low dose groups)
23	0 (observation period high dose groups)

The pattern of the intermittent dosing was 1 dosage-free wk followed by 4 wk of dosing (5d/wk). Time-weighed average dose was calculated as the sum of (dosage x wk received) divided by 78 wk.
The doses applied were adjusted according to the last mean group body weights.
Selection of the initial dose was based on the results of a range finding study (6 wk dosage, 2 wk observation).

Groups of 20 male and 20 female rats received corn oil alone and were used as matched vehicle controls. Another groups of 20 male and 20 female rats remained untreated.
During evaluation of the results the vehicle control groups were pooled with those from other experiments conducted in parallel, thus yielding 60 pooled control animals per sex.

EXAMINATIONS
Body weights were determined prior to initiation of the study. Body weights, food consumption, and clinical sign observations were recorded at weekly intervals for the first 10 wk and monthly thereafter. All animals were necropsied. Histopathological examination consisted of gross and microscopical examination of major tissues, organs, or gross lesions. Slides were prepared for skin, subcutaneous tissue, lungs and bronchi, trachea, bone marrow, spleen, lymph nodes, thymus, heart, salivary gland, liver, gallbladder, pancreas, esophagus, stomach, small and large intestine, kidney, urinary bladder, pituitary, adrenal, thyroid, parathyroid, testis, prostate, brain, tunica vaginalis, uterus, mammary gland, and ovary. Statistical analyses included Fisher exact test and Cochran-Armitage test to compare tumor incidences in test and control animals, with and without time-adjustment, and calculation of relative risks and confidence intervals.

The untreated control group was not used for analyses of tumor incidences because the test conditions of the vehicle controls more closely resembled those of the treated groups.

Test substance : Technical grade 1,2-dichloroethane was obtained from Dow Chemical Corp. Purity was reported to be >90%. 11 minor contaminants were present, but on these no further data were reported. According to Ward (1980) purity was 98-99%.

Conclusion : Oral administration of 1,2-dichloroethane to male and female Osborne-Mendel rats over a period of 78 wk caused severe mortality in high dose animals of both sexes receiving 95 mg/kg bw/d. At the low dose (47 mg/kg bw/d) survival was similar to control animals.

Significantly enhanced tumor formation was seen in both high- and low-dose males as evidenced by subcutaneous fibroma; squamous-cell carcinomas in forestomach; hemangiosarcomas in spleen and other sites.

Significantly enhanced tumor formation in female rats was seen as increased numbers of adenocarcinomas in the mammary gland (high-dose animals) and hemangiosarcomas low- and high-dose rats).

There are, however, limitations of the study due to methodological deficiencies. Amongst several others, poor degree of TS purity (>90%) should be mentioned.

Reliability : (2) valid with restrictions
Meets scientific standards, well documented, acceptable for assessment of a principal carcinogenic potential (see Remarks)

Flag : Critical study for SIDS endpoint

25.06.2002 (122) (184) (186)

Species : mouse
Sex : male/female
Strain : B6C3F1
Route of admin. : gavage
Exposure period : 78 wk
Frequency of treatm. : 5 d/wk
Post exposure period : 12 - 13 wk
Doses : m: 97 and 195 mg/kg bw /d ; f: 149 and 299 mg/kg bw /d
Result : positive
Control group : other: yes, concurrent vehicle and concurrent no treatment
Method : other: Carcinogenicity
Year : 1978
GLP : no data
Test substance : other TS: purity > 90 %; impurities: unspecified (11 different substances)
Method : Carcinogenicity bioassay. Similar to OECD 451, major deficiencies outlined under Remark
Remark : Experimental design differs largely from current test procedure and requirements: Limitations include questionable, unclear TS purity with contaminants not being characterized, potential of influence from other chemicals being tested in the same room (e.g. 1,1-dichloroethane, dibromopropane, trichloroethylene, and carbon disulfide), only 2 dose levels tested, poor survival at the high dose (top dose was distinctly too high contrary to requirements), lack of a third non-toxic lower dose, adjusted and intermittent dosage including prolonged higher doses than the average makes believe, low number of controls, risk irrelevant application mode (gavage) with poor practical relevance.

Technical grade TS was used in this study. Data on degree of purity given in this study and in the publication of Ward (1980) are conflicting. According to Maltoni et al. (1980; page 4), technical product was found to contain up to 7% of bis(2-chloroethyl)ether amongst other impurities.

However, this study has been regarded as valid key study and the results were used by EPA to derive carcinogenicity potency factors (e.g. unit risk values).

Result : Clinical observation
Appearance and behavior of treated mice was generally comparable with that in control animals, although decreased survival was evident during the second year. From experimental week 6 abscesses at body and extremities as well as generalized and/or localized alopecia were noted. Body weight development was only influenced in high dose females as early as week 15. Mean group body weight was ca. 22 g in this group at week 75 compared to ca. 33 g of the untreated and ca. 30 g of the treated control animals.

Mortality

Of the high-dose males, 50% survived at least 84 weeks and 42% survived until end of study. 72% (36/50) of the high-dose female mice died between week 60 & 80. 69% of these (25/36) had one or more tumors, therefore deaths were possibly tumor-related.
In low-dose groups, 52% (26/50) of males survived less than 74 weeks, but 68% (34/50) of females survived until end of study. In vehicle control groups, 55% (11/20) of males and 80% (16/20) of females survived until end of study.

In males mean survival was not significantly different from controls whereas in females a significant ($p<0.001$) association between dosage and mortality was demonstrated. However, survival was lowest in untreated male controls, followed by low dose males, high dose males, and vehicle control. In females survival was similar in all groups except from the high dose group.

Tumor formation
The numbers of animals with tumors and total number of tumors were significantly greater in male and female mice treated with the higher dose level, and in female mice treated with the low dose, than in controls. Increased incidence of the following neoplasms were observed:

Males (low and high dose, resp.)
Lung, alveolar/bronchiolar adenoma: 1/47 (NS) and 15/48 ($p<0.001$)
Hepatocellular carcinoma: 6/47 (NS) and 12/48 ($p=0.009$)

Females, (low and high dose, resp.)
Lung, alveolar/bronchiolar adenoma: 7/50 ($p=0.046$) and 15/48 ($p<0.001$)
Mammary adenocarcinomas: 9/50 ($p=0.001$) and 7/48 ($p=0.003$).

Further tumors were seen in male and female animals (cf. Ward, Weisburger) in various organs but these were not significantly different (NS) when compared with pooled controls. An increased incidence of endometrial stromal polyps plus sarcomas in the uterus (high dose 11%; low dose 10%, vehicle controls 0%) was noted in females. In the absence of statistical adjustment for early mortality, Ward (1980) has suggested that additional weight should be placed on the slightly increased incidence of uterine adenocarcinomas and squamous cell carcinomas of the forestomach of high dose females (9% and 10%, respectively, and about 0 and 5% in controls). 7 mice developed metastatic tumors.

Source : Wacker Chemie GmbH, Burghausen, Germany.

Test condition : TEST ANIMALS
B6C3F1 mice, 5 wk old, were used. Animals were housed in groups of 10 per cage.
EXPOSURE
Groups of 50 male & 50 female mice were administered technical-grade 1,2-dichloroethane in corn oil (concentration 5-7.5%) by gavage on 5 consecutive days/wk for a total of 78 wk. The time-weighted average doses were 195 and 97 mg/kg body wt/day for high- and low-dose males and 299 and 149 mg/kg bw/d for high- and low-dose females. The experimental design of the low and high dose groups was as follows:
1) males

weeks	dose (mg/kg bw/d)
8	75 and 150
70	100 and 200
12	0 (observation period low dose groups)
13	0 (observation period high dose groups)

2) females

weeks	dose (mg/kg bw/d)

8 125 and 250
3 200 and 400
67 150 and 300
13 0 and 0 (observation period all dose groups)

Time-weighed average dose was calculated as the sum of (dosage x wk received) divided by 78 wk.
The doses applied were adjusted according to the last mean group body weights.
Selection of the initial dose was based on the results of a range finding study (6 wk dosage, 2 wk observation).

Groups of 20 male and 20 female mice received corn oil alone and were used as matched vehicle controls. Another groups of 20 male and 20 female mice remained untreated. During evaluation of the results the vehicle control groups were pooled with those from other experiments conducted in parallel yielding 60 pooled control animals per sex.

EXAMINATIONS
Body weights were determined prior to initiation of the study. Body weights, food consumption, and clinical sign observations were recorded at weekly intervals for the first 10 wk and monthly thereafter.
All animals were necropsied. Histopathological examination consisted of gross and microscopical examination of major tissues, organs, or gross lesions. Slides were prepared for skin, subcutaneous tissue, lungs and bronchi, trachea, bone marrow, spleen, lymph nodes, thymus, heart, salivary gland, liver, gallbladder and bile duct, pancreas, esophagus, stomach, small and large intestine, kidney, urinary bladder, pituitary, adrenal, thyroid, parathyroid, testis, prostate, brain, tunica vaginalis, uterus, mammary gland, and ovary.
Statistical analyses included Fisher exact test and Cochran-Armitage test to compare tumor incidences in test and control animals, with and without time-adjustment, and calculation of relative risks and confidence intervals.

Test substance : Technical grade 1,2-dichloroethane was obtained from Dow Chemical Corp. Purity was reported to be >90%. 11 minor contaminants were present, but on these no further data were reported. According to Ward (1980) purity was 98-99%.

Conclusion : Oral administration of 1,2-dichloroethane to mice at dose levels of 97 and 195 mg/kg bw/d (males) and 149 and 299 mg/kg bw/d (females) over a period of 78 wk, 5 d/wk resulted in:

- slightly enhanced mortality in male low- and high-dose mice compared to vehicle controls
- significant increase in alveolar/bronchiolar adenoma of the lung in high dose males
- significant increase in hepatocellular carcinoma in high dose males
- clearly enhanced mortality in high dose females, but not in low-dose females
- significant increase in mammary adenocarcinoma in both low- and high-dose females
- significant increase in alveolar/bronchiolar adenoma of the lung in both low- and high-dose females

There are, however, limitations of the study due to serious methodological deficiencies. Amongst several others, poor degree of TS purity (>90%) should be mentioned.

Reliability : (2) valid with restrictions
Meets scientific standards, well documented, acceptable for assessment of a principal carcinogenic potential (see Remarks)

Flag : Critical study for SIDS endpoint

25.06.2002 (122) (184) (186)

Species	:	rat
Sex	:	male/female
Strain	:	Sprague-Dawley
Route of admin.	:	inhalation
Exposure period	:	78 wk
Frequency of treatm.	:	7 h/d, 5 d/wk
Post exposure period	:	ca. 70 wk
Doses	:	21, 41, 206 and 617 or 1028 mg/m3 (5, 10, 50 and 150 or 250 ppm)
Result	:	negative
Control group	:	other: two groups of 180 rats each
Method	:	other: Carcinogenicity
Year	:	
GLP	:	no data
Test substance	:	other TS: purity 99.82 %; impurities: 1,1-dichloroethane, tetrachloromethane and trichloroethene 0.02 %, respectively, tetrachloroethene 0.03 % and benzene 0.09 %
Method	:	Carcinogenicity bioassay. Similar to OECD 451, major deficiencies outlined under Remark
Remark	:	1) Intervals of body weight and food consumption recording differed from OECD 451. Details of statistical data evaluation (Chi-Square Test: see Tab. 11) are not contained in the publication. 2) Top concentration applied acceptable as it is close to the MTD. 3) Blood chemical parameters and pharmacokinetic data are contained in Spreafico et al., 1980 (see: 5.4).
Result	:	Clinical observations No body weight or other data were reported except that 250 ppm was too toxic (unspecified) and required lowering the concentration to 150 ppm (note: conclusive based on toxicity and pharmacotoxicity data.). No clear treatment-related hematological, blood chemistry or urinalysis changes were detected (see also Spreafico et al., 1980). Mortality Long-term survival rate low in both test and control males and observed mortalities reported to be comparable to controls . Survival rates at 52 weeks of age in rats: ---------- untreated 92.2% (males) controls: 97.8% (females) Chamber 88.9 (males) controls: 87.8 (females) 5 ppm: 98.9 % (males) 100 % (females) 10 ppm: 90.0 % (males) 96.7 % (females) 50 ppm: 96.7 % (males) 96.7 % (females) 250-150 ppm: 87.8 % (males) 93.3 % (females)

Survival rates at 104 weeks of age in rats:

untreated controls: 17.8% (males)
40.0% (females)

Chamber controls: 13.3% (males)
24.4% (females)

5 ppm: 50.0 % (males)
53.3 % (females)

10 ppm: 14.4 % (males)
28.9 % (females)

50 ppm: 18.9 % (males)
32.2 % (females)

250-150 ppm: 11.1 % (males)
23.3 % (females)

Tumor formation
No specific types of tumors and no relevant changes in the incidence of the tumors normally occurring in the strain of rats used were seen at any dose group. In female rats, an apparent increase in mammary tumors is due to fibromas and fibroadenomas rather than to malignant tumors. The increase of mammary fibromas and fibroadenomas was significant in the 250-150, 50 and 5 ppm groups when compared to chamber controls but not when compared to controls outside the exposure chamber. This difference was ascribed to the different survival rates in the groups, and was not treatment-related.

In conclusion, 1,2-dichloroethane was not considered carcinogenic in male and female Sprague Dawley rats under the conditions of the experiment.

Source : Wacker - Chemie GmbH, Burghausen, Germany.

Test condition : TEST ANIMALS
A total of 1080 Sprague-Dawley rats, 12 wk old, were used.
Animals were housed in cages in groups of 10.
EXPOSURE
90 animals/sex/dose group were used. Animals were placed into whole body inhalation chambers and exposed to the TS in air at concentrations of 0, 5, 10, 50, and 150-250 ppm. Because of marked toxic effects the highest concentration was reduced from 250 to 150 ppm (1028 mg/m3 to 617 mg/m3) after a few weeks. Animals were exposed 7hrs/d, 5d/wk, for 78 wk. Concurrent treated (chamber, 0 ppm) and untreated control animal groups of the same size (a nearby room), e.g. 90 animals/sex, were used.

After the exposure period, animals were allowed to live until spontaneous death.

EXAMINATIONS
Animals were controlled every 2 wk. Body weights were determined every 2 wk during the treatment and every 8 wk thereafter. Complete autopsy was performed on each animal. Histopathological examination consisted of gross and microscopical examination of the brain, Zymbal glands, retrobulbar glands, interscapular brown fat, salivary glands, tongue, lungs, thymus, diaphragm, liver, pancreas, kidneys, spleen, stomach, different segments of intestine, bladder, gonads, lymph nodes (axillary, inguinal, mesenteric), and any organ showing pathological lesions.

Details of statistical analysis were not reported.

Conclusion	:	No increases in any tumors (mammary, zymbal gland, leukemias nephroblastomas, hepatomas, forestomach, skin, s.c. sarcomas, encephalic tumors including neuroblastomas, and various others) were seen in Sprague-Dawley rats after exposure to 1,2-dichloroethane in an inhalation chamber at concentrations as high as 150 ppm for a period of 78 wk, 7hrs/d and 5 d/wk. Survival of treated rats was not significantly different from control animals.
Reliability	:	(2) valid with restrictions 2c Comparable to guideline study with acceptable restrictions
Flag	:	Critical study for SIDS endpoint
25.06.2002		(109) (156)
Species	:	Rat
Sex	:	male/female
Strain	:	Sprague-Dawley
Route of admin.	:	Inhalation
Exposure period	:	2 yr
Frequency of treatm.	:	5 d/wk, 7 hrs/d
Post exposure period	:	
Doses	:	50 ppm
Result	:	Negative
Control group	:	yes, concurrent vehicle
Method	:	other: carcinogenicity
Year	:	
GLP	:	no data
Test substance	:	as prescribed by 1.1 - 1.4
Method	:	Inhalation carcinogenicity bioassay similar to OECD 451. Major deficiency is noted under Remark.
Remark	:	Only one concentration tested. 50 ppm was the US occupational standard at that time. Further groups of animals received combined treatment with disulfiram or ethanol; details are omitted in this document.
Result	:	Clinical observations terminal body weights of treated animals were insignificantly increased compared to controls (m ca. 10%; f ca. 5%). Food consumption in treated animals was comparable to controls; water consumption was slightly increased. Mortality 2-yr survival was 58 and 54% in controls (m, f, resp.) and 60 and 64% in treated rats (m, f). Tumor formation No significant difference between control and treated rats of either sex were seen, e.g. incidences in primary tumors (m 69 vs 86; f 85 vs 87), animals with tumors (m 42 vs 45; f 47 vs 47); total benign or malignant tumors were seen in any of the examined tissues. Additional information 1) Terminal absolute liver weights were insignificantly increased in 1,2-dichloroethane treated males and females compared with controls; relative liver weights were identical to the respective controls. 2) Mean blood levels (n=5) of 1,2-dichloroethane after 7 h exposure was 0.28 and 0.26 µg/ml at 0.25 h and 0.22 and 0.28 µg/ml at 2.25 h after exposure (m and f, resp.). 3) Mean blood levels were ca. fold increased in animals receiving a combined disulfiram/1,2 -dichloroethane treatment. 4) Tumor incidence was increased in animals of both sexes after combined disulfiram/1,2-dichloroethane treatment in various organs (hepatic, testicular, mammary tumors).
Test condition	:	TEST ANIMALS

Rats, age 5.6 to 6 wk at initiation of the study. Animals were singly housed.
EXPOSURE
50 animals/sex were used as treated and control groups. Animals were placed into whole body inhalation chambers and exposed to the TS in air at concentrations of 50 ppm, controls received filtered air only. Exposure was continued for 24 months, 5d/wk, 7 hrs/d. Vapour concentration was determined hourly by GC.
EXAMINATIONS
Animals were examined twice daily for toxicity. Examinations of all animals for palpable masses were conducted prior to the initiation of the experiment and at weekly intervals after 4 months. Rats were weighed weekly for the first 8 wk and at monthly intervals thereafter.

At termination all animals were necropsied and weighed. Sections of major organs and tissues were routinely preserved (accessory sex organs, adipose tissue, adrenal glands, aorta, brain, esophagus, eyes, heart, kidneys, large intestine, larynx and pahrynx, liver, lungs, lymph nodes (thoracic and mesenteric), mammary tissue, nasal cavity and turbinates, ovaries, pancreas, parathyroid, pituitary, salivary glands, sciatic nerve, seminal vesicles, skeletal muscle, skin, skull, small intestine, spinal cord, spleen, sternum, vertebral bone and bone marrow, stomach, testes, thymus, thyroid, trachea, urinary bladder, uterus, and any gross lesions). Histopathological examination included adrenal gland bone, bone marrow, brain, colon, esophagus, heart, kidney, larynx, liver, lung, lymph node (thoracic and mesenteric), mammary gland, nasal cavity/mucus membrane, ovary, parathyroid, pituitary, pancreas, prostate, salivary gland, skin, small intestine, spleen, stomach, subcutis, testes, thymus, thyroid, trachea, urinary bladder, uterus, and any gross lesion.

Analysis of variance and Dunnett's test (organ & body weights, food & water consumption, blood levels, metabolism & DNA binding) and Fisher's exact probability test (mortality, histopathology) were used during statistical data analysis.

Test substance : 1,2-dichloroethane, purity >99%

Conclusion : No tumor formation was seen in male and female rats after 2 yr exposure to 50 ppm 1,2-dichloroethane. Animals were exposed 5d/wk, 7 h/d. Only one concentration was used.
Blood levels of TS were between 0.2-0.3 µg/ml in both sexes at 0.25 and 2.25 h after a 7-hr exposure to 50 ppm of TS.

Blood levels were ca. 5-fold increased when the animals received a combined 1,2-dichloroethane/disulfiram treatment.
Tumor incidences were increased in these animals in various organs (liver, testes, mammary gland).

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

Flag : Critical study for SIDS endpoint
15.05.2002 (43)

Species : Mouse
Sex : male/female
Strain : Swiss
Route of admin. : inhalation
Exposure period : 78 wk
Frequency of treatm. : 7 h/d, 5 d/wk
Post exposure period : remainder of normal life span
Doses : 21, 41, 206 and 617 or 1028 mg/m3 (5, 10, 50 and 150 or 250 ppm)
Result : negative
Control group : yes

Method : other: Carcinogenicity
Year :
GLP : no data
Test substance : other TS
Method : Carcinogenicity bioassay. Similar to OECD 451, major deficiencies outlined under Remark
Remark : Intervals of body weight and food consumption recording differed from OECD 451. Details of statistical data evaluation (Chi-Square Test for rats: see Tab. 11) are not contained in the publication.
Result : Clinical observations
No body weight or other data were reported except that 250 ppm was too toxic (unspecified) and required lowering the concentration to 150 ppm. No clear treatment-related hematological, blood chemistry or urinalysis changes were detected.

Mortality
Long-term survival rate low in both test and control males and observed mortalities reported to be comparable to controls .

Survival rates at 52 weeks of age in mice:

controls: 79.1 (males)
94.8 (females)

5 ppm: 60.0 % (males)
93.3 % (females)

10 ppm: 82.2 % (males)
95.6 % (females)

50 ppm: 75.6 % (males)
92.2 % (females)

250-150 ppm: 62.2 % (males)
83.3 % (females)

Survival rates at 78 weeks of age in mice:

controls: 36.6 (males)
56.8 (females)

5 ppm: 28.9 % (males)
75.6 % (females)

10 ppm: 37.8 % (males)
55.6 % (females)

50 ppm: 33.3 % (males)
54.4 % (females)

250-150 ppm: 28.9 % (males)
48.9 % (females)

There were no specific types of tumors and no relevant changes in the incidence of the tumors normally occurring in the strain of mice used. In conclusion 1,2-dichloroethane was not considered to exert carcinogenic effects in male and female Swiss mice under the conditions of the experiment.
Source : Wacker - Chemie GmbH, Burghausen, Germany.
Test condition : TEST ANIMALS

A total of 969 Swiss mice, 11 wk old at start, were used. Animals were housed in cages in groups of 10.
EXPOSURE
90 animals/sex/dose group were used. Animals were placed into whole body inhalation chambers and exposed to the TS in air at concentrations of 0, 5, 10, 50, and 150-250 ppm. Because of the marked toxic effects the highest concentration was reduced from 250 to 150 ppm (1028 mg/m3 to 617 mg/m3) after a few weeks due to marked toxicity. Animals were exposed 7hrs/d, 5d/wk, for 78 wk. A concurrent control animal group comprised 249 animals, 115 males and 134 females (kept in a nearby room).

After the exposure period, animals were allowed to live until spontaneous death.

EXAMINATIONS
Animals were controlled every 2 wk. Body weights were determined every 2 wk during the treatment and every 8 wk thereafter.
Complete autopsy was performed on each animal.
Histopathological examination consisted of gross and microscopical examination of the brain, Zymbal glands, retrobulbar glands, interscapular brown fat, salivary glands, tongue, lungs, thymus, diaphragm, liver, pancreas, kidneys, spleen, stomach, different segments of intestine, bladder, gonads, lymph nodes (axillary, inguinal, mesenteric), and any organ showing pathological lesions.

Details of statistical analysis were not reported.

Test substance : other TS: purity 99.82 %; impurities: 1,1-dichloroethane, tetrachloromethane and trichloroethene 0.02 %,tetrachloroethene 0.03 %, benzene 0.09 %

Conclusion : No tumors were seen in Swiss mice after exposure to 1,2-dichloroethane in an inhalation chamber at concentrations as high as 150 ppm for a period of 78 wk, 7hrs/d and 5 d/wk. Survival of treated mice was not significantly different from control animals.

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

Flag : Critical study for SIDS endpoint

25.06.2002 (109)

5.8.1 TOXICITY TO FERTILITY

Type	:	Fertility
Species	:	Rat
Sex	:	male/female
Strain	:	no data
Route of admin.	:	oral feed
Exposure period	:	2 yr, Fo producing 7 F1 generations
Frequency of treatm.	:	continuous, interrupted by 10-d mating periods
Prem ating exposure period		
Male	:	6 weeks
Female	:	6 weeks
Duration of test	:	2 yr
No. of generation studies	:	1
Doses	:	250, 500 ppm in diet (20-30 and 40-60 mg/kg bw/d)
Control group	:	Yes
NOAEL parental	:	= 40 - 60 mg/kg bw
NOAEL F1 offspring	:	= 40 - 60 mg/kg bw

Result : Negative
Method : other
Year : 1976
GLP : no data
Test substance : as prescribed by 1.1 - 1.4
Method : Similar to OECD 415: "multifold one-generation study" with 7 consecutive matings of the Fo generation, 5 could be reasonably evaluated due to natural decrease in fertility and vitality.
Limitations:
Only two doses were administered. The highest dose did not cause toxic effects in parental animals (In a preliminary study, liver content of total fat and triglycerides were significantly increased after 7 wk 1600 ppm TS, whereas liver fat content was unchanged after 5 wk at 600 ppm TS in the diet).
No histopathological examination of parental animals or litters was performed.
Result : TS uptake
Uptake was estimated to range between 20-30 mg/kg bw/d and 40-60 mg/kg bw/d in the low- and high-dose group, respectively, based on the daily food intake (10-30 g/d), body weight at the start and the end of the 2-yr study (100 to 400 g), the TS content, and TS loss of 30% due to evaporation.

Mortality, body weight
Mortality, food consumption, and body weight development of animals receiving 250 or 500 ppm TS in the diet was comparable to control animals.

Fertility and reproduction data
Parental animals
Male and female fertility were unaffected when compared to controls. In yr 2, the female fertility dropped steadily due to age: after the 5th pregnancy only few females conceived.

Pups
Litter size and foetal weight were unaffected. Mean body weights at birth and at weaning were comparable to controls. Mortalities of young at birth and at weaning were comparable to controls.

The authors proposed a tolerance value of 10 ppm of 1,2-dichloroethane in human food. Intake estimate was 0.07 mg/kg bw/d.
Source : Wacker Chemie GmbH, Burghausen, Germany.
Test condition : TEST ANIMALS
Locally bred rats. 90 male and 90 female litter mates were divided into 5 groups, with 18 animals per sex in each group. Animals were housed at six animals per cage. Age ca. 6 wk.
EXPOSURE/ADMINISTRATION
Animals received a diet containing 250 and 500 ppm of TS twice a day. The evening portion contained 80% of the daily intake. Animals were trained to eat rapidly in order to reduce TS losses due to evaporation. Food was weighed before and after feeding. Doses were selected based on results from preliminary studies with 300, 500 and 1600 ppm TS.
MATING
After 6 wk on experimental diet feeding females were mated with untreated males, and thereafter in 2-monthly intervals with treated males, for 10 days. Control diet was fed during this time. Females were weighed twice per wk and singly housed until parturition when they had gained 60 g. After 10 days pup were again counted, litters weighed, and dams were returned to communal cages.

EXAMINATIONS
Parent animals and litters were observed until 10 days after parturition.
Observations included
1. Parent animals:
signs of toxicity, mortalities, bodyweight changes (weekly up to wk 13, every second wk thereafter), pregnancy rate (percentage of paired females that became pregnant).
2. Litter data for rats to litter normally:
The young were counted and weighed at birth and after 10 d.
Further clinical chemistry parameters were examined in control and treated animals (3-5 animals per group) at termination of the experiment after 2 yr.
Effects on liver were examined in the preliminary study.
STATISTICS
Analysis of variance, and multiple range test of Duncan.

Test substance : 1,2-dichloroethane. No degree of purity or other data reported.
Conclusion : Reproductive performance of rats receiving 250 and 500 ppm TS in the diet was not disturbed during pregnancies 1 through 5 in a 2 yr study.
Reliability : (2) valid with restrictions
2e Meets generally accepted scientific standards, well documented and acceptable for assessment, MTD not reached, no histopathology.
Flag : Critical study for SIDS endpoint
25.06.2002 (4)

Type : One generation study
Species : Rat
Sex : male/female
Strain : Sprague-Dawley
Route of admin. : Inhalation
Exposure period : 176 exposures: males; none from gestation day 21 until lactation day for (females: for F1A and F1B litter))
Frequency of treatm. : exposures day 1 through 60: 6 h/d, 5 d/wk; exposures day 61 through 176: 6 h/d, 7 d/wk
Premating exposure period
Male : 60 d
Female : 60 d
Duration of test : 176 exposures (Bred twice to produce two F1 generations)
No. of generation studies : 1
Doses : 0, 25, 75 and 150 ppm (0, 103, 308, 616 mg/m³)
Control group : yes, concurrent no treatment
NOAEL parental : = 150 ppm
NOAEL F1 offspring : = 150 ppm
Method : other: Similar to OECD 415
Year :
GLP : no data
Test substance : as prescribed by 1.1 - 1.4
Method : Similar to OECD 415.
The highest dose did not cause toxic effects in parental animals, but at close to MTD.
Remark : Dose selection was not based on results of a range finder study. It was rather derived from results of other, comparable studies: 40 and 165 exposures, 7h/d, to 400 ppm TS was fatal to rats (Spencer et al., 1951); 300 ppm caused severe maternal toxicity in rat (Schlachte, 1979).

Mating of one male each with one female for a period of four days to produce F1A-generation; necropsy of F1A-generation between postnatal day 21 and 25, respectively. After further 7 days second mating of parental animals and necropsy of produced F1B -generation between postnatal days 21 and 25 as well.

Result : F0 parental animals
No deaths at 75 or 150 ppm exposure levels. One female control and one male and female low dose animal died.
Examinations revealed that this was not related to the TS.
No clinical signs of intoxication, no treatment-related changes in food consumption or body weight reported.
Relative organ weights of liver, kidneys, testes, uterus and ovaries were comparable to controls.

Offspring (both F1 generations)
No changes in the fertility indices, in the number of pups/litter, gestation survival, pup survival indices on days, 1, 7, 14 and 21, sex ratio at day 21, neonatal body weight and growth observed.
No substance related macroscopical and histopathological changes of liver and kidneys. No substance related external, visceral and skeletal malformations or retardations/variations observable in both F1 -generations.

Source : Wacker - Chemie GmbH, Burghausen, Germany.

Test condition : TEST ANIMALS
Male and female Sprague-Dawley rats, 6-7 wk of age. Animals were identified by a metal ear tag. Animals were housed singly, and in groups of 5-6 during periods of exposures. Control groups consisted of 30 and treated groups of 2 0 animals per sex and dose.
EXPOSURE/ADMINISTRATION
Treated animals were exposed to TS in a whole body inhalation chamber for 6 h/d under dynamic airflow conditions. TS was pumped into a vaporization vessel and heated to 90°C. Vapors were swept to the main chamber by compressed air and diluted as required. Concentration was monitored 2-3 times per hour using an infrared spectrometer.

During the first 60 exposures, the exposure period was 5d/wk. The exposure period of exposures 61-176 were 7d/wk, 6h/d. Maternal animals were not exposed from gestation through the 4th d post partum. Males continued to be exposed.
MATING
After 60 exposures the F0 animals were bred (1:1 within treatment groups) to produce the F1A generation. 7 d after sacrifice of the last F1A litter, the F0 animals bred again to produce the F1B litters.

EXAMINATIONS
Food consumption and body weight of all F0 animals was recorded weekly prior to mating; records were continued for males. Weights of rats showing vaginal smears were recorded on days 0, 6, 14, and 21 of gestation.
Parent animals and litters were observed until 21 days after parturition.
Observations included
1. Parental animals:
signs of toxicity, mortalities, bodyweights on d 1,7, 14, 21 post partum.
Date of parturition; fertility index (proportion of pregnant rats) was calculated.
2. Litter data for rats to litter normally:
Number of live and dead newborn, number and sex of live pups on days 1, 7, 14, and 21 post partum and individual pup body weights on day 21, any alterations of neonates. The indices for gestational survival and survival at days 1, 7, 14, and 21 were calculated.

NECROPSY, PATHOLOGY
All weanlings were sacrificed at 21 to 25 days of age and subjected to gross necropsy. Organ weights of kidneys and liver from one male and female weanling from 5 litters/dose were recorded, and tissue sections were preserved.

Gross pathological examination of F0 animals was performed and kidney and liver organ weights were recorded. Liver, kidneys, ovaries, uterus, and testes were preserved. Salivary glands with gross alterations were preserved and histologically examined. Microscopic examination of those tissues from 10 randomly selected rats per sex of control and top dose level were made.

STATISTICAL EVALUATIONS
Methods included Fisher's exact test for fertility index;
Wilcoxon test for survival indices and incidence of alterations in weanlings;
Dunnett's test was for body and organ weight data. Level of significance chosen was always
$p<0.05$.

Test substance : Purity 99.98 %: Contaminants at the beginning of the study: ethyl chloride 10 ppm, 1,1-dichlorethane 30 ppm, 1,2 -dichloroethylene 20 ppm, carbon tetrachloride 60 ppm, methylene chloride not detected. Contaminants at the end of study: ethyl chloride 20 ppm, 1,1 -dichlorethane 20 ppm, 1,2-dichloroethylene 70 ppm, carbon tetrachloride not detected, methylene chloride 10 ppm.

Reliability : (2) valid with restrictions
2e Meets generally accepted scientific standards, well documented and acceptable for assessment

Flag : Critical study for SIDS endpoint

25.06.2002 (120) (138)

Type : Two generation study
Species : Mouse
Sex : male/female
Strain : ICR
Route of admin. : drinking water
Exposure period : none during pregnancy and lactation
Frequency of treatm. : Daily
Premating exposure period
Male : 5 weeks (Fo); 11 weeks (F1)
Female : 5 weeks (Fo); 11 weeks (F1)
Duration of test : 25 wk and 24 wk in F0 and F1B animals, resp.
No. of generation studies :
Doses : ca. 0, 5, 15 or 50 mg/kg bw/d (30, 90 or 290 mg/l)
Control group : yes, concurrent no treatment
NOAEL parental : ca. 50 mg/kg bw
NOAEL F1 offspring : ca. 50 mg/kg bw
NOAEL F2 offspring : ca. 50 mg/kg bw
Result : NOAELs provisional; cf Conclusions
Method : other: Two generation reproductive toxicity test
Year : 1982
GLP : no data
Test substance : as prescribed by 1.1 - 1.4

Method : Similar to OECD 416. Major limitations described under Remarks
Remark : Limitations included
-Dosing: 35 d premating dosing only. No exposure during pregnancy and lactation. No MTD reached: No toxic effect noted at any of the doses used.

-Examination: Necropsy performed on pups, but no pathology and histopathology documented. No sperm parameters.

Result : Reproduction and fertility:
-Parental animals findings
Adult mice (F0 and F1B) showed no significant changes in water consumption, body weight or fertility index and gestation index (number of

females with live litters/number of females pregnant). Mortalities were seen only in the F0 animals (2/10 m, 3/30 f) at the lowest dose, e.g. effect was not dose related. At scheduled necropsy (after week 24 or 25 of dosing), neither chemical- nor dose-related gross pathology was observed in either generation.

-Litter findings
Among the offspring of F0 and F1B animals (F1A, F1B, F2A), no significant changes were seen in mean litter size, mean post-natal body weights (measured on days 7, 14 and 21), or survival (measured on days 4 and 21). There was no evidence of dose-dependent gross pathology or congential external, visceral or skeletal malformations although no details or data were given.

Source : Wacker Chemie GmbH, Burghausen, Germany.

Test condition : TEST ANIMALS
Male and female mice, 6-7 wk of age. Males were housed singly, females were kept three per cage, except during parturition and lactation when they were kept one per cage. Groups of10 males and 30 females were selected randomly.

EXPOSURE/ADMINISTRATION
TS was administered with the drinking water containing 1% Emulphor EL-620 at 0.03, 0.09, and 0.29 mg/ml, designed to yield doses of 5, 15, or 50 mg/kg bw/d. The highest dose was chosen to provide approx. 1/10 th of the LD50.

MATING, EXPERIMENTAL DESIGN
After 35 days of treatment, F0-generation was mated to produce an F1A generation (10 males, 30 females). Two wk after weaning of the offspring, the same adults were mated again to produce an F1B generation and subsequently an F1C generation applying the same mating regimen.
The F1A generation was subjected to necropsy on postnatal day 21, i.e. after weaning, while F1B mice were mated after weaning (three wk) and a further 11 wk of treatment to produce F2A and, two wk after weaning of the F2A generation,
F2B.

The F2A generation was autopsied on postnatal day 21.

EXAMINATIONS
Food consumption and body weight of all F0 animals was recorded weekly prior to mating; records were continued for males. Weights of rats showing vaginal smears were recorded on days 0, 6, 14, and 21 of gestation.
1) Reproduction study
Parent animals and litters were observed until 21 days after parturition.
Observations included
1.1) Parental animals:
Weekly body weight and twice-weekly fluid consumption was determined.
Mortalities were calculated at the termination of each generation (25 wk of dosing for F0; 24 wk for F1B).
Fertility index (proportion of pregnant rats) and gestation index were calculated.
1.2) Litter data for rats to litter normally:
21-day survival data collected on litters from F1A, F1B, F2A matings. Litter size recorded on days 0, 4, 7, 14, and 21. Litters culled to 10 pups on each day 4. Offspring were weighed collectively on days 7 and 14 and individually on day 21. Viability and lactation indices were calculated.

NECROPSY
All pups from each litter were sacrificed at 21 days of age and subjected to

gross necropsy.

STATISTICAL EVALUATIONS
Group differences in body weight and fluid uptake: Duncan's multiple range test. Adult reproductive performance was evaluated by fertility and gestation indices. Evaluation of litter data included Kruskal-Wallis test and Dunn's test. Level of significance chosen was always $p<0.05$.

Test substance : Purity >99%
Reliability : (2) valid with restrictions
2e Meets generally accepted scientific standards, limited documentation, acceptable for assessment, MTD not reached (see also Remarks)
Flag : Critical study for SIDS endpoint
25.06.2002 (103)

5.8.2 DEVELOPMENTAL TOXICITY/TERATOGENICITY

Species : rat
Sex : female
Strain : Sprague-Dawley
Route of admin. : inhalation
Exposure period : days 6-15 gestation
Frequency of treatm. : daily
Duration of test : 10 d, 7 hrs/day
Doses : 0 (30 females), 100 (30 females), 300 ppm (16 females)
Control group : yes
NOAEL maternal tox. : = 100 ppm
NOAEL teratogen. : > 100 ppm
NOAEL Embryotoxicity : = 100 ppm
Result : negative
Method : other
Year :
GLP : no data
Test substance : as prescribed by 1.1 - 1.4
Method : Similar to OECD 414
Remark : Limitation
Only two concentrations tested instead of 3.
Due to high mortality no teratogenicity effects could be studied at the highest dose.

Inhalation route was chosen because it was deemed the most important route of human exposure.

Result : No maternal deaths and no signs of toxicity observed in rats at 100 ppm. Maternal body weight was significantly increased compared to controls. Severe maternal toxicity was seen in rats at 300 ppm. Lethargy, ataxia, decreased body weights and food intake, some vaginal bleeding was seen prior to deaths in 10/16 dams.

Rats exposed to 100 ppm and their offspring no differences were seen when compared to controls in mean litter size, incidence of resorptions, foetal body weight and length. The incidence of malformations was comparable to or lower than those observed in control fetuses for total major malformations, soft tissue and skeletal malformations.

In contrast, there was only one litter from the survivors exposed to 300 ppm. All of the 14 implantations of this litter were resorbed (100%; for comparison: controls 7%, low dose 3%). Thus no fetuses were obtained from the high dose animals for further examinations.

Source : Wacker Chemie GmbH, Burghausen, Germany.

Test condition : TEST ANIMALS
Female rats, ca. 250 g bw. The rats were bred by the supplier.
EXPOSURE/ADMINISTRATION
Groups of rats were exposed to filtered air (30 control rats), 100 ppm (30 rats) or 300 ppm of TS (16 rats) in a 4.3 m³ inhalation chamber for 7 h/d through days 6-15 of gestation under dynamic airflow conditions. TS atmospheres were generated by pumping TS into a h eated vaporisation vessel (90°) from where the vapor was swept to the inhalation chamber and diluted as required. Nominal concentrations were calculated daily. Concentrations were monitored 2-3 times per hour using an IR spectrophotometer. Doses were selected based on the results of Spencer (1951).
MATING, EXPERIMENTAL DESIGN
The rats were bred by the supplier. Rats were sacrificed on day 21 of gestation.

EXAMINATIONS
Animals were observed and weighed periodically.
NECROPSY
After sacrifice, the number of corpora lutea and number and position of live, dead, and resorbed fetuses were recorded. Fetuses were weighed, measured for length, sexed, and examined for cleft palate and external alterations. 1/3rd of the fetuses of each litter were examined immediate ly for soft tissue alterations by dissection under a microscope. All fetuses were stained with alizarin red-S to permit examination for skeletal alterations.

STATISTICAL EVALUATIONS
Modified Wilcoxon test was used to evaluate incidences of fetal alterations, survival incidences, and resorptions.
Level of significance chosen was always $p<0.05$.

Test substance : Purity 99.9%

Conclusion : Findings after inhalation exposure of pregnant rats for 7h/d during days 6-15 of gestation at 100 ppm and 300 ppm:

- No signs of maternal toxicity, developmental or embryotoxicity, or teratogenicity at 100 ppm.

- Severe maternal toxicity and ca. 60% maternal mortality. Only 1 litter was detected which was 100% resorbed. Due to high mortality no evaluation of embryotoxicity and teratogenicity possible.

Thus, under the conditions of this study the NOAEL was 100 ppm for maternal toxicity, embryotoxicity, and teratogenicity.

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

Flag : Critical study for SIDS endpoint

25.06.2002 (138) (172)

Species : Rat
Sex : female
Strain : Sprague-Dawley
Route of admin. : inhalation
Exposure period : days 6-20 of gestation
Frequency of treatm. : 1x/d
Duration of test : 6 h/d
Doses : 150, 200, 250, 300 ppm
(= 600, 800, 1000, 1200 mg/m³)
Control group : yes, concurrent no treatment
NOAEL maternal tox. : = 250 ppm

NOAEL teratogen.	:	= 300 ppm
NOAEL Embryotoxicity	:	= 300 ppm
NOAEL Fetotoxicity	:	= 300 ppm
Result	:	negative
Method	:	other: no data
Year	:	1995
GLP	:	no data
Test substance	:	as prescribed by 1.1 - 1.4
Result	:	26 female rats were used per group with 24 to 15 litters delivered. At 300 ppm: 2/26 dams died. Maternal toxicity was indicated by intermittent decreased weight gains (day 6 - 21; 13 - 21) and expressed in a negative trend of the absolute weight gain of dams in surviving dams. No embryo- or fetotoxicity, no exposure-related changes in numbers of implantations, resorptions, and live fetuses, fetal sex ratio or body weights, or external, visceral, or skeletal development teratological effects were induced at any dose as compared to the control.
Test condition	:	Analytical chamber concentrations were: 150 +-5; 194 +-8; 254 +-11; 329 +-18 ppm.
Conclusion	:	No embryo- or fetotoxicity or teratogenicity noted at concentrations which caused maternal toxicity.
Reliability	:	(1) valid without restriction Comparable to guideline study, well documented.
Flag	:	Critical study for SIDS endpoint

25.06.2002 (130)

Species	:	rabbit
Sex	:	female
Strain	:	New Zealand white
Route of admin.	:	inhalation
Exposure period	:	days 6-18 gestation
Frequency of treatm.	:	daily
Duration of test	:	13 days, 7 hrs/day
Doses	:	0, 100 or 300 ppm
Control group	:	yes, concurrent no treatment
NOAEL teratogen.	:	= 300 ppm
	:	ppm
NOAEL Embryotoxicity	:	= 300 ppm
Result	:	negative
Method	:	other
Year	:	
GLP	:	no data
Test substance	:	as prescribed by 1.1 - 1.4
Method	:	Similar to OECD 414
Remark	:	Limitations Only 2 concentrations used. Maternal toxicity was >10% at either concentration. Thus, the study does not fully comply with the current OECD 414.
Result	:	At both 100 ppm and 300 ppm, maternal deaths in 4/21 (19%) and 3/19 (16%) dams occurred, respectively, no deaths in the control. Unclear cause of mortality, particular at 100 ppm: no dose-response, no treatment-related pathological changes on necropsy. Gross necropsy did not reveal any treatment-related pathological changes in these dams. In survivors and their offspring no differences were seen when compared to controls in mean litter size, fetuses per litter, incidence of resorptions, foetal body weight and length, sex ratio. The incidence of malformations was comparable to or lower than those

observed in control fetuses for total major malformations, soft tissue and skeletal malformations. Significantly lower incidences were seen in 13 ribs in litters at 100 ppm and in lumbal spurs among litters at 100 and 300 ppm. These alterations are considered to be minor skeletal variants without toxicological significance.

Severe multiple malformations were seen in 0/101 control fetuses, 1/75 low-dose and 1/85 high-dose fetuses. The fetus at 100 ppm showed misshapen vertebrae, hemivertebrae, delayed ossification of thoracic vertebrae, and unfused thoracic centra. The fetus at 300 ppm exhibited several external malformations (acephaly, omphalocele, kyphosis, bilateral ectrodactyly and anonychia), soft tissue alterations (missing thymus, diaphragmatic hernia, heart anomalies), and skeletal malformations (delayed ossification of ribs and vertebrae, bilobed and unfused thoracic centra, misshapen sternebrae). Alterations were, however, not significantly increased over controls.

Source : Wacker Chemie GmbH, Burghausen, Germany.

Test condition : TEST ANIMALS
Female New Zealand white rabbits, ca. 3.5-4.5 kg bw. The rabbits were allowed at least 3 wk for acclimation before the study started.
EXPOSURE/ADMINISTRATION
Groups of rabbits were exposed to filtered air (20 controls), 100 ppm (21 animals) or 300 ppm of TS (19 animals) in a 4.3 m^3 inhalation chamber for 7 h/d through days 6-18 of gestation under dynamic airflow conditions. TS atmospheres were generated by pumping TS into a heated vaporisation vessel (90°) from where the vapor was swept to the inhalation chamber and diluted as required. Nominal concentrations were calculated daily. Concentrations were monitored 2-3 times per hour using an IR spectrophotometer. Doses were selected based on the results of Spencer (1951).
MATING, EXPERIMENTAL DESIGN
The rabbits were artificially inseminated. Rabbits were sacrificed on day 29 of gestation.

EXAMINATIONS
Animals were observed and weighed periodically.
NECROPSY
After sacrifice, the number of corpora lutea and number and position of live, dead, and resorbed fetuses were recorded. Fetuses were weighed, measured for length, and examined for cleft palate and external alterations. 1/3rd of the fetuses of each litter were examined immediately for soft tissue alterations by dissection under a microscope. Rabbit fetuses were sexed according to internal genitalia. All fetuses were stained with alizarin red-S to permit examination for skeletal alterations.

STATISTICAL EVALUATIONS
Modified Wilcoxon test was used to evaluate incidences of fetal alterations, survival incidences, and resorptions.
Level of significance chosen was always $p<0.05$.

Test substance : Purity 99.9%, from Dow Chem.

Conclusion : Findings after inhalation exposure of pregnant rabbits for 7h/d during days 6-18 of gestation at 100 ppm and 300 ppm:

- No clear treatment-related maternal toxicity at both 100 and 300 ppm, but in 19% and 16% maternal mortality, respectively.

- No changes were seen at either 100 or 300 ppm regarding pregnancy rate, litter size, implantation loss, sex ratio, fetal size and weights.

- No changes seen at either 100 or 300 ppm regarding incidences of

external, or soft tissue, or skeletal malformations.

Thus, under the conditions of this study the LOAEL was 100 ppm for maternal toxicity. With regard to embryotoxicity and teratogenicity the NOAEL was 300 ppm.

Reliability : (2) valid with restrictions
2c Comparable to guideline study with acceptable restrictions.
Flag : Critical study for SIDS endpoint
25.06.2002 (138) (172)

Species	:	rat
Sex	:	female
Strain	:	Sprague-Dawley
Route of admin.	:	gavage
Exposure period	:	days 6-20 of gestation
Frequency of treatm.	:	1x/d in corn oil (2ml/kg bw)
Duration of test	:	
Doses	:	1.2, 1.6, 2.0, 2.4 mmol/kg bw/d (= 118, 158, 198, 238 mg/kg bw/d)
Control group	:	yes, concurrent vehicle
NOAEL maternal tox.	:	ca. 160 mg/kg bw
NOAEL teratogen.	:	ca. 240 mg/kg bw
NOAEL Embryotoxicity	:	ca. 160 mg/kg bw
NOAEL Fetotoxicity	:	ca. 240 mg/kg bw
Result	:	negative
Method	:	other: no data
Year	:	
GLP	:	no data
Test substance	:	as prescribed by 1.1 - 1.4
Method	:	26 female rats were used per group with
Result	:	26 female rats were used per group with 23 to 16 litters delivered.

Maternal toxicity was indicated by decreased absolute weight gain at the two highest oral dose levels.

At 240 mg/kg, 3 dams delivered pre-term on day 20. All fetuses of these litters were dead and were excluded from further final analysis of reproductive parameters due to possibility of cannabalism.

No significant effect was noted on the mean number of implantation sites and live fetuses, fetal sex ratio, and fetal body weights.

No embryo- or fetotoxicity, changes in fetal growth or teratological effects were induced at any dose. All malformations and variations seen were scattered among all groups with no indication of treatment-related effect.

There was only some embryolethal effects (increase in non-viable implants and resorption sites per litter), significant at 200 mg/kg and higher ($p<0.05$).

Test substance : Purity>99%, from Merck
Conclusion : No embryo- or fetotoxicity or teratogenicity noted at concentrations which caused maternal toxicity.
Reliability : (1) valid without restriction
Comparable to guideline study, well documented.
Flag : Critical study for SIDS endpoint
23.05.2002 (130)

5.8.3 TOXICITY TO REPRODUCTION, OTHER STUDIES

5.9 SPECIFIC INVESTIGATIONS

5.10 EXPOSURE EXPERIENCE

Type of experience : other: General Effects in Humans

Remark : Ethylene dichloride is a central nervous system depressant that produces symptoms ranging from nausea, vomiting, headache, lightheadedness and weakness to stupor, dysequilibrium, coma, and respiratory arrest. Typically, in severe cases, central nervous system signs appear first within several hours of exposure and are followed by a quiescent period. On the second day, oliguria and hepatic transaminasemia may develop. Subsequently, over the next several days, hepato-renal failure can occur. Severe ingestions produce widespread organ damage (especially kidney, liver, and adrenal gland) as well as gastrointestinal bleeding. Hepatic and renal dysfunction has been complicated by fatal massive midzonal hepatic necrosis, acute tubular necrosis, hypoglycemia, hypercalcemia, hypoprothombinemia, reduced clotting factors, adrenal necrosis,& gastrointestinal hemorrhage. Heavy exposure produces a bluish purple discoloration of the skin, dermatitis, & corneal abrasions.

Source : Wacker Chemie GmbH, Burghausen, Germany.
Reliability : (2) valid with restrictions
Flag : Critical study for SIDS endpoint
27.06.2002 (56)

Type of experience : other: Acute oral Toxicity in Humans
Remark : Accidental oral ingestion of a single dose of 0.5-1.0 g/kg has been reported to result in death; autopsy revealed liver necrosis and focal adrenal degeneration and necrosis.
Source : Wacker Chemie GmbH, Burghausen, Germany.
Reliability : (2) valid with restrictions
Flag : Critical study for SIDS endpoint
27.06.2002 (123)

Type of experience : other: Chronic poisoning in humans
Remark : Experience after Chronic Poisoning From inhalation or skin absorption: Weight loss, low blood pressure, jaundice, oliguria, or anemia may occur after repeated exposure.
Source : Wacker Chemie GmbH, Burghausen, Germany.
Reliability : (2) valid with restrictions
Flag : Critical study for SIDS endpoint
27.06.2002 (53)

Type of experience : other: Local Effects after Repeated Contact
Remark : Repeated contact with liquid can produce a dry, scaly, fissured dermatitis. Liquid and vapor may also cause eye damage, including corneal opacity. Acute exposures can lead to death from respiratory and circulatory failure. Autopsies have revealed widespread bleeding and damage in most internal organs.
Source : Wacker Chemie GmbH, Burghausen, Germany.
Reliability : (2) valid with restrictions
Flag : Critical study for SIDS endpoint
27.06.2002 (152)

Type of experience : other: General Findings in Humans after Ingestion
Remark : In man, death has resulted from the ingestion of 20 to 50 ml. Ethylene dichloride is hepato- and nephro-toxic. Acute exposure also leads to central

nervous depression, reduced blood pressure, and cardiac impairment. In humans, signs of intoxication are headache, nausea, vomiting, dizziness, watery stool, internal bleeding, cyanosis, weak and rapid pulse and loss of consciousness. In one human poisoning by ingestion, hypoglycemia, increased clotting time and hypercalcemia were prominent laboratory findings. Symptoms developed slowly; death occurred after six days. Extensive necrosis of liver, kidney and adrenal glands was found at autopsy.

Source : Wacker Chemie GmbH, Burghausen, Germany.
Reliability : (2) valid with restrictions
Flag : Critical study for SIDS endpoint
27.06.2002 (64)

Type of experience : other: Toxicity of a Solvent Mixture
Remark : Fatal dichloromethane poisoning in two workers following inhalation exposure was described. The two men (50 and 55 years old) were employed at an Italian chemical factory and were found dead in a 2 meter deep well where they had been burying barrels of chemical waste. The barrels contained mixed solvent and solid wastes. On site air sampling found dichloromethane vapor concentrations ranging up to 582 mg/l. Concentrations below 6 mg/l of 1 2-dichloroethane, l,l,l-trichloroethane and styrene were also detected. Blood samples collected 24 hours after death contained 571.6 and 600.9 mg/l dichloromethane. Smaller concentrations of 1,2-dichloroethane, 1,1,1 -trichloroethane and styrene were also found. Blood carboxyhemoglobin concentrations of 30% saturation were also found. Autopsies revealed extensive brain and lung edema and congestion, gastric congestion and erosive multifocal gastritis in both victims. Kidney congestion was manifested as tubular swelling and degeneration, glomerular swelling and congestion of the vessels. Congestion was also seen in the liver, spleen and adrenals. Both deaths were caused by acute inhalation of extremely high dichloromethane vapor concentrations.
Source : Wacker Chemie GmbH, Burghausen, Germany.
Reliability : (4) not assignable
Flag : non confidential
25.06.2002 (110)

Type of experience : other: Biochemical Study with Human Liver Fractions
Remark : In vitro experiments with human liver microsomes showed that oxidative metabolism of 1,2 -dichloroethane is mediated mainly by cytochrome P450 2E1.
Source : Wacker Chemie GmbH, Burghausen, Germany.
25.06.2002 (67)

Type of experience : other: Elimination(Clearance) after Inhalation
Remark : On the basis of results derived from animal studies (inhalation), a pulmonary clearance of 17 l/h (12 %) (with an assumed alveolar ventilation rate of 336 l/h) and a metabolic clearance of 130 l/h (88 %) has been calculated. This indicates very short hal-life in the body.
Source : Wacker - Chemie GmbH, Burghausen, Germany.
25.06.2002 (148)

Type of experience : other: Skin contact
Remark : After intermittent immersion of the hands of 3 men into 1,2-DCE a during 4 hours, a severe dermatitis developed, which was assigned to the degreasing ability of 1,2-dichloroethane.
Species: human
Exposure route: hand immersion
Source : Wacker Chemie GmbH, Burghausen, Germany.
Reliability : (2) valid with restrictions
Flag : Critical study for SIDS endpoint

25.06.2002 (191)

Type of experience : other: Genotoxicity in Humans: SCE
Result : It was found that smoking and exposure to EDC around 1 ppm was associated with an increased sister chromatic exchange frequency. In contrast, no association of age with SCE-rates was observable as was the consumption of alcohol. However, according to the reported histories alcohol consumption of the workers examined was low.

An increase of SCE frequencies as compared to controls was found and was correlated with increased EDC exposure: The mean increase vs. the unexposed control for the low EDC group was about 7 % (not statistically significant), and for moderate was about 24 % ($p<0.01$) (Tab. 3); SD or variance not given.

It was contended that relatively small amounts of EDC cause an increase in SCE frequency. This increasewas also obvious in non-smoking workers.
Source : Wacker - Chemie GmbH, Burghausenm, Germany
Test condition : 71 workers of a vinyl chloride manufacturing plant exposed to different level of a mixture of vinyl chloride monomer (VCM) and ethylene dichloride (EDC) were examined.

Exposure categories were defined:
---
low VCM/low EDC (VCM:0.25 - 0.39 ppm; EDC: 0.20 - 0.29ppm);

low VCM/moderate EDC (VCM:0.16 - 0.27ppm; EDC: 0.69 - 1.31ppm);

moderate VCM/moderate EDC (VCM: median of 1.63ppm; EDC: median of 0.77ppm);

A generally accepted protocol for isolation and preparation of peripheral lymphocytes and for the determination of SCE frequency was applied. The smoker status, alcohol consumption habits and a detailed medical and occupational history of the workers examined found consideration.
Reliability : (2) valid with restrictions
Study acceptably documented, but the low number of people per exposure group (8 to 23) as well as the low increases associated with an appreciable variance appears to limit a definite statement.
Flag : Critical study for SIDS endpoint
27.06.2002 (45)

Type of experience : Direct observation, poisoning incidents
Result : An ingestion of approx. 15 ml by a 14-year old boy resulted in fatal hepatorenal failure.
25.06.2002 (56) (194)

5.11 ADDITIONAL REMARKS

Type : Metabolism
Remark : After oral and i.p. administration as well as after inhalation 1,2-dichloroethane is being extensively metabolised. The far majority (48 - 86 %) of resorbed 1,2-dichlorethane is being transformed to metabolites excreted with urine. Only a minor quantity is metabolised to carbon dioxide (4 - 18 %) while 8 - 42 % of administered material is exhaled as unchanged compound.

Urinary metabolites were identified as thiodiacetic acid, the corresponding

sulfoxide and S-carboxymethylcysteine suggesting a role for glutathione in the biotransformation.
Small amounts of chloroacetic acid and very low concentrations of S,S´-ethylene-bis-cysteine and chloroethanol have been found in the urine also.

Metabolism of 1,2-dichloroethane is being mediated by both the glutathione pathway and mixed functional oxidases, i.e. by enzymes of the cytochrome P450 family where cytochromes P450 make a larger contribution. Both metabolic routes produce reactive metabolites where chloroacetaldehyde and chloroethanol is being formed by cytochromes P450 and an episulfoniumion via glutathione conjugation which is capable of binding to macromolecules of the DNA.

Source : Wacker Chemie GmbH, Burghausen, Germany.
Reliability : (2) valid with restrictions
Flag : Critical study for SIDS endpoint
27.06.2002 (68) (173) (193)

Type : other: ADME
Remark : In animal studies 1,2-dichloroethane is being resorbed rapidly after oral and dermal administration and after inhalation.

In light of its lipophilicity the compound is mainly distributed to fatty tissue with maximum values reached in these tissues after 45 to 60 minutes when administered orally. Maximum liver concentrations were observed after 10 minutes with declining concentrations thereafter.

After inhalation elimination rates of resorbed 1,2 -dichloroethane were slowest from fatty tissues and fastest from the lungs.

Ninety percent of resorbed compound is eliminated from rats and mice after oral administration and by rats after inhalation within 48 hours. After i.p. injection to mice 90 % of the administered dose was exreted within 24 hours.

The far majority (48 % after i.p. injection to mice and 86 % after oral administration to rats) of resorbed 1,2-dichlorethane is being excreted with urine. Only a minor quantity is exhaled as carbon dioxide (4 - 18 %) while 8 % (after oral administration to mice) to 42 % (after i.p. injection to mice) of administered material is exhaled as unchanged compound. Regardless of the route of administration excretion via the faeces is negligible.

Source : Wacker - Chemie GmbH, Burghausen, Germany.
Reliability : (2) valid with restrictions
Flag : Critical study for SIDS endpoint
27.06.2002 (12) (87) (116) (141) (156) (173) (174) (193)

Type : other: Bioavailability oral/inhalation
Method : Blood levels, distribution, and elimination of DCE was determined in male SD rats after single exposures (i.v.,oral, and inhalation). Inhalation was 6 h, which allowed to reach a kind of steady state, while oral administration was by gavage, which failed to arrive at equilibrium. Summary results of full pharmacokinetics including calculation of the AUCs and elimination plots are presented.
Remark : COMPARISON ORAL/INHALATION
- 50 ppm (non toxic after prolonged exposure): Based on the kinetic profile including AUC and peak levels, no relationship can be established for any oral dose: even at 25 mg/kg, all corresponding tissue values are significant higher. This suggests that 50 ppm correlates to an oral dose significantly below 25 mg/kg.

- 250 ppm (clearly toxic after prolonged exposure): Based onthe kinetic

profile including AUC and peak levels, no clear relationship can be established for any oral dose, but there are overlaps with 50 mg/kg and 25 mg/kg. This may indicatethat this concentration may correlate to a dose between 25and 50 mg/kg (which exhibited no or only low toxicity afterprolonged oral administration).

- AUCs for blood after inhalation are generally significantly smaller than after oral gavage application, although doses are said to be of the same order (Reitz et a., 1982; Spreafico et al., 1980): e.g. the 14C-balance after inhalation exposure arrived only at about 1/3 of recovery as compared with that after oral exposure, although the specific radioactivities of the applied test materials for both 150 mg/kg(oral) and 150 ppm(inh.) were the same (see p. 195; Tab. 1/p. 196). This, too, indicates that either bioavailability or metabolism/distribution of DCE after inhalation are not comparabel with the oral gavage scenario.

Reliability : (2) valid with restrictions
Flag : Critical study for SIDS endpoint
25.06.2002 (141) (156)

Type : other: Toxicokinetics/ADE

Method : Blood levels, distribution, and elimination of DCE was determined in male SD rats after single exposures (i.v., oral, and inhalation). Inhalation was 6 h, which allowed to reach a kind of steady state, while oral administration was by gavage, which failed to arrive at equilibrium.

Summary results of full pharmacokinetics including calculation of the AUCs and elimination plots are presented.

Remark : Spreafico et al; S. 22: "On this basis, a mechanism similar to that advanced for vinyl chloride bei Heiner et al. (1975) and Watanabe et al (1976), could in principle be postulated. According to this hypothesis, the liver metabolic capacity for EDC is saturable, (Filser and Bolt 1979), so that when confronted with lower quantitites of the chemical non oncogenic metabolites are produced, such as for instance chloroethylglutathione, a biotransformation product of EDC known to be a potent mutagen (Rannug and Beije 1979). In the absence of direct data on the levels and relative biological activity of the metabolites formed after oral and inhalatory exposure to EDC, such a mechanism remains purely hypothetical and its relevance in carcinogenicity testing unproven, also considering the possibility that a significant biotransformation of EDC may take place also at extrahepatic sites in organs possibly possessing different saturation rates and exhibiting different kinetics of EDC accumulation".

Result : 1. ABSORPTION during inhalation exposure (from Tab. 7/8):
At 50 ppm for 6 h, steady states are reached after 2 h with respect to constancy of blood, lung, liver and adipose-tissue levels. At 250 ppm for 6 h, steady states are reached after >3 h with respect to blood and tissue levels.

The 5-fold increase in the exposure concentration led to a multifold enhancement of DCE in tissues:

At 250 ppm as compared to respective levels at 50 ppm (Fig. 3 A,B, Tab. 6):
- in blood about 23x
- in liver about 20x
- in lung about 35x
- in adipose about 27x.

This indicates limitation of elimination mechanisms (saturation) at the high exposure level, although the elimination rate remains extremely high and is

only slowed down at a factor of about 2 (see below).

2. Blood and liver ELIMINATION kinetics

After single oral administration (gavage, olive oil, 1.5 ml/kg) (data from Tab. 6 and Fig. 2/3):

	Blood Peak level [ug/ml]	Blood t/2 [min]	Liver Peak level [ug/g]	Liver t/2 [min]
25 mg/kg	13.3	25	30	19
50 mg/kg	32	44	55	42
150 mg/kg	67	57	92	65

After single 6-h inhalation (data from Tab. 6 and Fig. 2/3):

	Blood Peak level [ug/ml]	Blood t/2 [min]	Liver Peak level [ug/g]	Liver t/2 [min]
50 ppm	1.4	13	1.0	11
250 ppm	31	22	22	18

3. TISSUE CONCENTRATIONs
- Adipose tissue levels:
Highest concentrations are found in fat tissue, although also the elimination rate (second kinetic phase) was high throughout and in the range of the other tissues documented, T/2 generally <= 30 min except for 250 mg/kg (oral) with a T/2 of about 60 min.

The peak adipose levels for 150 mg/kg (oral) was similar to that found after 250 ppm (inh.) at about 260 ug/g each. At 25 mg/kg (oral), this level was 11x higher than after exposure to 50 ppm (110 vs. 10 ug/g).

- Lung tissue levels:
After oral administration of the selected doses, no exponential increase of DCE was seen in the lung (like in the other tissues), in contrast to inhalation exposure (like in the other tissues) [see above: absorption]. At a dose 25 mg/kg, the lung level was at about 7.5x higher than that seen after 50 ppm (inhal.). After 50 or 150 mg/kg, it became relatively lower than in the lung from animals exposed to 250 ppm (approx. 0.7 to 0.5x).

- Liver levels:
All liver levels after oral dosing were significantly higher than those found after inhalation even to the highest concentration (see Table above).

Reliability : (1) valid without restriction
Flag : Critical study for SIDS endpoint
13.05.2002 (156)

Type : other: Toxicokinetics/ADE
Result : The distribution, blood or tissue concentrations of 1,2-dichloroethane in rats following repeated oral administration of 50 mg/kg (10 daily doses) was not different from those observed after single dose. This finding suggests that bioaccumulation of 1,2-dichloroethane does not occur with repeated oral exposure.
Reliability : (2) valid with restrictions

Flag : Critical study for SIDS endpoint
13.05.2002 (156)

Type : other: Toxicokinetics/blood levels
Result : After a 7-h inhalation period within the scope of a 2-years study (see entry under 5.4), mean blood levels of unchanged DCE in rats were as follows (from Tab. 9, p. 256):

	Time interval after exposure [h] 0.25	2.25
Male [ug/ml]	0.28 +-0.13	0.22 +-0.13
Female [ug/ml]	0.26 +-0.08	0.28 +-0.04

average of 5 SD rats per group
(air concentration: 50 ppm)
Analysis by GC
Remark: The time points and frequency of measurements during the course of the study not specified.

After previous prolonged exposure, DCE-blood levels did not or only slightly decrease after an additional 2 hours, which is contrary to findings after single exposure (see Reitz et al., 1982; Spreafico et al, 1980).

Note: In combination with disulfiram (0.05 %) in the feed, the blood level increased at about a factor of 5 (approx. 1.5 ug/ml), presumably due to inhibition of the aldehyde dehydrogenase, associated with increased toxicity. (Cheever et al., 1990)

Reliability : (2) valid with restrictions
Flag : Critical study for SIDS endpoint
13.05.2002 (43)

Type : other: Toxicokinetics/blood levels
Result : After 6- to 7-h inhalation exposure, the following DCE concentrations in blood were analysed (p. 118) (see also entry under 5.4):

Species (No.)	DCE exposure conc. [ppm]	blood level [ug/ml]
rabbit (3)	3000	40, 57, 79
rabbit (3)	1500	20, 25, 25
dogs (2)	1500	27, 40
dogs (21)	1000	average 23 (range: 8-30)

Note: DCE conc. were lethal or toxic.

Reliability : (2) valid with restrictions
Flag : Critical study for SIDS endpoint
13.05.2002 (77)

Type : other: Toxicokinetics/blood levels
Method : Blood levels, distribution, and elimination of DCE was determined in male Osborne-Mendel rats after single exposures (oral: 150 mg/kg, and inhalation: 150 ppm). Inhalation was 6 h, which allowed to reach a kind of steady state, while oral administration was by gavage, which failed to arrive at equilibrium.

The study further included: Distribution of 14C-DCE, DNA covalent binding

Summary results of full pharmacokinetics including calculation of the AUCs and elimination plots are presented.

Remark : Blood level and toxicity (acc. to author): "Thus it appears that a saturation of EDC metabolism may exist in both strains of rats at about 5 to 10 µg EDC/ml blood. As long as blood levels of EDC were below this saturating level, EDC was readily eliminated. However, once the EDC-blood levels exceeded the KM, elimination of EDC became saturated, resulting in increased half-lives and disproportionately increased AUCs. As discussed elsewhere, such a situation may result in unexpected toxicity when blood levels ries above the saturation level."

Result : 1. After inhalation (150 ppm):
Blood level after 4 h: 8.3 +-1.9 ug/ml = 92 % of the 6-h value (n = 4), indicating steady state after this time.
Blood level after 6 h: 8 - 10 ug/ml. The T/2 were approx. 10 min (rapid phase) and approx. 30 min (second phase):
About 80 % of DCE disappeared from blood within about 30 min., >97 % after 80 min.

2. After oral administration (150 mg/kg)
Peak blood level (after 15 min): 30 to 44 ug/ml, 4 to 5x higher than after inhalation. T/2 was about 90 min (second phase), but appeared to accelerate at about 10 ug/ml (not found in the study by Spreafico et al., 1980). About 80 % of DCE disappeared from blood within about 3 h (= 10 ug/ml-blood level): i.e. that very blood concentration after oral gavage which correlates to the initial peak level after inhalation was surpassed for about 3 h after gavage dosing. Complete elimination from blood took about 6 h.

Reliability : (2) valid with restrictions
Flag : Critical study for SIDS endpoint
13.05.2002 (141)

Type : other: Toxicokinetics/placental transfer
Method : Oral administration of an oral dose of 1.6 mmol/kg DCE, radiolabeled, to pregnant rats on gestation day 12 and 18: Time-dependent distribution of the radioactivity was followed in maternal and foetal compartments.

Result : Radioactivity increased in all maternal and foetal tissue after 1 to 4 h and then declined rapidly to 8 - 33 % of the maximal levels 48 h after treatment. The disappearance was slower in the uterus and conceptus than in other tissues.

Unchanged DCE and/or its metabolites traverse well the placental barrier, their levels in the placenta and fetus were comparable to those in maternal plasma after oral administration in late gestation.

Reliability : (2) valid with restrictions
Flag : Critical study for SIDS endpoint
25.06.2002 (130)

6.1 ANALYTICAL METHODS

6.2 DETECTION AND IDENTIFICATION

7.1 FUNCTION

7.2 EFFECTS ON ORGANISMS TO BE CONTROLLED

7.3 ORGANISMS TO BE PROTECTED

7.4 USER

7.5 RESISTANCE

8.1 METHODS HANDLING AND STORING

8.2 FIRE GUIDANCE

8.3 EMERGENCY MEASURES

8.4 POSSIB. OF RENDERING SUBST. HARMLESS

8.5 WASTE MANAGEMENT

8.6 SIDE-EFFECTS DETECTION

8.7 SUBSTANCE REGISTERED AS DANGEROUS FOR GROUND WATER

8.8 REACTIVITY TOWARDS CONTAINER MATERIAL

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10.1 END POINT SUMMARY

10.2 HAZARD SUMMARY

10.3 RISK ASSESSMENT