FOREWORD INTRODUCTION

1,1,2,2-TETRACHLOROETHANE

CAS N°:79-34-5

SIDS Initial Assessment Report

For

SIAM 15

Boston, Massachussetts, 22-25 October 2002

1. Chemical Name: 1,1,2,2-Tetrachloroethane

2. CAS Number: 79-34-5

3. Sponsor Country: France
National SIDS Contact Point in Sponsor Country:
Mme Laurence Musset
Ministère de l'Environnement et de l'Aménagement du Territoire
20, avenue de Ségur
75302 Paris 07 SP
France

4. Shared Partnership with:

5. Roles/Responsibilities of the Partners:

- Name of industry sponsor /consortium
- Process used

6. Sponsorship History

- How was the chemical or category brought into the OECD HPV Chemicals Programme ?

7. Review Process Prior to the SIAM: The national peer review consisted of a presentation and critical discussion at a national panel of experts in toxicology and ecotoxicology from administration, university and industry and nominated by the ministry of environment. In parallel, a review was performed by the national institute on environmental and industrial risk (INERIS) by request from the ministry of environment. For this particular substance, only the verification of the most relevant underlying study reports or publications was performed (e.g. long-term aquatic toxicity).

8. Quality check process:

9. Date of Submission: 9 August 2002

10. Date of last Update:

11. Comments:

SIDS INITIAL ASSESSMENT PROFILE

CAS No.	79-34-5
Chemical Name	1,1,2,2-Tetrachloroethane
Structural Formula	$Cl_2HC - CCl_2H$

SUMMARY CONCLUSIONS OF THE SIAR

1,1,2,2-Tetrachloroethane is a colourless volatile liquid with chloroform-like odour.

Human Health

Based on the large body of past human experience, 1,1,2,2-tetrachloroethane can be considered as very toxic to humans exposed acutely. It is irritating to skin and eye. Repeated exposure observations in laboratory animals and cases reported in humans indicate that it is mainly toxic to the liver and the kidney; it can also damage the nervous system and the hematological system. No standard reproductive toxicity studies in laboratory animals are available. The available data are conflicting and no conclusion can be made regarding effects of 1,1,2,2-tetrachloroethane on reproductive organs. The database for developmental toxicity is poor and adverse developmental effects were reported in rats and mice at doses known to be clearly toxic to pregnant females. It is not possible to draw a valid assessment from these studies on developmental toxicity. Some potential for genotoxicity of 1,1,2,2-tetrachloroethane has been demonstrated *in vitro.* The overall results observed *in vivo* and *in vitro* indicate that 1,1,2,2-tetrachloroethane might have some genotoxic potential. In an oral long term bioassay, 1,1,2,2-tetrachloroethane has been shown to induce hepatocellular carcinoma in mice but it was not carcinogenic in rats.

From the past experience, the threshold chronic toxicity by inhalation in human has been estimated around 70 mg/m^3, a value ten time higher than the current occupational exposure limit and several thousand times higher than the ambient and indoor air for the general population. The lowest oral threshold dose in rats was found around 3 mg/kg bw/day indicating large margins of safety when comparing with the trace levels of 1,1,2,2-tetrachloroethane when it is detected in food or drinking water in northern America.

Environment

Based on its physico-chemical properties, (vapor pressure: 6 hPa; solubility: 2.9 g/l) 1,1,2,2-tetrachloroethane released to the environment will mainly partition into the atmosphere. It has an average atmospheric lifetime of 92 days. Its impact on stratospheric ozone, its greenhouse effect and its contribution to the formation of tropospheric ozone is expected to be low. Observed intermediate products formed during the atmospheric oxidation are phosgene, C(=O)ClH and dichloroacetylchloride. Decomposition in the atmosphere of phosgene and C(=O)ClH should lead to the formation of HCl and CO_2 by hydrolysis in atmospheric water whereas, dichloroacetylchloride will form HCl and dichloroacetic acid which will be further removed from the atmosphere by rain water.

If released to water, 1,1,2,2-tetrachloroethane will be removed rapidly by volatilization. It is not readily biodegradable. It is expected to undergo dehydrochlorination under hydrolytic alkaline conditions to trichloroethylene (see SIDS for trichloroethylene: CAS No. 75-01-6) and to biodegrade under anaerobic conditions. Based on its partition coefficient (logKow = 2.39) and its bioconcentration factor (BCF = 4.2-13.2), it is not likely to bioaccumulate. Due to its low Koc value of 46, it is not expected to adsorb to suspended solids, sediments and soils.

1,1,2,2-Tetrachloroethane is toxic to aquatic organisms, *Daphnia magna* being the most sensitive species with a 48h EC50 of 9.3 mg/l. On the basis of the NOEC determined from the chronic tests (32 day NOEC *Pimephales promelas* = 1.4 mg/; 28 day NOEC *Daphnia magna* = 6.9 mg/l; 72h EC10 *Scenedesmus subspicatus* = 9.8 mg/l), a PNEC of 140 µg/l is proposed applying a factor of 10 to the lowest NOEC available with fish.

Exposure

The historic production level of 1,1,2,2-tetrachloroethane in the 1960–70's was over a hundred thousand tonnes/year. Since then, because of its disappearance as a solvent, the production has dramatically decreased. The substance is no longer on the market but it is exclusively produced and consumed on site. There are no publicly available production data but it is estimated that the current production level is between 10,000 and 100,000 tons/year. According to the Sponsor country, 1,1,2,2-tetrachloroethane is only used in OECD countries as a feedstock in closed system for the production of other chlorinated hydrocarbons. It may also be an incidental by-product of other production processes for chlorinated hydrocarbons such as the production of vinyl chloride.

Personal exposure monitoring conducted during production, processing and maintenance activities shows that potential for exposure of workers to 1,1,2,2-tetrachloroethane is extremely low. The available monitoring data range from 0.01 to 0.2 ppm. These values are well below the Occupational Exposure Limit (TWA/8h) of 1 ppm (7 mg/m^3).

The recent data from the US and the European Union show that the release of 1,1,2,2-tetrachloroethane into the environment through its production and uses is low. Its concentration in surface water was found far below the Predicted No Effect Concentration (PNEC) of 140 µg/l proposed for the substance.

RECOMMENDATION

The chemical is currently of low priority for further work.

RATIONALE FOR THE RECOMMENDATION AND NATURE OF FURTHER WORK RECOMMENDED

The chemical possesses properties indicating a hazard for human health. Based on data presented by the Sponsor country, exposure to humans is anticipated to be low, and therefore this chemical is currently of low priority for further work. Countries may desire to investigate any exposure scenarios that were not presented by the Sponsor country.

FULL SIDS SUMMARY

CAS NO: 79-34-5		SPECIES	PROTOCOL	RESULTS
PHYSICAL-CHEMICAL				
2.1	Melting Point			-43.8 to -36 °C
2.2	Boiling Point			146.5°C
2.3	Density			1.59449 at 20°C
2.4	Vapour Pressure			4.1to 6.5 hP at 20°C
2.5	Partition Coefficient log Pow		measured	2.39
2.6.	Water Solubility			2,870 mg/l at 20°C
2.7	logKoc		Measured	1.66
ENVIRONMENTAL FATE AND PATHWAY				
3.1.1	Photodegradation		Calculated	Atmospheric lifetime = 92 days 1/2 lifetime = 63 days
3.1.2 2	Stability in Water		Hydrolysis	Half lives : Neutral pH =1-3 months Basic pH = <= 1day
3.3	Transport and Distribution		Mackay level 1	Air : 92.26 % Water : 7.46 % Soil : 0.14 % Sediments : 0.14 %
3.5	Biodegradation	Aerobic	OECD 301C	Not readily biodegradable
		Anaerobic		Degradable
3.6	Bioaccumulation	*Lepomis macrochirus*	EPA	BCF = 8 (14 d)
		Cyprinus carpio	OCDE 305C	BCF = 4.2 - 13.2 (42 d)
ECOTOXICOLOGY				
4.1	Acute Toxicity to Fish	*Pimephales promelas*	US EPA	96 h LC50 = 20.3 mg/l
		Jordanella floridae	US EPA	96 h LC50 = 18.5 mg/l
4.2	Acute Toxicity to Aquatic Invertebrates (*Daphnia)*	*Daphnia magna*	US EPA	48h EC50 = 9.3 mg/l
4.3	Toxicity to aquatic plants e.g. Algae	*Scenedesmus subspicatus*	OCDE 201	72 h EC50 = 47 mg/l 72 h EC10 = 9.8 mg/l

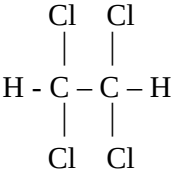
CAS NO: 79-34-5		SPECIES	PROTOCOL	RESULTS
4.4	Chronic toxicity to fish	*Pimephales Promela*	Early life stage test	32d NOEC = 1.4 mg/l 32d LOEC = 4 mg/l
		Jordanella floridae	Carcinogenicity	No carcinogenic effect
		Poecilia reticula	Carcinogenicity	No carcinogenic effect
4.5	Chronic toxicity to aquatic invertebrates	*Daphnia magna*	Reproduction	28d NOEC =6.9 mg/l 28d LOEC = 14mg/
TOXICOLOGY				
5.1.1	Acute Oral Toxicity	rat		LD50 = 250-800 mg/kg
5.1.2	Acute Inhalation Toxicity	rat		LC50/4h = 8.6 mg/l
5.1.3	Acute Dermal Toxicity	rabbit		LD50 = 3990-8140 mg/kg
5.2.1	Skin Irritation	rabbit		Irritant
5.2.2	Eye Irritation	rabbit		Irritant
5.4	Repeated Dose Toxicity	Human		LOAEL – inhal. : *ca* 10 ppm (70 mg/m3)
		rat		LOAEL – oral : *ca* 3 mg/kg/d
5.5	Genetic Toxicity In Vitro			
A.	Bacterial Test (Gene mutation)	*Salmonella typhimurium*		Positive / negative
B.	Non-Bacterial In Vitro Test (Chromosomal aberrations)	CHO		Negative
5.6	Genetic Toxicity In Vivo	*Drosophila*		Negative
5.8	Toxicity to Reproduction	rat	Sexual organs	Inconclusive effects on testes
5.9	Developmental Toxicity/ Teratogenicity	rat		Effect at maternally toxic doses
5.10	Carcinogenicity	rat		Inactive
		mouse		Hepatocarcinogenic effect
5.11	Experience with Human Exposure	Acute		Toxic via all routes
		chronic		Toxic via all routes
HUMAN EXPOSURE				
6;1	Workers	TWA / 8h		1 ppm (7 mg/m3)
6.2	Consumers			None
6.3	Indirect via the environment	Ambient air		<0.1- 0.25
		Drinking water		0-6 µg/l

SIDS Initial Assessment Report

1 IDENTITY

1.1 Identification of the Substance

CAS Number: 79-34-5
IUPAC Name: 1,1,2,2-Tetrachloroethane
Molecular Formula: $C_2H_2Cl_4$
Structural Formula:



Molecular Weight: 167.85
Synonyms: Ethane, 1,1,2,2- tetrachloro; acetylene tetrachloride

1.2 Purity

> = 80%

Main impurities**:** 1,1,1,2-tetrachloroethane

Pentachloroethane

1.3 Physico-Chemical properties

Table 1 Summary of physico-chemical properties

Property	Value
Physical state	colorless to pale-yellow liquid
Odour	chloroform-like
Melting point	-43.8°C to -36 °C
Boiling point	146.5 °C
Vapour pressure	4.126 hPa to 6.5 hPa at 20° C 7 hPa at 25° C
Water solubility	2.9 g/l at 20° C
Partition coefficient n-octanol/water (log value)	2.39 (measured)
Flammability	Non-flammable
Conversion factors	1 ppm (v/v) = 6.87 mg/m^3 1 mg/m^3 = 0.146 ppm (v/v)

2 GENERAL INFORMATION ON EXPOSURE

2.1 Production Volumes and Use Pattern

Uses and Functions

1,1,2,2-Tetrachloroethane is produced in closed systems by direct chlorination or oxychlorination utilizing ethylene as feedstock, by catalytic chlorination of ethane or by chlorination of 1,2-dichloroethane. High purity 1,1,2,2-tetrachloroethane is made by chlorinating acetylene.

The principal use of 1,1,2,2-tetrachloroethane is as an intermediate in the manufacture of other chlorinated hydrocarbons, such as 1,2-dichloroethane, trichloroethylene, and tetrachloroethylene. In most cases, 1,1,2,2-tetrachloroethane is not isolated, but immediately thermally cracked at 454 deg C to give the desired trichloroethylene and tetrachloroethylene product (Kirk-Othmer, 1991). When isolated, it is stored in controlled on-site facilities and used on the same site in closed system. It may also be an accidental by-product of other production processes for chlorinated hydrocarbons such as the production of vinyl chloride.

In the past, it was also used as a solvent in cleaning and decreasing metals, in paint removers, varnishes and lacquers, in photographic films, and as an extractant for oils and fats. Although at one time it could be used as an insecticide, fumigant and weedkiller, it presently is not registered for any of these purposes (ATSDR, 1994).

Due to 1,1,2,2-tetrachloethane's toxicity and new processes for manufacturing chlorinated ethylenes, the manufacture of 1,1,2,2-tetrachloethane as an end product now appears to be very limited.

Production Volume

The historic production level of 1,1,2,2-tetrachloroethane in the 60-70s was over a hundred thousand tonnes/year. Since then, because of its disappearance as a solvent, production has dramatically decreased. The substance is no longer on the market but it is exclusively produced and consumed on site. There are no publicly available production data but it is estimated that the current production level is between 10,000 and 100,000 tonnes/year.

The producers and locations are listed below:

United States:	DOW CHEMICAL
Europe:	ATOFINA (France), INEOS,
Japan:	TOAGOSHEI
China :	Beijing Beihua Fine Chemical Products Co; Shangaï Chemical Reagent Co; Shanghaï Dannier Chemical Corporation, Tianjin City N°1 Reagent Factory.

2.2 Environmental Exposure and Fate

2.2.1 General Discussion:

Based on the fugacity model level 1of Mackay, 1,1,2,2-tetrachloroethane released to the environment will partition mainly into the atmosphere.

1,1,2,2-Tetrachloroethane has an average atmospheric lifetime of 91days. It has negligible impact on stratospheric ozone and greenhouse effect and minor contribution to the formation of

tropospheric ozone. Observed intermediate products formed during the atmospheric oxidation are phosgene, C(=O)ClH and dichloroacethylchloride. Decomposition in the atmosphere of phosgene and C(=O)ClH should lead to the formation of HCl and CO_2 by hydrolysis in atmospheric water whereas, dichloroacethylchloride will form HCl and dichloroacetic acid further removed from the atmosphere by rain water.

1,1,2,2-Tetrachloroethane that is released in the water will be removed rapidly by volatilization. It is expected to hydrolyze under alkaline conditions and to biodegrade under anaerobic conditions. It is not likely to bioaccumulate and is not expected to adsorb to suspended solids, sediments and soils**.**

2.2.2 Fate in Waste Water Treatment Plants

In waste water treatment plants, it has been found that 1,1,2,2-tetrachloroethane will be eliminated by stripping to the air and not by biodegradation (Kincannon et al., 1983).

2.2.3 Distribution in Air, Water and Soil

A theoretical distribution of 1,1,2,2-tetrachloroethane has been calculated at 20° C using the fugacity model level 1 of Mackay with a vapor pressure of 6 hPa and a solubility of 2.9 g/l. Approximately 92.26 % of 1,1,2,2-tetrachloroethane released into the environment will enter the atmosphere, 7.46 % the water compartment, 0.14 % the soils and 0.14 % the sediments.

1,1,2,2-Tetrachloroethane released to surface water is rapidly lost through volatilization to the atmosphere.

Dilling et al. (1975) measured the evaporation of 1,1,2,2-tetrachloroethane from a dilute solution (1mg/l) at 25° C. The time for 50 % evaporation was 56 minutes and greater than 120 minutes for 90 % evaporation. In later experiments (Dilling et al., 1977) using the same technique (constant stirring at 200 rpm), the measured half-life for evaporation was 55,2 minutes.

Chiou et al. (1980) reported a half life of 9.2 minutes for 1,1,2,2-tetrachloroethane (2270 ppm) at about 24 °C under stirring conditions of 100rpm

The volatilization half-life from a model river (1 m deep flowing 1m/sec with a wind speed 3 m/sec) has been estimated to be 6.3 hours (Lyman et al., 1982).and 3.5 days from a model pond which considers the effects of adsorption (USEPA,EXAMS II, 1987).

Due to a measured Koc of 46 (Chiou et al., 1979), 1,1,2,2-tetrachloroethane is not expected to adsorb to soils and sediments.

2.2.4 Abiotic and Biotic Degradation in Air, Water and Soil

2.2.4.1 Abiotic degradation

2.2.4.1.1 Water

Data reported indicate that 1,1,2,2-tetrachloroethane is expected to hydrolyze under environmental conditions to form trichloroethylene.

In one study, the half-lives at 25 °C and pH 7 and 9 based on a second order elimination reaction was estimated to be 102 days and 1.02 days respectively (Cooper et al., 1987). In another study, half lives of 575 days at pH 6.05, 36 days at pH 7.01 and 6.6 to 12.8 hours at pH 9 were calculated

at 25 °C in pure water. The hydrolysis yielded trichlorethylene as the major if not sole product. In pore water sediments the half-life was found to be 29.1 days at 25° C. (Haag and Mill , 1988).

An environmental hydrolysis half-life (25° C, pH 7) of 0.4 year was found by Jeffers et al. (1989).

From the above studies, it appears that 1,1,2,2-tetrachloroethane will undergo hydrolysis to form trichlorethylene (see corresponding assessment documents for trichloroethylene CAS No 75-01-6) under neutral and alkaline conditions, hydrolysis increasing with increasing pH. At 25°C, half lives of 36 days to 102 days were estimated under neutral pH while half lives from 6.6 hours to 1.02 days were determined under alkaline conditions (pH9).

2.2.4.1.2 Atmosphere

Atmospheric life time

Reaction with the atmospheric OH radicals.

Method

Principle of the method: OH radicals are generated from the photolysis of a precursor which can be H_2O, H_2O_2 or HNO_3. The concentration of the substance is put in excess and considered constant during the experiment. The rate constant can be inferred from the rate of disappearance of the OH radical. An extensive study was done using that technique (Jiang et al,1993).

Results:

$k\ (OH) = 2.72 \pm 0.42\ 10^{-12}\ (T/300)^{0.22} \exp(-(915 \pm 62)/T)$

$k\ (OH) = 1.26\ 10^{-13}\ cm^3\ mol^{-1}s^{-1}$ at 298 K.

Previous results have been reported a review (Atkinson, 1994)

$k = 2.37 \pm 4.8\ 10^{-13}\ cm^3\ mol^{-1}s^{-1}$ at 292 K

$k = 2.26 \pm 4.6\ 10^{-13}\ cm^3\ mol^{-1}s^{-1}$ at 298 K

$k = 2.66 \pm 5.4\ 10^{-13}\ cm^3\ mol^{-1}s^{-1}$ at 312 K

The results from Jiang et al. because of the experimental technique used and control of impurities seem the most reliable.

Atmospheric lifetime of 1,1-2,2-tetrachloroethane.

Assuming an average OH° concentration of $10^6\ cm^{-3}$ it is possible to calculate a 1/2 lifetime of 63 days or an atmospheric lifetime of 92 days on the basis of the Jiang et al. rate constant.

Atmospheric degradation

The possible atmospheric oxidation scheme of 1,1-2,2-tetrachloroethane is described below:

$CHCl_2\text{-}\ CHCl_2 + OH° \rightarrow CHCl_2\text{-}\ C°Cl_2 + H_2O$

$CHCl_2\text{-}\ C°Cl_2 + O_2 + NO \rightarrow CHCl_2\text{-}\ CCl_2O° + NO_2$

At this stage two pathways can be considered:

Carbon-carbon bond cleavage leading to the formation of phosgene:

$CHCl_2$- $CCl_2O°$ $\rightarrow$ $C(=O)Cl_2$ + $C°HCl_2$

$C°HCl_2$ + O_2 + NO $\rightarrow$ $CHCl_2O°$ + NO_2

$CHCl_2O°$ $\rightarrow$ C(=O)HCl + Cl°

Chlorine atom abstraction leading to the formation of chloroacetylchloride:

$CHCl_2$- $CCl_2O°$ $\rightarrow$ $CHCl_2$- C(O)Cl + Cl°

Phosgene will further hydrolyze in atmospheric water to give HCl and CO_2. The removal of phosgene by wet deposition has an estimated lifetime of 70 days. Dichloroacethylchloride should also undergo hydrolysis in atmospheric water to form dichloroacetic acid removed by rain.

These reaction products have been observed by Spence et al. (1978)

Ozone depleting potential

Organic substances containing chlorine, if primarily present in the atmospheric compartment and if their lifetime is long enough can reach the stratosphere and decompose through photolysis and other chemical reaction (e.g. with OH°). Chlorine atoms can then participate in the catalytic ozone destruction cycles.

In the case of 1,1,2,2-tetrachloroethane the atmospheric lifetime is too short to enable a significant fraction of the compound emitted to reach the stratosphere. Similar conclusion was taken in the last scientific assessment for ozone depletion (WMO 1998) as far as short-lived substances containing chlorine are concerned.

The ozone depletion potential cannot be calculated with conventional methods such as those used for the long-lived species like CFCs and most HCFCs and will depend on the place of emission of that substance (Olsen et al., 2000). A study using algorithm approach (Nimitz et al., 1992) attempted to estimate the ODP of 1,1-2,2-tetrachloroethane with a result of less than 0.001 and an estimated lifetime of about 1 month. However this method cannot take into account the specific behavior of short-lived species as explained in Olsen et al. Therefore, although it can be concluded that the ODP of 1,1,2,2-tetrachloroethane is very small, no accepted number has been calculated.

Global Warming potential and contribution to the greenhouse effect:

Although no GWP value is reported, the direct global warming potential of 1,1,2,2-tetrachloroethane should be small essentially because of its short atmospheric lifetime. The GWP values of substances with comparable lifetime are generally less than 100. (IPCC, 2000).

Contribution to the formation of ozone at ground level.

1,1,2,2-Tetrachloroethane reacts too slowly with the OH° radical to be considered a significant contributor to the formation of tropospheric ozone. Halocarbon with comparable reactivity with OH° are reported to have low Photochemical Ozone Creation Potential value e.g. chloroform, methylene chloride, tetrachloroethylene show POCP of less than 10 (100 for ethylene). (Derwent et al., 1998)

2.2.4.2 Biodegradation

Aerobic biodegradation

1,1,2,2-Tetrachloroethane is persistent under aerobic conditions. It is not readily biodegradable (0% after 28 days in an OECD 301C test, CSCL, 1992).

No significant biodegradation was found in an aerobic degradability test with adaptation utilizing biochemical oxygen demand dilution water containing 5 mg of yeast extract per liter, as synthetic medium, 5 ppm and 10 ppm of 1,1,2,2-tetrachloroethane, a 7-day static incubation at 25°C in the dark followed by three weekly subcultures and incorporating settled domestic wastewater as microbial inoculum (Tabak et al., 1981).

Anaerobic biodegradation

1,1,2,2-Tetrachloroethane undergoes degradation under anaerobic conditions.

In an anaerobic biodegradability test using a methanogenic laboratory-scale continuous flow fixed-film reactor supplied with 27 µg/l of 1,1,2,2-tetrachloroethane, 97% steady state removal was achieved after 4 month of operation. The production of 1,1,2-trichloroethane was reported as a result of 1,1,2,2-tetrachloroethane transformation (Bower et al., 1983).

The rates of disappearance of halogenated ethanes were studied in anoxic sediment-water systems. A half life of 6.6 days was found for 1,1,2,2-tetrachloroethane (Jafvert and Wolfe,1987). Reductive dechlorination or reductive hydrogenolysis is a common transformation of 1,2-carbon chlorinated aliphatics under methanogenic conditions. The production of trichlorethylene and 1,1,2-trichlorethane was reported. The products of abiotic and anaerobic transformations of 1,1,2,2-tetrachloroethane were determined under methanogenic conditions. 1,1,2,2-Tetrachloroethane degradation started without lag with municipal digester sludge. 1,1,2-trichloroethane, trans-1,2-dichloroethene and cis-1,2-dichloroethene were products of anaerobic transformation while trichloroethylene resulted from abiotic degradation. Trichloroethylene was further transformed to vinyl chloride and ethene. 1,1,2-Trichloroethane was converted in 1,2-dichloroethane, then further degraded to chloroethane and ethane (Chung Chen et al., 1996).

2.2.5 Bioaccumulation

Results from fish bioaccumulation are summarized in the following table

Species	Method	Exposure (day)	Water concentration µg/l	Elimination DT 50 day	BCF	Reference	Reliability
Lepomis macrochirus	Flow-through	14	9.6 (^{14}C)	<1	8	Barrows et al., 1978	2
Cyprinus carpio	OCDE 305 C	42	26 260		4.1-13.1 4.5-13.2	CSLC Japan, 1992	2
Pimephales Promelas	-	32			8	Ahmad et al., 1984	4

Based on the above measured BCF and on a logKow of 2.39 (Hansch and Leo, 1979), 1,1,2,2-tetrachloroethane is not expected to bioaccumulate.

2.2.6 Predicted Environmental Concentration

1,1,2,2-Tetrachloroethane is produced and used as a chemical intermediate on a limited number of industrial sites. The release into the environment through its production and uses is expected to be low.

According to the TRI database (1999) an estimated total of 5,215 lbs (2365 kg) of 1,1,2,2-tetrachloroethane was discharged to air in the US. The release to surface water and land was estimated to be about 1 lb (0.45 kg) and 15 lb (6.8 kg) respectively.

In Europe, the concentration of 1,1,2,2-tetrachloroethane in the receiving surface water of a production plant was estimated to be about 10 µg/l.

Data on 1,1,2,2-tetrachloroethane in environmental media based on a review done by WHO - IPCS CICAD (1998) mainly in the US and Canada are presented in the table of section 2.3.3.

Mean concentrations of 1,1,2,2-tetrachloroethane in ambient air in cities in Canada ranged from <0.1 to 0.25 µg/m^3. Maximum concentrations of up to 79 µg/m^3 have been detected in the vicinity of waste sites in the USA (ASTR, 1994).

Limited data are available in surface waters. Levels of 1,1,2,2-tetrachloroethane in Canada, the USA and Germany range from< 0.005 to 4 µg/l, from <10 µg/l to a maximum reported value of 180 µg/l and from <0.03 to 10 µg/l, respectively. 1,1,2,2-Tetrachloroethane was not detected (detection limits 0.001-0.05 µg/l) in the surface waters in Japan.

Very low concentrations of 1,1,2,2-tetrachloroethane in German rivers (from <0.01 to 0.69 µg/l) were also reported in a review done by BUA (1998). Results are given in the following table (extracted from BUA report 210, 1998):

River (region), Year(s)	Concentration (ug/l)	Reference Source
Rhine (NRW), 1990	≤ 0.02	LWA NRW, 1991
Rhine (NRW), 1991	≤ 0.01	LWA NRW, 1992
Rhine (NRW), 1992	< 0.01	LWA NRW, 1993
Elbe (Schnackenburg), 1991	0.07-0.69	ARGE Elbe, 1992
Elbe (Schnackenburg), 1992	< 0.01 – 0.39	ARGE Elbe, 1993
Elbe (Schnackenburg), 1993	< 0.01 – 0.39	ARGE Elbe, 1994
Elbe (Hamburg-Teufelsbrück), 1991	< 0.01 – 0.32	ARGE Elbe, 1992
Elbe (Hamburg-Zollenspieker), 1992	< 0.01 – 0.29	ARGE Elbe, 1993
Elbe (Hamburg-Seemannshöft), 1992	< 0.01 – 0.26	ARGE Elbe, 1993
Elbe (Hamburg-Zollenspieker), 1992/93	≤ 0.30	Hamburg, 1995
Elbe (Hamburg-Seemannshöft), 1992/93	≤ 0.27	Hamburg, 1995
Elbe (Hamburg-Zollenspieker), 1993	< 0.01 – 0.25	ARGE Elbe, 1994
Elbe (Hamburg-Seemannshöft), 1993	< 0.01 – 0.23	ARGE Elbe, 1994
Elbe (Brunsbüttel), 1992	< 0.01-0.07	ARGE Elbe, 1993
Elbe (Brunsbüttel), 1993	< 0.01-0.08	ARGE Elbe, 1994
Elbe (Cuxhaven), 1993	< 0.01	ARGE Elbe, 1994

2.3 Human Exposure

2.3.1 Occupational Exposure

Potential exposures to 1,1,2,2-tetrachloroethane can occur primarily as a result of loading/unloading and uses as a chemical intermediate. Exposure can also occur in the remaining uses as a solvent. Workers in chemical industry and related industries can be exposed via inhalation or dermal contact.

Personal exposure monitoring conducted during production, processing and maintenance activities shows that potential for exposure of workers to 1,1,2,2-tetrachloroethane is extremely low. The

monitoring data collected at the ATOFINA and Dow sites range from 0.01 to 0.2 ppm. These values are well below the Occupational Exposure Limit (TWA/8h) of 1 ppm (7 mg/m^3).

2.3.2 Consumer Exposure

Currently there are no known uses of 1,1,2,2-tetrachloroethane in consumer products. A survey of 1159 household products conducted in the USA in 1992 did not detect 1,1,2,2-tetrachloroethane above the limit of detection of 0.1% (CICAD, 1998).

2.3.3 Indirect Exposure via the Environment

According to the review done by WHO-IPCS (see following table extracted from CICAD, 1998), relevant data on 1,1,2,2-tetrachloroethane in environmental media were found essentially in North America :

Levels of 1,1,2,2-tetrachloroethane in various media (Data from 1,1,2,2-tetrachloroethane CICAD, 1998)

Medium	Location	Year	Concentration	Reference
Ambient air	Canada	1989-1990	<0.1-0.25 µg/m3 (means)	Environment Canada, unpublished data 1992
Ambient air	USA	pre-1987	0.7 µg/m3 (mean)	Shah & Heyerdahl, 1988
Indoor air	Canada	1991	<0.1 µg/m3 (mean)	Fellin et al., 1992
Indoor air	USA	pre-1987	0.098 µg/m3 (mean)	Shah & Heyerdahl, 1988
Drinking-water	Canada	1988-1991	<0.05 µg/litre	P. Lachmaniuk, Personal communication, 1991
		1990	<1.0 µg/litre	Ecobichon & Allen, 1990
Drinking-water	USA	pre-1986	<0.5 µg/litre	ATSDR, 1994
		1984-1992	ND (a)-5.8 µg/litre	Storm, 1994
Surface water	Canada	1985	<1.0-4.0 µg/litre	COARGLWQ, 1986
		1981	<0.005-0.06 µg/litre	Kaiser & Comba, 1983
Surface water	USA	1980-1988	<10-180 µg/litre	ATSDR, 1994
Surface water	Japan	1976	<0.001, <0.002, <0.05 µg/litre	Environment Agency Japan, 1976
Surface water	Germany	1989-1990	<0.03-10 µg/litre	Wittsiepe, 1990
Food (34 groups)	Canada	1991	<50 µg/kg (solids), <1 µg/litre (liquids)	Enviro-Test Laboratories, 1991
		1992	<5 µg/kg (solids), <1 µg/litre (liquids)	Enviro-Test Laboratories, 1992
Food (231 items)	USA		<13 µg/kg, <20 µg/kg	Daft, 1988
Consumer products (1159 items)	USA		<0.1%	Sack et al., 1992
Sediment	Japan	1976	<0.05 µg/g, <1 µg/g	Environment Agency Japan, 1976

(a) Detection limit not specified.

Mean levels in residential indoor air in Canada and the USA are generally below the detection limit (i.e. <0.1 µg/m3). The mean intake of the general population due to inhalation of indoor air is estimated to be <0.03 µg/kg BW per day.

The surveys of food and drinking water in northern America indicate that 1,1,2,2-tetrachloroethane is rarely detected (detection limits of 0.05-1 µg/l in water and 5-50 µg/kg in solid food ingredient). Consequently food and drinking water probably do not represent significant sources of exposure to 1,1,2,2-tetrachloroethane based on its volatility and low potential for bioaccumulation.

Therefore ambient air is likely the main medium of exposure of the general population to 1,1,2,2-tetrachloroethane.

3 HUMAN HEALTH HAZARDS

3.1 Effects on Human Health

3.1.1 Toxicokinetics, Metabolism and Distribution

1,1,2,2-Tetrachloroethane is readily absorbed following inhalation, ingestion, and dermal exposure and rapidly distributed in tissue compartments by passive processes. Respiration is the route of excretion for non-transformed 1,1,2,2-tetrachlororethane, volatile metabolites and terminal metabolite CO_2. Most of the metabolites are excreted by the urinary route but also by the faeces and skin. In mice, urinary metabolites represent about 1/3 of the absorbed dose. Based on data on the metabolism of 1,1,2,2-tetrachloroethane in mice, Yllner (1971) suggested that the principal pathway of degradation involves stage wise hydrolytic cleavage of the carbon-chlorine bonds and oxidation to dichloroacetaldehyde hydrate, dichloroacetic acid (the major metabolite), and eventually glyoxylic acid. The glyoxylic acid is then metabolized to oxalic acid, glycine, formic acid, and carbon dioxide. A small proportion of the parent compound is probably non-enzymatically dehydrochlorinated to trichloroethylene, which is further converted to trichloroacetic acid and trichloroethanol. In addition, a minor amount of 1,1,2,2-tetrachloroethane may be oxidized to tetrachloroethylene, which, in turn, is metabolized to trichloroacetic acid and oxalic acid. It has also been proposed that 1,1,2,2-tetrachloroethane may be metabolized via cytochrome P-450 to dichloroacetyl chloride, which is hydrolysed to dichloroacetic acid (Halpert, 1981). In addition to the liver, metabolism may also occur in the epithelia of the respiratory tract and upper alimentary tract (Eriksson & Brittebo, 1991).

3.1.2 Acute Toxicity

The acute toxicity of 1,1,2,2-tetrachloroethane in experimental animals is slight to moderate :

- By inhalation LC50s of 8.6 mg/l (1200 ppm) and 4.5 mg/l (640 ppm) were reported for a 4 h exposure in rats (Schmit et al, 1980) and a 8 h exposure in mice (Plohkova, 1966) respectively.

- By the oral route, LD50s values were reported to lay between 250 and 800 mg/kg in rats (Smyth et al., 1969; Henschler, 1972 ; Izmerov et al., 1982)

- By the dermal route the reported LD50 in rabbits were 3990 mg/kg (Schmid, 1979) and 4900-8140 mg/kg (Smyth et al., 1969).

After sub-lethal concentration exposure, the main target organs were the central nervous system with an initial stimulation followed by delayed anesthesia-like symptoms, and the liver with degenerative lesions observed at the end of the two-week observation period.

1,1,2,2-tetrachloroethane was irritating to rabbit skin (Smyth et al., 1969) and eyes (Truhaut et al., 1974). There is no skin sensitization data available.

3.1.3 Repeated Dose Toxicity (effects in animals)

Although many studies on repeated exposure toxicity were conducted on 1,1,2,2-tetrachloroethane over the last four decades, there are no conventional studies available that allow a clear NOAEL identification and many of these studies are not fully reliable. However most of the data gave consistent results allowing target organs identification and finally allowing establishing a LOAEL for the inhalation exposure route and possibly for the oral route.

All available data are presented in the following two tables.

Repeated exposure toxicity studies by oral route

Species	Test conditions	Results	Effect level	Reliability	Reference
Rat	5 Fisher344 males/group, gavage 104 and 208 mg/kg/d for **3 weeks** ; no hematology and blood biochemistry ; urinalysis of several enzymes; histopathology of main organs	High dose : all rats died or euthanasied before end of study ; lethargy, diarrhea, breathing difficulties. Low dose : normal growth; normal urinalysis ; liver enlargement and cytoplasmic vacuolisation of hepatocytes ; no changes in kidney, testis and other organs	NOAEL and LOAEL <104 mg/kg/d	2	Butcher, 1996
Rat	50 male or female Osborne-Mendel/group; gavage for **78 weeks** , 5d/w; followed by a 32 week observation period ; males : TWA 62 or 108 mg/kg ; females : TWA 43 or 76 mg/kg/d; Control : 40males or females; Histopathology on main organs; no blood exams	High dose: increased mortality; decreased bodyweight ; no increase incidence of non-neoplastic lesions Low dose: decreased bodyweight ; no increase incidence of non-neoplastic lesions	NOAEL and LOAEL <62 (M) and 43 (F) mg/kg/d	2	NCI, 1978
Rat	10 males/group ; gavage for 6 weeks 8 or 20 mg/kg/d; gavage for **27 weeks** 3.2 or 8 mg/kg/d; no hematology; blood biochemistry of certain enzymes; histopathology of main organs	High dose : damages reported in liver, kidneys, testes and thyroid; Low dose : minor hepatic effects	NOAEL <3.2 mg/kg/d LOAEL = 3.2 mg/kg/d	3	Gohlke et al, 1977
Mouse	50 male or female B6C3F1-/group; gavage for **78 weeks**, 5d/w; followed by a 12 week observation period; TWA 142 or 284 mg/kg /d Control : 40males or females; Histopathology on main organs; no blood exams	Dose-related increase in mortality ; moderate dose-related decrease in bodyweight ; No incidence increase of non-neoplastic lesions in any organ/tissues examined	NOAEL and LOAEL <142 mg/kg/d	2	NCI, 1978

Repeated exposure toxicity studies by the inhalation route

Species	Test conditions	Results	Effect level	Reliability	Reference
Rat	20-21 male Wistar and Brown Norway/ group; control groups : 10-14 males; whole body exposure ; 5h/d, 5d/w for **13 weeks** to concentration fluctuating	- Bodyweight: decreased - Biochemistry : no effect on ASAT, ALAT and creatinine at any time for both strains - Urinalysis : proteinuria was lower in exposed rats of both strains versus their respective	NOAEL and LOAEL: <108-516 ppm (742-3545 mg/m^3)	2	Danan et al., 1983

	from 108 to 516 ppm; biochemistry : creatinine, ASAT, ALAT ; urinalysis : proteins; organs examined at necropsy : kidney	controls - Histopathology: minimal glomerulotoxicity in both strains (only visible with electronic microscopy).			
Rat	110 Sprague Dawley females were divided into one control group and 1 treated groups and exposed whole body by inhalation for **15 weeks** to 0 or 560 ppm (single tested concentration), 5-6h/d, 5d/wk. Blood cytology and macroscopic and microscopic examination of liver, kidney, adrenals, ovaries, uterus; Also hepatic DNA neosynthesis	- Transient CNS depressing effects during first exposures. - Bodyweight decreased during the last weeks of exposure - Slight decrease of hematocrit, red and white cells - Hepatotoxicity: increased liver weight, hyperplasia and increased DNA biosynthesis with hepatocellular lesions were seen during the first weeks ; these effects regressed after 19 exposures and disappeared after 39 exposures. - All other organs examined were normal.	NOAEL and LOAEL <560 ppm (3850 mg/m^3)	2	Truffert et al., 1977
Rat	210 males equally divided in one exposed and one control group ; single dose tested : 13.3 +/- 0.24 mg/m3 (1.94 ppm); whole body exposure 4h/d, 5d/wk for **9 months** ; Blood exams comprised: cytology, SGOT, SGPT, BSP excretion, serum albumin, serum globulin, total fat in the liver and kidney, ACTH activity of pituitary gland. SHD, alc Phosphatase and unspecified Esterases. Organ exams: hypophysis, brain, thyroid, thymus, lung, heart, liver, spleen, kidney, adrenals and testes.	- Mortality: no significant difference between treated and control animals. - Bodyweight gain : minimal effect (less than 5% decrease) - Hematology: some increase in leukocyte count after 110 days. No data on WBC were mentioned thereafter. - Clinical biochemistry: serum globulin, fat content of the liver increased in treated animals; the ACTH activity in hypophysis was decreased at interim and final sacrifices (65 % to 13 %). - Organ weights : decrease relative weight of thyroid - Histopathology: mild liver changes; follicular desquamation in thyroid; no changes in other organs.	NOAEL <1.94 ppm (13.3 mg/m^3) LOAEL : Approx. 1.94 ppm (13.3 mg/m^3) ?	3	Schmidt et al., 1972
Rat	6 exposed and 2 controls male rats; whole body exposure 2h/d, 2d/wk for **4 weeks** at 9000 ppm (single tested concentration). Exams : hemoglobin, blood cells counts; histology of liver and main organs (not specified)	All animals survived; hypermotility followed by CNS depression including almost complete loss of consciousness ; no effect on bodyweight ; tendency to decreased hemoglobin and red blood cell counts; congestion and fatty degeneration of the liver.	NOAEL and LOAEL <9000 ppm (61830 mg/m^3	3	Horiuchi et al., 1962

		Congestion of other main organs.			
Mouse	9 male mice whole body exposed to 7000 ppm (single tested concentration) 2h/d, once a week for **4 weeks**. Exams : Histology of liver and main organs (not specified)	All nine mice died within the 4 week test period Slight to moderate congestion and fatty degeneration of the liver ; congestion of other organs	NOAEL and LOAEL <7000 ppm (48100 mg/m^3	3	Horiuchi et al., 1962
Rabbit	Rabbits exposed to 15 ppm , 3-4 h/d for 7-11 month	Slight effects on liver	NOAEL and LOAEL <15 ppm (100 mg/m^3)	4	Patty, 1994
Rabbit	Rabbits exposed to 100-160 ppm , 8-9 h/d for 4 weeks	No effect ; no typical organ changes were found	NOAEL => 160 ppm (1100 mg/m^3)	4	Patty, 1994
Cats	Cats exposed to 100-160 ppm, 8-9 h/d for 4 weeks	No effect ; no typical organ changes were found	NOAEL >/= 160 ppm (1100 mg/m^3)	4	Patty, 1994
Monkey	A male cynomolgus maccaca was whole body exposed to 1000-4000 ppm , 2h/d, 6d/wk for 9 months Exams: hematology, urinalysis; histology of liver, heart, lung, kidney, pancreas, spleen, testis.	- diarrhea, anorexia; almost complete unconsciousness occurred at 2000-4000 ppm 20min to 1h after exposure to vapors. - Minimal bodyweight changes - Slight increase in white blood cells and decrease of red blood cells and hemoglobin. - Urine no changes in albumin and urobilinogen - Slight to moderate congestion and fatty degeneration of the liver. Congestion of spleen. No changes in other organs.	NOAEL and LOAEL <1000ppm (6870 mg/m^3	3	Horiuchi et al., 1962

Most of the above results observed on different animal species have shown that the main target organ of 1,1,2,2-tetrachoroethane on repeated exposure by inhalation and by the oral route is the liver. The central nervous system and possibly the hematopoietic system appear also as target organs but at much higher doses. The NOAEL was not established in any of the studies conducted by oral route or by inhalation although one old unreliable study in cats and rabbits reported a NOAEL of 160 ppm (1100 mg/m^3) which is in contradiction with all other studies (Patty, 1994) and the experience in humans (ATSDR, 1994). Based on a limited study (Schmidt et al., 1972), the LOAEL by inhalation in rats could be located around 2 ppm (14 mg/m^3) with an exposure by inhalation during 9 months as findings may be considered minimal at the single tested concentration of 1.94 ppm. The LOAEL by the oral route could be 3 mg/kg/day based on a limited gavage study over 27 weeks (Gohlke et al., 1997).

3.1.4 Genotoxicity

3.1.4.1 Genotoxicity and cell transformation *in vitro*

Test system	End point	Result		Reference	Reliability
		- S9	+ S9		
Salmonella typhimurium. TA 1535, 1537, 98, 100	Reverse mutations	+	+	Eriksson et al., 1992	2
Salmonella typhimurium. TA 97, 98, 100, 102	Reverse mutations	+	+	Mersch-Sundermann, 1989	2
Salmonella typhimurium TA 1535, 1537, 98, 100	Reverse mutations	-	-	Milman er al., 1988	2
Salmonella typhimurium TA 100	Reverse mutations	-	-	Warner et al., 1988	4
Salmonella typhimurium TA 97, 98, 100, 104	Reverse mutations	+	+	Strobel and Grummt, 1987	2
Salmonella typhimurium TA 1535, 1537, 98, 100	Reverse mutations	-	-	Mitoma et al., 1984	2
Salmonella typhimurium. TA 1535, 1537, 98, 100	Reverse mutations	-	-	Haworth et al., 1983	2
Salmonella typhimurium. TA 1535, 1537, 1538,98, 100	Reverse mutations	-	-	Nestman et al., 1980	2
Salmonella typhimurium TA 1530, 1535, 1538	Reverse mutations	+	NT	Rosenkranz, 1977	4
Salmonella typhimurium TA 1530, 1535, 1538	Reverse mutations	+	NT	Brem et al., 1974	2
Saccharomyces cervisiae D7 and XV185-14C	Reverse mutation	-	NT	Nestman and Lee, 1983	2
Salmonella typhimurium BA13 and BAL13	Forward mutation	-	-	Roldan-Arjona et al., 1991	2
Saccharomyces cervisiae D7 and D4	Mitotic gene conversion and recombination	+	NT	Callen et al., 1980	2
Aspergillus nidulans P1 and 35	Chromosome malsegregation	+	NT	Crebelli et al., 1988	2
Chinese hamster ovary WB1	Chromosome aberration	-	-	Galloway et al., 1987	2
Chinese hamster ovary WB1	Sister Chromatide Exchanges	+	+	Galloway et al., 1987	2
Bacillus subtilis H17 and M45	DNA repair damage	-	-	Matsui et al., 1989	2
Escherichia coli B/r WP2s	DNA repair damage	-	+	DeMarini et al., 1992	2
Escherichia coli Pol A1-/Pol A+-	DNA repair damage	-	NT	Rosenkranz, 1977	4
Escherichia coli Pol A1-/Pol A+-	DNA repair damage	-	NT	Brem et al., 1974	2

Escherichia coli ?	DNA repair damage	+?	+?	Upton et al., 1984	4
Escherichia coli PQ 37	SOS-repair system (SOS Chromotest)	-	-	Mersch-Sundermann et al, 1989	2
F344 rat hepatocyte primary culture	UDS – DNA repair	-	NT	Williams et al., 1989	2
Osborne-Mendel rat hepatocyte primary culture	UDS – DNA repair	-	NT	Milman et al., 1988	2
B6C3F1 mouse hepatocyte primary culture	UDS - DNA repair	-	NT	Milman et al., 1988	2
Osborne-Mendel rat hepatocyte primary culture	UDS – DNA repair	-	NT	Williams, 1983	2
B6C3F1 mouse hepatocyte primary culture	UDS - DNA repair	-	NT	Williams, 1983	2
Wistar rat liver, kidney, lung, stomach cells	DNA covalent binding	+	NT	Colacci et al., 1987	2
BALB/c mouse liver, kidney, lung, stomach cells	DNA covalent binding	+	NT	Colacci et al., 1987	2
BALB/c 3T3 mouse Clone A31	Cell transformation - with amplification	 +	 +	Colacci et al., 1993	2
BALB/c 3T3 mouse Clone A31	Cell transformation - without amplification - with amplification	 - +	 NT NT	Colacci et al., 1992	2
BALB/c 3T3 mouse Clone A31	Cell transformation - without amplification - with amplification	 - +	 - +	Colacci et al., 1990	2
BALB/c 3T3 mouse Clone C1 1-13	Cell transformation - without amplification	 -	 NT	Milmann et al., 1988	2
BALB/c 3T3 mouse Clone C1 1-13	Cell transformation - without amplification	 -	 NT	Tu et al., 1983 Little AD, 1983	2

Data on the many gene mutation in vitro assays conducted on 1,1,2,2-tetrachloroethane gave mixed results with positive effects in the presence and the absence of metabolic activation, as well as negative effects on the same testing systems. A chromosome malsegregation assay on yeast was positive. However an assay on mammalian cells (CHO) did not show chromosomal aberration effects, while it did show an increase in Sister Chromatide Exchanges. The DNA repair assays conducted on bacteria gave negative results as well as the UDS DNA repair assays conducted on rat and mouse hepatocyte primary cultures. The chemical was able to bind covalently with DNA extracted from several mouse and rat tissues. In cell neoplastic transformation assays on BALB/c 3T3 cultures, 1,1,2,2-tetrachloroethane was active only when using a special amplification procedure. The significance of such findings is unclear.

3.1.4.2 Genotoxic and related effects in Animals

Assay	Test conditions	Result	Reference	Reliability
Rat cytogenetic assay	Chromosome aberration determination after 5 days exposure by inhalation to 349 mg/m^3 (50 ppm)	Ambiguous.	Mc Gregor, 1980 (quoted in CICAD, 1998)	4
Dominant lethal assay in rat	determination of DL effect after 5 day exposure by inhalation to 349 mg/m^3 (50 ppm)	Negative	Mc Gregor, 1980 (quoted in CICAD, 1998)	4
Drosophila melanogaster eye mosaïc assay	Treatment of Leiden Standard larvae by inhalation (500-1000 ppm) Determination of interchromosomal mitotic recombination	Negative	Vogel and Nivard, 1993	2
Drosophila melanogaster Sex linked recessive lethal mutations	Adult male Canton S treated by feeding and injection for testing SLRL at the meiotic and postmeiotic germ cell stage.	Negative	Woodruff et al., 1985	2
Drosophila melanogaster Sex linked recessive lethal mutations	No data available	Negative	Mc Gregor, 1980(quoted in CICAD, 1998)	4
Mouse hepatocytes Unscheduled DNA Synthesis	Male and female B6C3F1 mice received single gavage at doses of 0, 50, 200, 600 and 1000 mg/kg. UDS determined 2 or 12 h after.	Negative	Mirsalis et al., 1989	2
Rat and mouse DNA Covalent Binding	Male Wistar rats an BALB/c mice. i.p. single injection of C14 labeled test material. DNA, RNA and protein binding determined in liver, kidney, lung, stomach sampled 22h after treatment	Positive	Colacci et al., 1987	2
Rat liver Foci Assay	Partly hepatectomised Osborne-Mendel male rats administered 200 mg/kg p.o. / 7 weeks. GGT+ as indicator	Positive	Milman et al., 1988	2

1,1,2,2-Tetrachloroethane was reported to give an ambiguous effect in a rat chromosome aberration study. It did not induce clastogenic effects in three different studies in Drosophila and was reported as negative in a Dominant lethal assay in male rats. It did not induce unscheduled DNA in hepatocytes of mice treated orally although it was shown to have covalently binded with macromolecules, including DNA, from various tissues of mice and rats exposed by the intraperitoneal route. In an initiation/promotion assay where gammaglutamyl-transpeptidase was used as a putative preneoplastic indicator, 1,1,2,2-tetrachloroethane has shown some intrinsic initiation effect as well as some promoting effect.

3.1.4.3 Genotoxicity overall conclusion

With possible exception of the equivocal result for chromosomal aberrations in rats by inhalation (Mc Gregor, 1980 reported by CICAD, 1998), the weight of evidence from *in vivo* and *in vitro*

studies suggests that 1,1,2,2-tetrachloroethane might have some genotoxic potential, acting through a mechanism that results in gene conversion and induction of sister chromatide exchange.

3.1.5 Carcinogenicity (experience in experimental animals)

In the USA, an oral rat and mouse carcinogenicity bioassay were performed by NCI (1978) with 1,1,2,2-tetrachloroethane.

In the rat study, groups of 50 animals/per sex/dose were fed during 78 weeks with 62 or 108 mg/kg/d (males) and with 43 or 76 mg/kg/d (females) 1,1,2,2-tetrachloroethane. No statistically significant excess of neoplastic lesions were observed in both sexes although 2 hepatocellular carcinomas and 1 neoplastic nodule were observed out of 49 males compared *versus* 0/20 males in vehicle controls.

In the mouse study, groups of 50 males and 50 females received 142 or 284 mg/kg/d 1,1,2,2-tetrachloroethane. There was a dose related increase of mortality and a slight dose related decrease of bodyweight. Large statistically significant excess of hepatocellular carcinomas were found in males (6%, 26% and 90% in control, low and high dose group respectively) and in females (0%, 63% and 91% in control, low and high dose group respectively). These tumors appeared earlier in mice of the high dose group.

Theiss et al., 1977 conducted a pulmonary tumor response bioassay in Strain A mouse. 1,1,2,2-Tetrachloroethane was injected i.p. at 80, 200 or 400 mg/kg/d for 15 to 21 weeks. Lung tumor incidences were increased in treated groups *versus* the control but the differences were not statistically significant. Although the highest dose group reached nearly statistical significance ($p = 0.059$), the biological significance of this result is limited due to poor survival (5/20 versus 15/20 in controls).

Liver tumours induced by some chemicals in mice appear to be of limited relevance to man for the assessment of hazard in human (Hughes et al., 1994). However the mechanism of liver tumour induction in mice exposed to 1,1,2,2-tetrachloroethane has not been established. Review of the carcinogenicity and related mechanistic data in mice available on all the potential metabolites of 1,1,2,2-tetrachloroethane indicate that some of the tumors induced by these metabolites may not be relevant to humans, or that humans are less susceptible (Hughes et al., 1994). This is notably the case for dichloroacetic acid, the primary metabolite of 1,1,2,2-tetrachloroethane. Its toxicity profile has been reviewed by ECETOC (1994).

3.1.6 Toxicity for Reproduction

3.1.6.1 Effects in Animals on Reproductive Capabilities

There have been no standard reproductive toxicity testing on 1,1,2,2-tetrachloroethane. However the data in laboratory animals reported in the following table suggest that this chemical does not selectively affect the reproductive system.

Reproductive toxicity

Species	Test conditions	Results	Effect level	Relia-bility	Reference
		INHALATION			
Rat	*One generation study* 9 months male parental exposure 4h/d, 5d/wk to 13.3 mg/m3 (1.94 ppm)	no effect on male fertility no effect on offsprings born from exposed father + unexposed mother	NOAEL : > 13.3 mg/m^3 (males)	2	Schmidt et al., 1972
Rat	*Sub-chronic toxicity study* Females exposed 15 weeks 560 ppm,(3850 mg/m3) 5-6h/d, 5d/wk	No effect on female sexual organs.	NOAEL >3850 mg/m^3 (females)	2	Truffert et al., 1977
Rat	*Dominant Lethal assay* Males exposed 5 days at 349 mg/m3 (50 ppm)	Small statistical increase in one type of sperm abnormalities (result considered by authors as being of questionable biological significance)	NOAEL <349 mg/m^3 ?? (males)	4	Mc Gregor, 1980 (quoted in CICAD, 1998)
Rat	*Sub-acute toxicity study* Males exposed 4 to 10 days at 13.7 mg/m3 (2 ppm)	Conflicting results : After 10 days : no effect After 4 days : some atrophy of seminal vesicles, decrease of spermatogenesis	NOAEL - 10 d exp: > 13.7 mg/m^3 - 4 d exp : < 13.7 mg/m^3	3	Golke and Schmidt, 1972
Monkey	*Chronic toxicity study* One single male cynomolgus maccaca , whole body exposed to 6870 - 27480 mg/m3 (1000-4000 ppm) , 2h/d, 6d/wk for 9 months	No significant histological changes in testis	NOAEL >27480 mg/m^3 (male)	3	Horiuchi et al., 1962
		ORAL			
Rat	*Chronic toxicity study* Animals treated up to 108 mg/kg/d (males) and 76 mg/kg/d (females) during 78 weeks	No significant histological changes in male and female sexual organs	NOAEL: > 108 mg/kg/d (males); > 76 mg/kg/d (females)	2	NCI, 1978
Rat	Sub-chronic toxicity study Male rats treated at 3.2, 8 and 20 mg/kg/d during 17 weeks and at 3.2 and 8 mg/kg/d during 27 weeks	At the highest doses : - Testis : High incidence of interstitial edema ; clumped sperm ; epithelial cells present in the tubular lumen ; partial necrosis and totally atrophied tubules , giant cells two-row germinal epithelial cells ; disturbed spermatogenesis - In parallel there were damages in liver, kidney and thyroid gland.	NOAEL : = 3.2 mg/kg/d (males)	3	Golke et al., 1977
Rat and Mouse	Sperm motility and vaginal cytology evaluation 10 males and 10 females F344 rats and B6C3F1 mice	Male mice: ↓ terminal body weight at 700 and 1400 mg/kg feed ↓ epididymal sperm motility	NOAEL: 175 mg/kg feed for male and female mice	2	NTP, 1993

	were exposed via dosed feed for 13 weeks. Doses were 0, 37, 75 and 150 mg/kg feed for rats and 0, 175, 700 and 1400 mg/kg feed for mice. The endpoints include body weight, testicular, epididymal and caudal weights, sperm motility, sperm number/g caudal tissue, and testicular spermatid head count for male and body weight and estrual cyclicity for female animals	at 1400 mg/kg feed Female mice: ↓ terminal body weight at 700 and 1400 mg/kg feed ↑ average estrous cycle length at 1400 mg/kg feed Male rats: ↓ terminal body weight at 75 and 150 mg/kg feed ↓ epididymal sperm motility at all tested doses Female rats: ↓ terminal body weight at 75 and 150 mg/kg feed ↑ frequency of diestrus stage at 150 mg/kg feed	LOAEL: 37 mg/kg feed for male rats NOAEL: 37 mg/kg feed for female rats		
Mouse	*Chronic toxicity study* Males and females treated up to 284 mg/kg/d during 78 weeks	No significant histological changes in male and female sexual organs	NOAEL: > 284 mg/kg/d (males and females	2	NCI, 1978

Although all available data have limitations, reproductive effects have been observed only in experimental animals exposed to oral or inhalation levels of 1,1,2,2-tetrachloroethane that are also associated with decreases in bodyweight and/or other signs of toxicity (mainly liver damages). Furthermore the data describing adverse findings on reproductive organs, generally at rather low dose levels, were in contradiction with data reporting no effects at much higher doses and longer exposure periods.

3.1.6.2 Effect in Animals on Developmental Toxicity

There are no standard developmental toxicity studies available on 1,1,2,2-tetrachloroethane.

Decreased fetal bodyweight and/or increased resorptions were reported in range-finding studies in rats and mice exposed via their food during gestation at doses equal or higher than those that induced maternal toxicity (increased mortality or decreased bodyweight gain), respectively (NTP, 1991a, b) (reliability : 2).

The data on these two studies are presented in the following table.

Range finding developmental toxicity studies

Species	Test conditions	Results	Effect level	Relia-bility	Reference
Rat	8-9 Sprague-Dawley pregnant females/group were exposed via dosed feed at 0, 30, 90, 180, 270 and 360 mg/kg/d from GD4 to GD20. The in live endpoints include body weight gain food consumption, clinical signs and mortality. At necropsy on GD20, number of implantation sites, resorptions, dead fetuses and live fetuses, and uterine weight were recorded.	Maternal toxicity: clinical signs at ≥ 270 mg/kg/d, decrease body weight gain at ≥ 90 mg/kg/d, decrease food consumption at all dose levels. Foetotoxicity: decrease fetal weight at ≥ 90 mg/kg/d, total resorptions in 4/9 dams at 360 mg/kg/d, respectively	NOAEL for maternal and fetal toxicity: 30 mg/kg/d	2	NTP 1991a
Mouse	5-11 CD-1 pregnant females/group were exposed to feed dosed at 0, 0.5, 1.0, 1.5, 2.0 and 3.0% from GD6 to GD15. The in live endpoints include body weight gain food consumption, clinical signs and mortality. At necropsy on GD17, number of implantation sites, resorptions, dead fetuses and live fetuses, and uterine weight were recorded.	Maternal toxicity: clinical signs at ≥ 1.0%, maternal mortality at ≥ 1.0%, decrease body weight gain at ≥ 1.0%, decrease food consumption at ≥ 1.0%, abnormal liver at ≥ 0.5%, Foetotoxicity: total resorptions in 2/8, 1/1 and 1/2 dams at 1.0, 1.5 and 2.0% mg/kg/d, respectively	NOAEL for maternal toxicity < 0.5% NOAEL for fetal toxicity = 0.5%	2	NTP, 1991b

In a study with 1,1,2,2-tetrachloroethane administered by the intra-peritoneal route during gestation in mice of two different strains there were no effect at the dose of 300 mg/kg. At the dose of 700 mg/kg some embryotoxic effects (increased post-implantation lost versus controls) and increased malformations were found in one strain while questionable results were found in the other strain. Fetal bodyweight were similar in control and all treatment groups. Unfortunately it is not possible to check for maternal toxicity as no maternal data were provided. The authors concluded that the test material is a faintly teratogenic compound by the i.p. route (Schmidt 1976)(reliability : 3).

Schmidt et al (1972) did not found adverse developmental effects on offsprings born from unexposed dams mated with male rats previously exposed by inhalation to 13.3 mg/m3 1,1,2,2-tetrachloroethane vapor, 2h/d, 5d/week, for 9 months (reliability : 3).

In conclusion, it is not possible to draw valid assessment from these limited data on developmental toxicity.

3.1.7 Experience in humans

Experience in human is based on the reported numerous cases of suicidal or accidental poisonings mainly by oral and inhalation exposures, and on the many cases of chronic intoxications in workers or studies on volunteers exposed by inhalation and dermal contacts. Limited epidemiological surveys in workers are available. Many reviews of this large human experience on 1,1,2,2-

tetrachloroethane are available (INRS, 1987 ; BUA, 1989 ; Lauweris, 1990 ; ACGIH, 1991 ; ATSDR, 1994 ; IARC, 1999). They can be summarized as follows :

ACUTE/SUB-ACUTE INTOXICATION :

Acute intoxication by 1,1,2,2-tetrachloroethane may combine the following :

- Signs of mucosae irritation : digestive signs if ingested ; respiratory and ocular signs if inhaled.

- Signs of depression of the central nervous system: confusion, loss of equilibrium, drowsiness, then coma, sometimes with convulsions..

- Liver cytolysis with, occasionally, renal tubular damages.

- Contacts with skin induce orthoergic irritation.

CHRONIC TOXICITY :

The initial phase may include : fatigue, sweating, anorexia, digestive troubles.

After a latency period of several days/weeks the following damages occur :

- liver : hepatitis, often icteric and initially apyretic, cirrhosis.

- kidney : nephritis

- nervous system (less frequently): central effects (tremor, headache, asthenia, mood troubles) and peripheral effects (tip polynevritis, cranial nerves damages)

- hematological effects (less frequently and sometimes late): hyperleukocytosis, mononucleosis, lymphocytosis, thrombocytosis, anemia.

EPIDEMIOLOGY :

No excess of cardiovascular lesions were observed in a study on 75 workers exposed in a production plant (mean exposure: 2.5 to 22 mg/m^3 ; peaks of 275 mg/m^3). Neurological signs (mainly tremor) and epigastric symptoms but not jaundice were seen in a survey of 380 workers exposed to 1,1,2,2-tetrachloroethane in pearl manufacturing plants (exposures from 63 to 686 mg/m^3). There was no significant excess of cancer mortality in a cohort of 3859 army personnel exposed to 1,1,2,2-tetrachloroethane (exposure not measured) used as a clothing impregnation solvent during World War II. Due to confounding factors the small excess of genital cancer and leukemia could not be confidently associated with the use of 1,1,2,2-tetrachloroethane.

QUANTITATIVE DATA :

- Oral: fatalities from 285 to 6000 mg/kg ; LOAEL : 100 mg/kg

- Inhalation: odor detected at 20 mg/m^3 ; NOAEL /10 minutes : 90 mg/m^3 ; LOAEL /30 minutes : 1000 mg/m^3 ; LOAEL/chronic exposure : 70 mg/m^3

3.2 Initial Assessment for Human Health

Because of the declining use of 1,1,2,2-tetrachloroethane, the toxicology data are generally confined to early limited studies that do not allow a refined characterization of its toxicology profile. For the initial assessment it is important to note that 1,1,2,2-tetrachloroethane is used as a chemical intermediate in closed system only and there are no known applications or uses as a consumer product. Consequently, although the general population can be exposed via the

environment, significant human exposure occurs primarily in the working areas where 1,1,2,2-tetrachloroethane is produced or used.

Assessment of acute toxicity:

Although animal data point to a substance moderately toxic, based on the large past human experience, 1,1,2,2-tetrachloroethane can be considered as very toxic by all routes, producing depressing effects on the central nervous system, mucosae irritation and liver and kidney lesions at doses around 1000 mg/m^3 by inhalation and 100 mg/kg by oral intake. 1,1,2,2-tetrachloroethane was irritating to skin and eye in rabbits. In human repeated skin contacts have induced orthoergic irritation. No skin sensitization data are available in animal or in humans. Because the workplace occupational exposure limits (TWA 8 h) have been set around 7 mg/m^3 in most countries and the environmental concentrations are so low, acute toxicity is not likely to be of concern under normal circumstances and current industrial hygiene practice, provided skin and eye contacts are strictly prevented.

Assessment of repeated exposure toxicity:

Studies on different animal species have shown that the main target organs of 1,1,2,2-tetrachoroethane on repeated exposure by inhalation and by the oral route is the liver. The central nervous system and possibly the hematopoietic system appear also as target organs but at much higher doses. The NOAEL was not established in any of these studies. Based on two limited studies, LOAELs in rats would be located around 14 mg/m^3 (2 ppm) with an exposure by inhalation during 9 months and possibly around 3 mg/kg in a gavage study over 27 weeks. However a large body of past human experience has established that the target organs after repeated exposures are the liver, the kidney and, less frequently, the nervous system (central and peripheral) and the hematopoietic system. The LOAEL in humans was estimated to be around 70 mg/m^3 (10 ppm) and based on that estimation the occupational exposure limit was fixed at 7 mg/m^3 (ACGIH, 1991).This leads to a margin of safety of 10 for workers and in excess of 10000 for the general population when considering the highest figures measured in ambient air in the USA and Canada. The oral LOAEL of 3 mg/kg in rats indicates large margins of safety when comparing with the low environmental levels of 1,1,2,2-tetrachloroethane (values:<50 µg/kg in food and <6 µg/l in drinking water).

Assessment from reproductive and developmental studies:

Although no standard reproductive toxicity studies are available on 1,1,2,2-tetrachloroethane, the data in laboratory animals suggest that this chemical does not selectively affect the reproductive system. The reproductive effects which have been observed in some limited studies occurred only in experimental animals exposed to levels of 1,1,2,2-tetrachloroethane that were also associated with decreases in bodyweight and other signs of toxicity (mainly liver damages). Furthermore these data were in contradiction with other more reliable studies describing no adverse findings on reproductive organs at much higher doses and with longer exposure periods.

There are also no standard developmental toxicity studies available on 1,1,2,2-tetrachloroethane. Decreased fetal bodyweight and/or increased resorptions were reported in range-finding studies in rats and mice exposed in feed during gestation at doses equal or higher than those that induced maternal toxicity (increased mortality or decreased bodyweight gain). In a mouse developmental toxicity study where 1,1,2,2-tetrachloroethane was administered by the intra-peritoneal route during gestation, some embryotoxic effects (increased post-implantation lost) and increased malformations were found but the fetal bodyweight were similar in control and all treatment groups. Unfortunately maternal effects were not checked but the high doses administered (300-700 mg/kg) were likely toxic to the dams based on knowledge from repeated dose toxicity by other routes.

It is not possible to draw valid conclusions from these limited data on developmental toxicity.

Assessment from genotoxicity and carcinogenicity studies

Some potential for genotoxicity of 1,1,2,2-tetrachloroethane has been demonstrated *in vitro* as mixed results have been reported for the induction of gene mutation and prokaryotic systems in the presence of metabolic activation.

With possible exception of the an equivocal result for chromosomal aberrations in rats by inhalation, the weight of evidence from *in vivo* and *in vitro* studies suggests that 1,1,2,2-tetrachloroethane might have some genotoxic potential, acting through a mechanism that results in gene conversion and induction of sister chromatide exchange.

1,1,2,2-Tetrachloroethane has been shown to be carcinogenic in a mouse oral long term bioassay, inducing large excess of hepatocellular carcinomas. No carcinogenic effect was found in a similar bioassay performed in rats. Liver tumours induced by some chemicals in mice appear to be of limited relevance to man for the assessment of hazard in human (Hughes et al. 1994). However the mechanism of liver tumour induction in mice exposed to 1,1,2,2-tetrachloroethane has not been established. Review of the carcinogenicity and related mechanistic data in mice available on all the potential metabolites of 1,1,2,2-tetrachloroethane indicate that some of the tumors induced by these metabolites may not be relevant to humans, or that humans are less susceptible (Hughes et al, 1994). IARC (1999) has considered that the animal carcinogenicity data available on 1,1,2,2-tetrachloroethane form "limited evidence" while the epidemiological data are "inadequate evidence" leading to the conclusion that this substance is "not classifiable as to its carcinogenicity to humans".

4 HAZARDS TO THE ENVIRONMENT

4.1 Acute toxicity to aquatic organisms.

4.1.1 Acute toxicity to fish

Several acute toxicity studies have been conducted on fish species

The results of the tests summarized in the following table show that 1,1,2,2-tetrachloroethane is slightly toxic to freshwater and marine species:

Species	**Duration**	**Results mg/l**	**Remarks**	**Methods**	**Reference**	**Reliability**
Pimephales promelas	72h	LC50 = 20.4 (20-20.9)	Flow-through,lake water,measured concentrations	US EPA-660/3-75-009, 1975	Ahmad et al., 1984	1
Oryzias latipes	48h	LC 50 = 31	semi-static test	Japanese Industrial Standard (JIS K 0102-1986-71)	CSCL Japan, 1992	1
Jordanella floridae	96h	LC50, semi-static = 26.8 LC50, flow-through=185 (16.4-20.8)	Flow through and semi-static tests, Dechlorinated Lake Superior water,no aeration nominal conc. for semi-static test, measured conc. for flow-through test.	US EPA-660/3-75-009, 1975	Smith et al., 1991.	2
Lepomis macrochirus	96h	LC50 = 20-22	Static test, well water, capped jars, nominal concentrations	US EPA-660/3-75-009, 1975	Buccafusco et al., 1984	3
Poecilia reticulata	7 days	LC 50 = 36.7	Semi-static test, daily renewal, vessels covered with glass, Unmeasured concentration	Alabaster, JS. And Abram F.S.H. (1964)	Köneman, 1981	2
Cyprinodon variegatus (saltwater)	96h	LC 50 = 12 (4.7-32)	Static test, naturel salt water,open system Nominal concentrations	US EPA-660/3-75-009, 1975	Heitmuller et al., 1981	3

4.1.2 Acute toxicity to invertebrates

The results of the tests conducted for determining the acute toxicity of 1,1,2,2-tetrachloroethane to invertebrates are summarized in the following table :

Species	Dura-tion	Results mg/l	Remarks	Methods	References	Reliability
Daphnia magna	48h	EC50unfed = 23 EC50fed = 25 LC50unfed,fed = 62,1 LC50fed = 57	static test, no renewal, no aeration,stoppered glass containers, measured concentrations.	ASTM (1980)	Ahmad et al., 1984	1
Daphnia magna	48h	EC50 = 9.3 (6.8-13)	Static, unaerated conditions, not completely filled closed containers, nominal concentrations	US EPA-660/3-75-009, 1975	Leblanc, 1980	2
Mysidopsis bahia (Marine species)	48h	EC50=9.02	Secondary reference	US EPA-660/3-75-009, 1975	Leblanc, 1984	4

Based on the above studies, 1,1,2,2-tetrachloroethane can be considered as slightly toxic to freshwater and marine invertebrates.

4.1.3 Acute toxicity to algae

Four toxicity studies on algae were identified: three on freshwater algae and one on a marine alga. Only one study could be considered as valid with restriction.

Results are given in the following table:

Species	Dura-tion	Results mg/l	Remarks	Methods	References	Reli-ability
Scenedesmus subspicatus	72h	EC50 = 47 EC10 = 9.8	Closed system. measured concentration (at the beginning of the test)	OCDE 201 modified for volatile substance	Behechti et al., 1995	2
Scenedesmus subspicatus	72h	EC 50 =76 (31.4-188)	Unmeasured concentrations		EPA, 1978	4
Selenastrum capricornutum	96h	EC50 = 136	Secondary reference		Leblanc, 1980	4
Skeletonema costatum (Sea water)	96h	EC50 = 6.44	Secondary reference	US EPA-660/3-75-009, 1975?	Leblanc, 1984	4

4.1.4 Toxicity to microorganisms (e.g. bacteria)

Toxicity studies were performed by Blum and Speece (1991) on three groups of bacteria : aerobic heterotrophs (seed bacteria obtained from the mixed liquor of an activated sludge wastewater treatment plant), methanogens (anaerobes from an enrichment culture maintained for >10 years) and *Nitrosomonas* (seed bacteria obtained from the mixed liquor of an activated sludge plant that treat meat-packing, rendering and hide-curing wastewater).

The activity of aerobic heterotrophs was measured by the oxygen uptake, the activity of methanogens by the inhibition of the gas production and the activity of *Nitrosomonas* by the inhibition of ammonia oxidation.

Nitrosomonas were the most sensitive to 1,1,2,2-tetrachloroethane with an EC 50 24h of 1.4 mg/l (EC50 methanogens = 4.1 mg/l; EC50 aerobic heterotrophs = 130 mg/l).

The 5 minutes EC50 of 1,1,2,2-tetrachloroethane to *Photobacterium phosphoreum* was found to be 5.43 mg/l and 8.6 mg/l in a Microtox test which measures the decrease in natural light emission from the luminescent bacteria (Blum and Speece, 1991; Curtis et al., 1979).

4.2 Chronic toxicity to aquatic organisms

4.2.1 Chronic toxicity to fish

Results of chronic toxicity studies performed on freshwater species are given in the following table:

Species	Dura-tion	Results mg/L	Remarks	Reference	Reli-ability
Pimephales Promelas (Freshwater)	32days	NOEC = 1.4 LOEC = 4	Early life stage test, extended beyond the larval stage to that of young fish	Ahmad et al., 1984	1
Jordanella floridae	28 days	NOEC,(hatchability) = 22 NOEC, 10d larval survival = 4.9 LOEC, 10d larval survival = 10.6 NOEC 28d juvenil survival = 6.15 LOEC,28d juvenile survival = 11.7	Early life stage test, flow-through test, measured concentrations	Smith et al., (1991)	2

For information, results of carcinogenic studies carried out with *Poecilia reticulata* and *Oryzias latipes* over a period of 90 days are given in the following table:

Species	Duration	Results	Remarks	Reference	Reli-ability
Poecilia reticulata	90 days	No evidence of carcinogenicity, on the basis of histopathological examination	Carcinogenicity study, flow through test, 2d old guppies exposed continously at 4mg/l TCE and once a week (24h)at 8 or 15 mg/l.	Hawkins, 1989	2
Oryzias latipes	90 days	No evidence of carcinogenicity, en the basis of histopathological examination	Carcinogenicity study, flow through test, 2d old medaka exposed continously at 4mg/l TCE and once a week (24h)at 8 or 15 mg/l	Hawkins, 1989	2

4.2.2 Chronic toxicity to aquatic invertebrates

Chronic 28-days toxicity studies were conducted on *Daphnia magna* by Ahmad et al. (1984) according to ASTM standards (1978) in closed glass containers with aeration and a renewal of the solutions three times each week.

The measured 28 day LOEC and NOEC values for reproductive impairment were 14 mg/l and 6.9 mg/l respectively.

4.3 PNEC for the aquatic compartment

The following results from the chronic tests are used to determine the PNEC :

Pimephales promelas : 32 day NOEC = 1.4 mg/l

Daphnia magna : 28 day NOEC = 6.9 mg/l

Scenedesmus subspicatus : 72h EC10 = 9.8 mg/l

The EC10 found with *Scenedesmus subspicatus* can be used as a NOEC

As a NOEC is available for three trophic level species (fish, daphnia and algae), a PNEC of 140 µg/l can be calculated applying a factor of 10 to the lowest NOEC obtained from fish.

4.4 Terrestrial effects

4.4.1 Toxicity to soil dwelling organisms

A LC50 of 14 µg/cm^2 was found in a 2 day contact filter paper test used to evaluate the impact of 1,1,2,2-tetrachloroethane on the earthworm *Eisenia fetida* (Savigny) according to the methodology developed by the EU Commission (1983).

4.4.2 Toxicity to terrestrial plants

Investigations were carried out more than 40 years ago on the effects on terrestrial plants, when 1,1,2,2-tetrachloroethane, a known insect-control fumigant, was also under consideration as a plant pesticide for fruit orchards. Studies by Gast and Early (1956) on various experimental plants (cotton, cucumbers, tomatoes, maize, beans) showed that a concentration of 0.5 % compound, applied to moist soil, had no adverse effect, except in beans, which exhibited "slight" damage. Ten times that amount caused weak to moderate plant damage. The authors did not provide details on the toxic effect.

4.5 Initial Assessment for the Environment

Based on its physico-chemical properties, (vapor pressure: 6 hPa; solubility: 2.9 g/l) 1,1,2,2-tetrachloroethane released to the environment will mainly partition into the atmosphere. It has an average atmospheric lifetime of 92 days. Its impact on stratospheric ozone, its greenhouse effect and its contribution to the formation of tropospheric ozone is expected to be low. Observed intermediate products formed during the atmospheric oxidation are phosgene, C(=O)ClH and dichloroacetylchloride. Decomposition in the atmosphere of phosgene and C(=O)ClH should lead to the formation of HCl and CO_2 by hydrolysis in atmospheric water whereas, dichloroacetylchloride will form HCl and dichloroacetic acid which will be further removed from the atmosphere by rain water.

If released to water, 1,1,2,2-tetrachloroethane will be removed rapidly by volatilization. It is not readily biodegradable. It is expected to undergo dehydrochlorination under hydrolytic alkaline conditions to trichloroethylene (see SIDS for trichloroethylene: CAS No. 75-01-6) and to biodegrade under anaerobic conditions. Based on its partition coefficient (logKow = 2.39) and its

bioconcentration factor (BCF = 4.2-13.2), it is not likely to bioaccumulate. Due to its low Koc value of 46, it is not expected to adsorb to suspended solids, sediments and soils.

1,1,2,2-Tetrachloroethane is toxic to aquatic organisms, *Daphnia magna* being the most sensitive species with a 48h EC50 of 9.3 mg/l. On the basis of the NOEC determined from the chronic tests (32 day NOEC *Pimephales promelas* = 1.4 mg/; 28 day NOEC *Daphnia magna* = 6.9 mg/l; 72h EC10 *Scenedesmus subspicatus* = 9.8 mg/l), a PNEC of 140 µg/l is proposed applying a factor of 10 to the lowest NOEC available with fish.

5 RECOMMENDATIONS

The chemical is currently of low priority for further work.

Environment

No further work proposed

Human Health

The chemical possesses properties indicating a hazard for human health. Based on data presented by the Sponsor country, exposure to humans is anticipated to be low, and therefore this chemical is currently of low priority for further work. Countries may desire to investigate any exposure scenarios that were not presented by the Sponsor country.

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I U C L I D

Data Set

Existing Chemical	:	ID: 79-34-5
CAS No.	:	79-34-5
EINECS Name	:	1,1,2,2-tetrachloroethane
EC No.	:	201-197-8
TSCA Name	:	Ethane, 1,1,2,2-tetrachloro-
Molecular Formula	:	C2H2Cl4

Producer related part

Company	:	Atofina
Creation date	:	24.04.2001

Substance related part

Company	:	Atofina
Creation date	:	24.04.2001
Status	:	
Memo	:	
Printing date	:	09.08.2002
Revision date	:	
Date of last update	:	09.08.2002
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	:	cooperating company
Name	:	2,4 Pentanedione Producers Association
Contact person	:	
Date	:	
Street	:	1250 Connecticut Avenue, NW, Suite 700
Town	:	20036 Washington, DC
Country	:	United States
Phone	:	
Telefax	:	
Telex	:	
Cedex	:	
Email	:	
Homepage	:	

Source : EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
10.07.2001

Type	:	
Name	:	Enichem S.p.A.
Contact person	:	
Date	:	
Street	:	Via Taramelli,26
Town	:	20124 Milan
Country	:	Italy
Phone	:	
Telefax	:	
Telex	:	
Cedex	:	
Email	:	
Homepage	:	

Source : EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
11.02.2000

Type	:	
Name	:	ICI Chemicals & Polymers Limited
Contact person	:	
Date	:	
Street	:	PO Box 14, The Heath
Town	:	WA7 4QF Runcorn, Cheshire
Country	:	United Kingdom
Phone	:	
Telefax	:	
Telex	:	
Cedex	:	
Email	:	
Homepage	:	

Source : EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
11.02.2000

1.0.2 LOCATION OF PRODUCTION SITE, IMPORTER OR FORMULATOR

1.0.3 IDENTITY OF RECIPIENTS

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 :
Colour :
Odour :

Source : EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
11.02.2000

1.1.2 SPECTRA

1.2 SYNONYMS AND TRADENAMES

1,1,2,2-czterochloroetan; 1,1,2,2-tetrachloorethaan; 1,1,2,2-tetrachloroaethan; 1,1,2,2-tetrachlorethane; 1,1,2,2-tetracloroetano; 1,1-dichloro-2,2-dichloroethane; Acetylene chloride; Dichloro-2,2-dichloroethane; Ethane, 1,1,2,2-tetrachloro

Source : Atochem Paris la Defense
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
17.03.1994

Ethane 1,1,2,2-tetrachloro; 1,1-dichloro-2,2-dichloroethene; acetylene tetrachloride; sym-tetrachloroethane; tetrachloroethane; TETRAS; 1,1,2,2-Tetracloroetano (Italian)

Source : Enichem S.p.A. Milan
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
29.05.1994

s-tetrachloroethane; sym-tetrachloroethane; Tetrachloroethane; Tetrachlorure d'acetylene; NCI-c03554; A13-04597; EPA Pesticide Chemical Code 078601; Westron; Acetosal; Acetylene tetrachloride; Cellon; Bonoform

Source : Atochem Paris la Defense
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
08.11.1993

Sym Tetrachloroethane

Source : ICI Chemicals & Polymers Limited Runcorn, Cheshire
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
02.06.1994

1.3 IMPURITIES

1.4 ADDITIVES

1.5 TOTAL QUANTITY

1.6.1 LABELLING

Labelling	:	as in Directive 67/548/EEC
Specific limits	:	yes
Symbols	:	T+, N, ,
Nota	:	, other RM: S,
R-Phrases	:	(26/27) Very toxic by inhalation and in contact with skin (51/53) Toxic to aquatic organisms, may cause long-term adverse effects in the aquatic environment
S-Phrases	:	(1/2) Keep locked up and out of reach of children (38) In case of insufficient ventilation, wear suitable respiratory equipment (45) In case of accident or if you feel unwell, seek medical advice immediately (show the label where possible) (61) Avoid release to the environment. Refer to special instructions/Safety data sets
Source	:	EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
11.02.2000		

1.6.2 CLASSIFICATION

Classified	:	as in Directive 67/548/EEC
Class of danger	:	dangerous for the environment
R-Phrases	:	(51) Toxic to aquatic organisms (53) May cause long-term adverse effects in the aquatic environment
Specific limits	:	
1st Concentration	:	
2nd Concentration	:	
3rd Concentration	:	
4th Concentration	:	
5th Concentration	:	
6th Concentration	:	
7th Concentration	:	
8th Concentration	:	
1st Classification	:	
2nd Classification	:	
3rd Classification	:	
4th Classification	:	
5th Classification	:	
6th Classification	:	
7th Classification	:	
8th Classification	:	
Source	:	EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
11.02.2000		
Classified	:	as in Directive 67/548/EEC

Class of danger	:	very toxic
R-Phrases	:	(26/27) Very toxic by inhalation and in contact with skin
Specific limits	:	
1st Concentration	:	
2nd Concentration	:	
3rd Concentration	:	
4th Concentration	:	
5th Concentration	:	
6th Concentration	:	
7th Concentration	:	
8th Concentration	:	
1st Classification	:	
2nd Classification	:	
3rd Classification	:	
4th Classification	:	
5th Classification	:	
6th Classification	:	
7th Classification	:	
8th Classification	:	

Source : EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
11.02.2000

1.6.3 PACKAGING

1.7 USE PATTERN

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 : MAK (DE)
Limit value : 7 mg/m3

Source : Atochem Paris la Defense
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
17.03.1994 (1)

Type of limit : TLV (US)
Limit value : 6.9 mg/m3

Source : Atochem Paris la Defense
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
17.03.1994 (2)

Type of limit : TLV (US)
Limit value : 6.9 mg/m3

Remark : Notation: skin
Source : Enichem S.p.A. Milan
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
29.05.1994 (3)

Type of limit : other: VME
Limit value : 7 mg/m3
Short term exposure limit value
Limit value : 35 mg/m3
Time schedule : 15 minute(s)
Frequency : 4 times

Country : France
Source : Atochem Paris la Defense
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
17.03.1994 (4)

Remark : Not listed UK HSE EH40
ICI Company Standard - 1ppm
Source : ICI Chemicals & Polymers Limited Runcorn, Cheshire
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
02.06.1994

1.8.2 ACCEPTABLE RESIDUES LEVELS

1.8.3 WATER POLLUTION

1.8.4 MAJOR ACCIDENT HAZARDS

1.8.5 AIR POLLUTION

1.8.6 LISTINGS E.G. CHEMICAL INVENTORIES

1.9.1 DEGRADATION/TRANSFORMATION PRODUCTS

1.9.2 COMPONENTS

1.10 SOURCE OF EXPOSURE

Remark : Continuous process.This chemical is an intermediate of the production of trichloroethylene.
One production site.
Effluents: as prescribed in the directive EEC 76/464
Source : Atochem Paris la Defense

EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)

07.06.1994

Remark : Minimal exposure used as intermediate.
Source : ICI Chemicals & Polymers Limited Runcorn, Cheshire
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)

02.06.1994

1.11 ADDITIONAL REMARKS

Remark : None
Source : ICI Chemicals & Polymers Limited Runcorn, Cheshire
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)

02.06.1994

1.12 LAST LITERATURE SEARCH

1.13 REVIEWS

2.1 MELTING POINT

Value : = -44 °C
Sublimation :
Method :
Year :
GLP : no data
Test substance :

Reliability : (2) valid with restrictions
Data from litterature.
10.09.2001 (5)

Value : = -43.8 °C

Reliability : (2) valid with restrictions
Data from Handbook
10.09.2001 (6)

Value : = -43 °C

Reliability : (2) valid with restrictions
Data from Handbook
10.09.2001 (7)

Value : = -36 °C

Reliability : (2) valid with restrictions
Data from Handbook
10.09.2001 (8)

2.2 BOILING POINT

Value : = 146.5 °C at 1013 hPa
Decomposition :
Method :
Year :
GLP : no data
Test substance :

Reliability : (2) valid with restrictions
Data from Handbook
10.09.2001 (9)

2.3 DENSITY

Type : density
Value : = 1.5953 at 20 °C
Method :
Year :
GLP : no
Test substance :

Reliability : (2) valid with restrictions

10.09.2001 (10)

Type : density
Value : = 1.5886 g/cm³ at 25 °C
Method :
Year :
GLP : no
Test substance :

Source : Atofina Paris la Defense
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Reliability : (2) valid with restrictions
07.09.2001 (11)

2.3.1 GRANULOMETRY

2.4 VAPOUR PRESSURE

Value : = 6.5 hPa at 20 °C
Decomposition :
Method :
Year :
GLP : no data
Test substance : no data

Reliability : (2) valid with restrictions
Data from Handbook
10.09.2001 (12)

Value : = 7.045 hPa at 25 °C
Decomposition :
Method :
Year :
GLP : no data
Test substance : no data

Reliability : (2) valid with restrictions
Data from Handbook
10.09.2001 (13)

Value : = 12.23 hPa at 30 °C
Decomposition :
Method :
Year :
GLP : no data
Test substance : no data

Reliability : (2) valid with restrictions
Data from Handbook
10.09.2001 (14)

2.5 PARTITION COEFFICIENT

Partition coefficient :
Log pow : = 2.39 at 25 °C

pH value :
Method : other (measured)
Year :
GLP : no data
Test substance :

Reliability : (2) valid with restrictions
10.09.2001 (15)

2.6.1 SOLUBILITY IN DIFFERENT MEDIA

Solubility in :
Value : = 2.9 g/l at 20 °C
pH value :
concentration : at °C
Temperature effects :
Examine different pol. :
pKa : at 25 °C
Description :
Stable :
Deg. product :
Method :
Year :
GLP : no data
Test substance :

Reliability : (2) valid with restrictions
Data from Handbook
10.09.2001 (16)

Solubility in :
Value : = 2.86 g/l at 25 °C
pH value :
concentration : at °C
Temperature effects :
Examine different pol. :
pKa : at 25 °C
Description :
Stable :
Deg. product :
Method :
Year :
GLP : no data
Test substance :

Reliability : (2) valid with restrictions
Data from Handbook
10.09.2001 (17)

2.6.2 SURFACE TENSION

Test type : other
Value : = 35.6 mN/m at 20 °C
Concentration :
Method :
Year :
GLP : no

Test substance : other TS: pure substance

10.09.2001 (18)

Test type : other
Value : = 34.4 mN/m at 30 °C
Concentration :
Method :
Year :
GLP : no data
Test substance : other TS: pure substance

10.09.2001 (19)

Test type : other
Value : = 33.3 mN/m at 40 °C
Concentration :
Method :
Year :
GLP : no
Test substance : other TS: pure substance

Reliability : (2) valid with restrictions
Data from Handbook
10.09.2001 (20)

2.7 FLASH POINT

28.06.2001

2.8 AUTO FLAMMABILITY

2.9 FLAMMABILITY

2.10 EXPLOSIVE PROPERTIES

2.11 OXIDIZING PROPERTIES

2.12 DISSOCIATION CONSTANT

2.13 VISCOSITY

2.14 ADDITIONAL REMARKS

Memo : Henry's Law constant at 25°C (measured) = 37.177 Pa.m3/mole

Remark : Distribution coefficients are reported for 21 chlorinated hydrocarbons plus C6H6 [71-43-2] and PhMe [108-88-3] in dil. air-water systems over the temperature range 0-30 °C.

The measurements were performed with a simple experimental apparatus consisting of an equil. cell followed by gas-chromatography analalysis.
This technique achieves a random error of less than .+-.1% and a systematic error, primarily attributable to gas-chromatography peak separation and integration error, of >5% for most of the compdounds considered which exhibit room-temperature distribution coefficients between 100 and 1000.

07.09.2001 (21)

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	:	2000000 molecule/cm³
Rate constant	:	< .0000000000001 cm³/(molecule*sec)
Degradation	:	= 100 % after 1160 day(s)
Deg. product	:	
Method	:	other (measured)
Year	:	
GLP	:	no data
Test substance	:	

Result : <0.1% loss per 12h sunlight day.
10.09.2001 (22)

Type	:	air
Light source	:	
Light spectrum	:	nm
Relative intensity	:	based on intensity of sunlight
INDIRECT PHOTOLYSIS		
Sensitizer	:	OH
Conc. of sensitizer	:	1000000 molecule/cm³
Rate constant	:	= .000000000000126 cm³/(molecule*sec)
Degradation	:	= 50 % after 63 day(s)

Attached document : Atmospheric fate of 1,1-2,2-tetrachloroethane

Reaction with the atmospheric OH radical.

Method

Principle of the method: OH radicals are generated from the photolysis of a precursor which can be H2O, H2O2 or HNO3. The concentration of the substance is put in excess and considered constant during the experiment. The rate constant can be inferred from the rate of disappearance of the OH radical. An extensive study was done using that technique by Jiang et al.(1)

Results:

k (OH) = 2.72 ± 0.42 10-12 (T/300)0.22 exp(-(915 ±62)/T)

k (OH)= 1.26 10-13 cm3 mol-1s-1 at 298 K.

Previous results have been reported in the review of Atkinson. (2).
k = 2.37 ± 4.8 10-13 cm3 mol-1s-1 at 292 K
k = 2.26 ± 4.6 10-13 cm3 mol-1s-1 at 298 K
k = 2.66 ± 5.4 10-13 cm3 mol-1s-1 at 312 K

The results from Jiang et al because of the experimental

technique used and control of impurities seams the most reliable.

Atmospheric lifetime of 1,1-2,2-tetrachloroethane.

Assuming an average OH° concentration of 106 cm-3 it is possible to calculate a 1/2 lifetime of t = ln2/k (OH°) of 63 days or an atmospheric lifetime of 92 days on the basis of the Jiang et al rate constant.

Atmospheric degradation products of 1,1-2,2-tetrachloroethane

It can be inferred from the structure that the oxidation of 1,1-2,2-tetrachloroethane should lead to the formation of phosgene and C(=O)HCl as the intermediate compounds which will further hydrolyze in atmospheric water to give HF and CO2. The removal of phosgene by wet deposition has an estimated lifetime of 70 days.(3)

3.1.4.1.2.2 Atmospheric degradation.

The possible atmospheric oxidation scheme of 1,1-2,2-tetrachloroethane is described below:

CHCl2- CHCl2 + OH° -> CHCl2- C°Cl2 + H2O

CHCl2- C°Cl2 + O2 + NO -> CHCl2- CCl2O° + NO2

At this stage two pathways can be considered:

Carbon-carbon bond cleavage leading to the formation of phosgene:

CHCl2- CCl2O° -> C(=O)Cl2 + C°HCl2

C°HCl2 + O2 + NO -> CHCl2O° + NO2

CHCl2O° -> C(=O)HCl + Cl°

Chlorine atom abstraction leading to the formation of chloroacéthylchloride:

CHCl2- CCl2O° -> CHCl2- C(O)Cl + Cl°

Phosgene will further hydrolyze in atmospheric water to give HCl and CO2. The removal of phosgene by wet deposition has an estimated lifetime of 70 days.(3) Dichloroacéthylchloride should also undergo hydrolysis in atmospheric water to form dichloroacétic acid removed by rain.

These reaction products have been observed by Spence et al.(1978) (8).

Reaction with stratospheric ozone.

Organic substances containing chlorine, if primarily present in the atmospheric compartment and if there lifetime is long enough can reach the stratosphere and decompose through photolysis and other chemical reaction (e.g. with OH°). Chlorine atoms can then participate to the catalytic ozone destruction cycles.

In the case of 1,1-2,2-tetrachloroethane the atmospheric lifetime is too short to enable a significant fraction of the compound emitted to reach the stratosphere. Similar conclusion was taken in the last scientific assessment for ozone depletion (3) as far as short-lived substances containing chlorine are concerned.

The ozone depletion potential cannot be calculated with conventional methods such as those used for the long-lived species like CFCs and most HCFCs and will depend on the place of emission of that substance (4). A study using algorithm approach (5) attempted to estimate the ODP of 1,1-2,2-tetrachloroethane with a result of less than 0.001 and an estimated lifetime of about 1 month. However this method cannot take into account the specific behavior of short-lived species as explained in (4). Therefore, although it can be concluded that the ODP of 1,1-2,2-tetrachloroethane is very small, no accepted number have been calculated.

Contribution to the greenhouse effect.

Although no GWP value are reported, the direct global warming potential of 1,1-2,2-tetrachloroethane should be small essentially because of its short atmospheric lifetime. The GWP values of substances with comparable lifetime are generally less than 100 . (6).

Contribution to the formation of ozone at ground level.

1,1-2,2-tetrachloroethane reacts too slowly with the OH° radical to be considered as a significant contributor to the formation of tropospheric ozone. Halocarbon with comparable reactivity with OH° are reported to have low Photochemical Ozone Creation Potential value e.g. chloroform, methylene chloride, tetrachloroethylene show POCP of less than 10 (100 for ethylene). (7)

Conclusion.

1,1-2,2-tetrachloroethane has an average atmospheric lifetime of 91 days. It has negligible impact on stratospheric ozone, greenhouse effect and minor contribution to the formation of tropospheric ozone. Decomposition in the atmosphere should be complete and produce HF and CO2. Expected intermediate products formed during the atmospheric oxidation are phosgene and C(=O)HCl.

Bibliography

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(3)- WMO 1998, Scientific assessment of Ozone Depletion, World Meteorological Organization, Global Ozone Research and Monitoring Project- Report N°. 44.

(4)- Olsen et al, Geophys. Res. Let., Vol. 27, N° 10, P; 1475-1478, May 15, 2000

(5)- J.S.Nimitz and S.R.Skaggs, Env. Sci. Technol. 1992, 26, 739-744

(6)- IPCC 2000, Climate Change 2000, The Science of Climate Change, Contribution of Working Group I to the third Assessment Report of the Intergovernmental Panel on Climate Change. In press.

(7)-Derwent et al, Atmospheric environment vol.32, N°14/15, pp. 2429-2441.

(8)-SPENCE, J.W. and HANST, P.L., 1978.Oxidation of chlorinated
ethanes.J. Air Poll. Contr. Assoc., 28, 250-253.

Reliability : (1) valid without restriction
Flag : Risk Assessment
10.09.2001 (23)

Type : air
Light source :
Light spectrum : nm
Relative intensity : based on intensity of sunlight
INDIRECT PHOTOLYSIS
Sensitizer : OH
Conc. of sensitizer : 500000 molecule/cm³
Rate constant : = .000000000003 cm³/(molecule*sec)
Degradation : = 50 % after 53 day(s)
Deg. product :
Method : other (calculated)
Year :
GLP : no
Test substance :

Reliability : (1) valid without restriction
10.09.2001 (24)

Result : The influence of UV radiation on the stability of 10 ppm 1,1,2,2-tetrachloroethane, mixed with 4 ppm chlorine gas has been investigated at 22.5 degree C.
After 2 minutes of radiation at a wave lenght of 360 nm, 35% of the mixture had been degraded to 0.2 ppm CO, 4 ppm HCl,

0.5 ppm CCl2O and 2.5 ppm CCl2HCOCl.

10.09.2001

Remark : Laboratory investigations under stratospheric conditions have shown an initial degradation to trichloroethylene (i.e. a splitting off of HCl as the primary breakdown stage).This trichloroethene then further reacts by chlorine-sensitized photooxidation to become dichloroacetylchloride (ref.1), which is degraded to CO2 and HCL, with phosgene as intermediate.Small amounts of trichloromethane and tetrachloromethane may occur as by-products, which are themselves degraded to CO2, HCl and H2O (ref.2).

10.09.2001 (25)

3.1.2 STABILITY IN WATER

Type : abiotic
t1/2 pH4 : at °C
t1/2 pH7 : = .4 year at 25 °C
t1/2 pH9 : at °C
Deg. product :
Method : other
Year :
GLP : no data
Test substance :
Deg. products : 79-01-6 201-167-4 trichloroethylene

Result : Kinetic analysis
Preliminary studies were made to find appropriate temperatures and base concentration range at which the reaction would proceed.
Th dependence of hydrolysis rate on concentration of base was determined by varying OH concentration by at least a factor of 10 within the range pH 7-14.
All reaction were found to be either first order in base or pH independent.
Solutions were made 0.001 M in HCl to measure the "neutral" hydrolysis rate in order to assure negligible reactions with OH-.There were no evidence of any acid catalysis.
The data were reduced as first order or pseudo first order, with naturel logarithm of reactant concentration plotted against time in minutes, the slope giving k (observ).
The second order rate constant for base-catalyzed reactions was obtained by dividing k (observ) by base concentration.
Each individual rate constant value was determined by 5-20 time-concentration points, with each sample analyzed in triplicate.

Under "neutral "conditions, measurements were performed at approximately 175, 159 and 85°C .
Under alkaline conditions, the temperatures were 49.5, 35, 21 and 0°C.

Arrhenius parameters :
NEUTRAL
A = (1.57+-0.50)e8 min-1
E (Activation Energy) = 92.4+-3.2 kJ
k (neutral,25°C) = 9.70e-9 min-1

BASIC
A = (1.54+-0.14)e15 1/mol min
E (Activation Energy) = 78.1+-1.0 kJ
kb (pH 7, 25°C) = 3.02e-6 min-1

k(observ) = k+kb = 3.03e-6

Test condition : Aqueous solutions were prepared by shaking the test substance for 2 min with deionized water, previously distilled and boiled.
Final solution (0.1M, pH7 phosphate buffered or diluted NaOH or HCl) were less than 10% saturated in the organic substrate.
All solutions were refrigerated, if not used immediately.
Hydrolysis experiments utilized either zero dead-volume stainless steel tubes (2 ml volume) or glass bulbs .The stainless steel tubes were filled by using a needle syringe.The bulbs were filled by capillary action.The ends were flamed sealed enclosing about 350 µl of liquid and a 10-15 µl air space.
The lower temperature were achieved by using water baths.
The reaction tubes/bulbs used for high-temperature runs were air thermostated by use of a gas chromatograph oven.
Adsorption on steel or glass was checked.

Analysis were performed by gas chromatography.

Test substance : obtained from Aldrich or Eastman or Pfaltz and Bauer.Highest purity available.

10.09.2001 (26)

Type : abiotic
t1/2 pH4 : at °C
t1/2 pH7 : at °C
t1/2 pH9 : at °C
Deg. product :
Method :
Year : 1987
GLP :
Test substance : no data

Result : A measured aqueous hydrolysis rate constant of Kb = 2.3*10E+7
mol-1 yr-1 at pH of 9 and 25 °C corresponds to half-lives of 1.1 and 111 days at pH of 9 and 7.

Reliability : (4) not assignable

10.09.2001 (27)

Type : abiotic
t1/2 pH4 : at °C
t1/2 pH7 : at °C
t1/2 pH9 : at °C
Deg. product :
Method : other
Year : 1988
GLP : no data
Test substance : no data
Deg. products : 79-01-6 201-167-4 trichloroethylene

Remark : No significant differences in the kinetics or products were observed in the sediment pores compared to those in water at

the same pH, indicating that the effects of ionic strengh, surface catalysis and adsorption are unimportant for the low-carbon sediment studied.

Neutral and base-catalysed hydrolyses of the test substance in pure water yielded trichloroethylene as essentially the sole degradation product.

Result : - Half-life calculated from kinetic data, according to Lyman's equation : t1/2=0.693/k (Ref. 2), for hydrolysis of 1,1,2,2-tetrachloroethane in pure water, at 25°C :

pH	10E+8 k, s-1	t1/2
6.05	1.4+-0.4	573 d
7.01	22.0+-3.5	36.5 d
9.0	1500+-250	12.8 h
9.0	2920+-640	6.6 h
10.0	12100+-1400	1.6 h

- Half-life in sediment pore-water at 25°C and pH between 7 and 7.5 was found to be 29.1 d.the kinetic constant (10E+8 k, s-1) was 27.6+-4.0.

Test condition : The focus of this work was to study hydrolysis under conditions approximating groundwater environments as closely as possible : most experiments were performed at 25 °C.

Sediments were provided by EPA Environmental Research Laboratory, Ada, Ok, as Lula C1, a sandy material collected at a depth of between 5.4 and 6.4 m.It was described as having a total organic carbon content of 0.02+-0.005%, a total surface area of 11+- 1 m2/g and a cation-exchange capacity of 2.5+- 0.2 maquiv NH'+/g.

Sediment-extracted pore water was obtained by saturating sediments samples with Milli-Q water, and recovering the water after equilibrated overnight .
The pore water was analyzed by ion chromatography, had a pH of about 7-7.5 and a buffering capacity of about 1 mM.
Aqueous solutions of the compounds were added to vials or ampules by a syringe.

Sediments (6.8 g) were added to the vials.Aqueous samples (1.35 ml) were injected slowly into the bottom of the sediments to displace the air.

Samples were incubated in a temperature-controlled bath (+-0.1 °C) at the desired temperature.
At appropriate time intervals, samples were cooled and stored at 2°C until analysis at the end of the run.

Halogenated compounds were analyzed by gas chromatography after extraction with hexane or isooctane.

Sorption of the compound was shown in experiments to be minor, as expected for a low-carbon sediment.

Test substance : Commercial source not specified, and used as received.

10.09.2001 (28)

Type : abiotic
t1/2 pH4 : at °C
t1/2 pH7 : = 102 day(s) at 25 °C

t1/2 pH9 : = 1 day(s) at 25 °C
Deg. product :
Method : other (calculated)
Year : 1987
GLP :
Test substance : no data
Deg. products : 79-01-6 201-167-4 trichloroethylene

Remark : Kinetics of elimination reaction
At each temperature, 3 or more independent sets of experimental data were obtained.
Each set daa consisted of 6-11 measurements of the concentration of both 1,1,2,2-tetrachloroethane and trichloroethylene.
In all cases, the disappearance of 1,1,2,2-Tetrachloroethane is balanced by a corresponding appearance of trichloroethylene.
The emimination reaction is also found to be base promoted for values of pH in the range 5-9.
Pseudo-first order rate constants were obtained.
According to the curve given in the publication, the duration of experiment was 80 hours.

Test condition : The abiotic elimination of HCl from the test substance was studied in 0.100M phosphate-buffered distilled water.
The reaction was investigated for pH 5-9 and at 11 different temperatures ranging from 30 to 95°C.

From the results, the half-life was calculated at 25°C at pH 7 and pH 9.

200 µl of a standard solution of the test substance in methanol was added to 60 ml of the desired buffer to give a nominal test substance concentration of 450 nmol/l.The sealed ampules containig the samples were incubated in a water bath maintained at a constant temperature within +-0.1°C.
After incubation, the ampules were placed in ice-water for rapid cooling and then stored in a refrigerator at 4°C.
The samples were analyzed as soon as possible, always within 24 h after refrigeration.
The neck of the ampules was broken and 50 ml of the sample was transferred into a serum vial, with 5 ml of pentane and analyzed by gas chromatography.
The adsorption of compounds on glass surfaces of the test vessels was examined.
Control experiments were conducted under sterile conditions to determine the extent of microbially mediated degradations.
No difference in the degradation rates was observed in sterile and non sterile ampules.

Test substance : 98 % from Aldrich chemical
10.09.2001 (29)

Type : abiotic
t1/2 pH4 : at °C
t1/2 pH7 : at °C
t1/2 pH9 : at °C
Deg. product :
Method :
Year : 1983

GLP :
Test substance :

Result : A study found that at ppm concentration levels, 1,1,2,2-tetrachloroethane undergoes hydrolytic dehydrohalogenation to trichloroethylene in a sterile, anaerobic solution at pH 7.
In 28 days, 25% of the chemical had degraded and the amount of degradation was not affected by contact with a sulfide redox buffer of hematin.
Reliability : (4) not assignable
10.09.2001 (30)

3.1.3 STABILITY IN SOIL

3.2.1 MONITORING DATA

10.09.2001 (31)

3.2.2 FIELD STUDIES

3.3.1 TRANSPORT BETWEEN ENVIRONMENTAL COMPARTMENTS

Type : adsorption
Media : soil - 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
Year :

Method : Not described.
Result : A Koc of 46 was determined on the basis of a soil- water equilibrium isotherm from water at 20°C onto a Willamette silt loam (1.6 % organic matter,26 % clay, 3.3% sand,69 % silt). this figure suggests that 1,1,2,2-tetrachloroethane will be highly mobile in soil.
10.09.2001 (32)

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
Year : 1975

Result : The time for 50% evaporation was 56 minutes and for 90% was greater than 120 minutes.

Test condition : -Ref 1
Hollow fiber-mass spectroscopic method of analysis was used.
Solutions of 1 ppm (weight basis) of the test substance were prepared by dissolving a known amount of 1,1,2,2-tetrachloroethane in 100 ml methanol and then mixing an aliquot (0.1 ml) with a liter of deionized water.
The solutions (200 ml) were poured into a 250 ml beaker and stirred at 200 rpm with a propeller stirrer.
After the starting of the stirrer, mass spectra were scanned after 1 minute and periodically thereafter.
The maximum peak height obtained was considered to be 1 ppm, and subsequent concentrations were determined from the peaks heights by assuming a linear relationship between peak height and concentration.
The solutions were at room temperature (25°C).

- Ref 2
In an another publication (same author), evaporation half-life from 1 ppm aqueous solutions were determined and compared to caluclated half-lifes.
The experimental conditions included 200 rpm stirring with a shallow-pitch propeller stirrer at around 25°C, and an average solution depth of 6.5 cm.
The experimental half life obtained was 55.2 minutes, while the calculated half-lifes were : Mackay's Formula = 12 minutes and Liss and Slater's formula = 40.5 minutes.

Test substance : Not specified.
10.09.2001 (33)

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
Year : 1980

Result : Evaporation half-life: t1/2 = 9.2 minutes at 2270 ppm (24.8°C)
t1/2 = 8.6 minutes at 0.1 ppm (24°C)

Test condition : Rates of evaporation were measured gravimetrically by a Mettler H54 balance.
A stop watch was used to record the time for weight loss.
Stainless-steel planchets (4.6 cm2) with a wall height of 6 mm were used as the sample containers.The liquid level was about 4 mm height.
The mechanical stirring was carried out by a Teflon magnetic stirring bar at a controlled speed of 100+-10 rpm.
The solutions were maintained at a depth of 1.7 cm, at a temperature of 24.8 °C.
The half-lives were measured at two drastically different intial concentrations. The high concentration (2270ppm) corresponds to about 80 % solubility limit.

Test substance : Not specified.
10.09.2001 (34)

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
Year	:	

Result : 1-The volatilization half-life from a model river (1m deep, flowing 1m/sec, with a wind speed 3m/sec, has been estimated to be 6.3 hours (ref:1).

2-The volatilization half-life from a model pond, which considers the effect of adsorption, has been estimated to be 3.5 days (ref:2).

10.09.2001 (35)

Type	:	fugacity model level I
Media	:	
Air	:	92.26 % (Fugacity Model Level I)
Water	:	7.46 % (Fugacity Model Level I)
Soil	:	.14 % (Fugacity Model Level I)
Biota	:	% (Fugacity Model Level II/III)
Soil	:	% (Fugacity Model Level II/III)
Method	:	
Year	:	

Test condition : Model used : Nord base

physico-chemical parameters :

Temperature : 20°C
Molecular weight : 170
Vapor pression : 600 Pa
Solubility : 2900 g/m3
Solubility : 17.06 mol/m3
Henry's law constant : 35.17 Pa.m3/mol
log octanol/water partition coefficient : 2.39
Organic C-water partition coefficient : 100.64
Air-water partition coefficient : 0.01
Soil-water partition coefficient : 3.02
Sediment-water partition coefficient : 6.04
Amount of chemical : 1 mole
Fugacity : 0.37477329e-6 Pa
Total VZ products : 2668279.78

10.09.2001

3.3.2 DISTRIBUTION

27.06.2001

3.4 MODE OF DEGRADATION IN ACTUAL USE

3.5 BIODEGRADATION

Type : aerobic
Inoculum : activated sludge
Concentration : 100 mg/l related to Test substance
related to
Contact time :
Degradation : = 0 (±) % after 28 day(s)
Result : under test conditions no biodegradation observed
Deg. product :
Method : OECD Guide-line 301 C "Ready Biodegradability: Modified MITI Test (I)"
Year :
GLP : no data
Test substance : no data

Test condition : - Test Conditions of cultivation
(1) Concentration of test substance : 100 mg/l
(2) Concentration of activated sludge [as the concentration of suspended solid] : 30 mg/l
(3) Volume of test solution:300 ml
(4) Cultivation temperature : 25 °C
(5) Cultivation duration : 28 days

- Measurement and analysis

- Total organic carbon analyzer : TOC
- Gas chromatography : GC

- Results : percentage biodegradation (average)

- TOC 0
- GC 10

Reliability : (1) valid without restriction
Flag : Critical study for SIDS endpoint
10.09.2001 (36)

Type : aerobic
Inoculum : predominantly domestic sewage, adapted
Deg. product :
Method :
Year : 1981
GLP :
Test substance : no data

Remark : - Result: No significant degradation under conditions of the test.
- 0% degradation at 7 day (5 and 10 mg/l)
29 and 23 % degradation at 28 day (5 and 10 mg/l respectively)
- 7% and 0% volatilization loss at 25°C (at 5 and 10 mg/l respectively)
Test condition : The author who incubated the tetrachloroethane with sewage seed for 7 days and followed that with three successive 7-day subcultures found no significant degradation under these conditions.

Test method :
- static-culture flask-screening procedure of Bunch and

Chambers, utilizing biochemical oxygen demand (BOD), dilution water containing 5 mg of yeast extract per liter, as the synthetic medium
- 2 concentrations of test compound: 5 and 10 mg/l
- Inoculum: domestic wastewater
- 7 day static incubation at 25°C in the dark, followed by 3 weekly subcultures (totaling 28 days of incubation)
- Analysis method: GC

Biodegradability studies were carried out in 250 ml glass - stoppered reagent bottles to minimize possible volatilization of the test compound.
The substrate containing media in reagent bottle was inoculated with prechilled yeast extract and 10 ml of prechilled settled domestic wastewater as inoculum.
Volatility controls were held at both refrigerated and 25°C temperatures for 10 days and then analyzed by GC and for TOC to determine loss of substance from volatilization.
Analysis were carried out by a direct injection method (without a solvant extraction) chromatographically.

Reliability : (3) invalid
10.09.2001 (37)

Type : aerobic
Inoculum : activated sludge, domestic, adapted
Deg. product :
Method :
Year : 1983
GLP : no data
Test substance : no data

Result : At a concentration of 201 mg/l of the test substance, it was shown that the main removal mechanism was a air-stripping process (93.5%) , assuming a 27% biodegradation.

Test condition : Complete-mix, bench-scale, continuous-flow activated-sludge reactors were used to treat a synthetic wastewater containing a "base mix" plus the pollutant(s) under study.
The base-mix included :
- ethylene glycol
- ethyl alcohol
- glucose
- glutamic acid
- aceic acid
- phenol
- ammonium sulfate
- phosphoric acid
- salts

The "base-mix" and pollutants were added so that the BOD5 of the wastewater would be approximately 250 mg/l.
The pollutants were studied as single-pollutant or in combinations of three to a system.

The activated sludge systems consisted of stainless steel internal recycle 3.0 l reactors.
The wastewater was pumped from a sealed feed tank to the reactor.The effluent from the settling unit flowed by gravity to a collection tank.The off-gas was pulled by a vacuum pump.

Activated sludge for initial seeding was obtained from a local municipal activated sludge plant.

Three individual systems were acclimated to the synthetic wastewater and the pollutant(s) to be evaluated.
The activated sludge systems were operated at mean cell residence times of 2,4 and 6 days.The mean cell residence times were maintained by wasting sludge once a day.
After a one-month acclimation period, influent, effluent, mixed liquor and offgas samples were collected for analyses over a 60-day period.

The treatment performances of the activated sludge systems were monitored with respect to BOD5, TOC, COD and specific pollutants analysis (gas chromatography).

10.09.2001 (38)

Type : aerobic
Inoculum :
Deg. product :
Method :
Year : 1982
GLP :
Test substance : no data

Remark : 41% degradation was obtained in 24 days in a modified shake flask biodegradability test using an unacclimated inoculum, and 19% degradation in a river die-away test while 5 other chlorinated ethanes and ethenes were undegraded.
Reliability : (4) not assignable

10.09.2001 (39)

Type : anaerobic
Inoculum :
Deg. product :
Method :
Year : 1983
GLP : no data
Test substance : other TS: reagent grade

Result : After a 9-12 weeks acclimation period, removal of 97+-3 % of the test substance, after a two-day flow-through period, with a test concentration of 27+-1 µg/l .
Test condition : Continuous-flow fixed-film studies with methanogenesis.
A fixed-bed reactor was used, which has initially been adapted to chlorinated aliphatic hydrocarbons for 12 months.

Anoxic conditions were achieved by connecting two laboratory-scale glass columns (2.5 cm*25 cm) in series .
Glass beds were used as the support medium for the biofilms in order to minimize adsorptive effects.
Sterile defined growth medium was continuously applied to the lead column with a syringe pump equipped with a 60 ml plastic syringe.The growth medium contained 250 mg/l acetate.
The lead column was initially seeded with primary sewage effluent and produced an anoxic effluent (dissolved oxygen by the winkler method was below the detection limit of 0.5 mg/l) that became the influent to the second anoxic column.

Primary digested sewage sludge was used to seed the second column for methanogenesis.
A mixture of halogenated aliphatic compounds (about 160 µg/l for each) was pumped to the second column influent feed.
The comumn system were operated at 22°C in the dark to prevent growth of photosynthetic organisms for 15 months.
The methanogenic growth medium was amended with molybdate at a concentration of 1.5 mM to inhibit sulfate reduction.

The anoxic column effluents were collected in 20 ml glass syringe barrel with tight-fitting teflon floats to prevent volatilization losses.
Extraction of organic ompounds were performed directly on samples on the syringes.

Analysis of halogenated aliphatic compounds with a detection limit of 0.1 µg/l in water were conducted using pentane-extraction, gas chromatography procedure with electron-capture detection.

Reliability : (2) valid with restrictions
10.09.2001 (40)

Type : anaerobic
Inoculum :
Deg. product :
Method :
Year : 1980
GLP :
Test substance : no data

Remark : A static test under anaerobic conditions showed that at concentrations up to 100 mg/m3 chlorinated compounds only inhibited the growth of clostridia and some facultative anaerobes within the first 3 to 5 days of a total period of 1 to 2 weeks.
This was followed by rapid bacterial growth, with 50 to 70% of organically bound chlorine being converted to chloride ions.Used strains has been isolated as hexachlorohexane degraders and exhibited a dechlorinating enzyme system.

Reliability : (3) invalid
lack of information on test conditions.
No specific information on 1,1,2,2- tetrachloroethane
10.09.2001 (41)

Type : anaerobic
Inoculum :
Deg. product :
Method :
Year : 1987
GLP :
Test substance : other TS: purity : 98 %

Remark : Products studies indicated that reduction by vicinal dehalogenation was the major fate process.

Result : Results of primary degradation :
At an initial 1,1,2,2-tetrachloroethane concentration of 3.5 E-7 mol/l of suspension, half-life time due to chemical hydrolysis and biodegradation was 6.6 days.

Test condition : The degradation of selected halogenated ethanes was studied in anoxic sediment-water suspensions at 1 to 20%

sediment concentration.
Batch kinetic experiments were used to quantify decay.

Sediment-water slurries were collected from ponds.

Kinetics experiments were performed using a batch method in which sediment-water aliquots were distributed into a series of test tubes and spiked with a known concentration of chemical under a nitrogen atmosphere.
Time-concentration data were collected by periodically sacrificing a tube for analysis.

A stock solution of the tested substance was made in acetonitrile such that 20 µl additions of chemical into 10 ml sediment-water gave the desired initial experimental concentration.

At specific intervals, the tubes were extracted with 4 ml hexane by vortex-mixing at high speed.The hexane was recovered from the tubes by centrifuging .The hexane layer was removed from samples not analyzed on the same day as extracted and placed in a clean tube.

Hexane extracts were analyzed using a Tracor model 220 gas chromatograph equipped with an electron-capture detector.

Reliability : (2) valid with restrictions
10.09.2001 (42)

Type : anaerobic
Inoculum :
Deg. product :
Method :
Year : 1996
GLP : no data
Test substance : other TS: purity :99 %

Result : Biotic transformations of TeCA :
TeCA removal in the first and second spikings occured without lag.
Trichloroethylene (TCE), cis-1,2-dichloroethene (cDCE) and trans-1,2-dichloroethene (tDCE) were formed simultanouesly during the first 6 days.Much smaller amounts of 1,1,2-trichloroethane (1,1,2-TCA) and 1,2-dichloroethane (1,2-DCA) appeared later.
The five products persisted in the first two spiking tests for at least 4 weeks.

Compound (%)

Spiking	1,1,2-TCA	1,2-DCA	TCE	tDCE	cDCE	ethane	ethene
First	3.2	1.3	16.5	21.4	51.6	0.3	0.6
Second	3.1	1.4	9.1	22.6	54.8	0.3	0.8

(For first spiking, mean values between day 6 and day 17.
For second spiking, mean values between day 6 and day 19.)

In the third and subsequent spikings, the transformation for the first 12 days was similar.

1,1,2-TCA and 1,2-DCA appeared earlier than in the earlier tests.

Compound (%)

Spiking	1,1,2-TCA	1,2-DCA	TCE	tDCE	cDCE	ethane	ethene
third	5.3	1.9	15.1	20.1	51.7	0.2	0.1
fourth	4.2	0.5	8.7	25.4	61.4	0.5	0.3

(For third spiking, mean values between day 3 and day 10.
For fourth spiking, mean values between day 7 and day 13.)

Abiotic transformations of TeCA :
It resulted in TCE formation in all bottles, the rate of conversion depending on the experimental conditions.
TeCA was converted to TCE by abiotic dehydrochlorination.

Test condition : - Culture media :
Reduced anaerobic mineral medium was used in all experiments.
- Source of organisms :
Anaerobic sludge from a laboratory-scale municipal sludge digester was used.
- Analytical methods :
Chlorinated compounds were analyzed by gas chromatography with an electrolytic conductivity detector.
- Experimental design :
Batch bottle tests were used in a serie of tests.
The sludge (30 ml each bottle) and reduced anaerobic mineral medium (130 ml each bottle) were dispensed into each bottle while purging with N2 and CO2.
Sterile syringes and needles were used for feeding chlorinated compound.
The bottles were incubated at 35°C.
Gas production and gas composition were periodically analyzed.Chlorinated compounds were measured daily during the first week and then every 2-3 days.

- 1,1,2,2-tetrachloroethane (TeCA) degradation was tested in a sludge seeded culture that was fed TeCA four times over about 4 months.
The TeCA concentration fed was about 60 µmol/l in the first spiking, 70 µmol/l in the second spiking, 80 µmol/l in the third spiking and 105 µmol/l in the fourth and following spikings.

- Abiotic tests with TeCA :
In order to understand abiotic transformations of TeCA under anaerobic conditions, reduced cell-free extracts were prepared.

Attached document : Teca.tif
Reliability : (2) valid with restrictions
10.09.2001 (43)

Type : anaerobic
Inoculum :

Result : The products of anaerobic biodegradation of the test

substance were determined in a 6-week study to be (in decreasng order):
cis-1,2-dichloroethylene, trans-1,2-dichloroethylene, trichloroethylene, 1,1,2-trichloroethane, 1,1-dichloroethylene and vinyl chloride.

Reliability : (4) not assignable
Document not available.

10.09.2001 (44)

3.6 BOD5, COD OR BOD5/COD RATIO

3.7 BIOACCUMULATION

Species	:	Cyprinus carpio (Fish, fresh water)
Exposure period	:	42 day(s) at 25 °C
Concentration	:	.26 mg/l
BCF	:	= 4.5 - 13.2
Elimination	:	no data
Method	:	OECD Guide-line 305 C "Bioaccumulation: Test for the Degree of Bioconcentration in Fish"
Year	:	1981
GLP	:	no data
Test substance	:	no data
Remark	:	At 0,26mg/l test substance, 4.5 was the lower limit value of BCF measured and 13.2 the upper limit value measured. At 0.026 mg/l test substance concentration the lower limit value of BCF was 4.1 and 13.1, the upper limit value.
Test condition	:	- Condition of acclimation Fish were reared in an acclimation tank according to flow through system at temperature of 25+-2°C for about 28 days.During this period, abnormal fish were removed. Then fish were transfered to test tanks and reared again at the same temperature for about one month. - weight : about 30 g length : about 10 cm lipid content : 2-6% - Feeding The amount corresponding to about 2% of the total body weight of test fish was fed twice a day by halves. - The test water was supplied at a rate of 200-800 ml/min in the glass tank of 100 l. - The concentration of dissolved oxygen was 6-8 mg/l. - Number of fish : 15-20 fish/level Analysis of test water and test fish: - test water analysis : twice a week - test fish analysis :every two weeks (n=2) - Control fish analysis :before the initiation and the termination of exposure (n=2)
Reliability	:	(1) valid without restriction
Flag	:	Critical study for SIDS endpoint

10.09.2001 (45)

Species	:	Lepomis macrochirus (Fish, fresh water)
Exposure period	:	14 day(s) at 16 °C
Concentration	:	9.62 µg/l
BCF	:	= 8
Elimination	:	yes
Method	:	other
Year	:	1978
GLP	:	no
Test substance	:	no data
Remark	:	- 1,1,2,2-tetrachloroethane was carbon-14 labelled on 1,2-14C (MW=167.86). - Elimination half-life in tissues < 1 day
Test condition	:	- Water hardness: 35 CaCO3 mg/l - Dissolved O2: 5.9 to 8.6 mg/l - pH: 6.3 to 7.9 - Test species : Bluegill sunfish (Lepomis macrochirus) , 0.37-0.95 g, 25-35 mm. - Test system : Studies were conducted in a flow-through system closed system). 100 bluegill were placed into an aquarium and continuously exposed to a sublethal concentration of the carbon 14 labeled substance. Representative water and fish samples were collected periodically (0,1,2,4,7,14,21,and 28 days) until apparent equilibrium between concentrations in fish tissue (whole body) and exposure water was observed. The remaining fish were transferred into an aquarium through which pollutant-free water flowed at a rate equivalent to that during exposure. In order to evaluate the persistence of the chemical, chemical analysis were performed on fish sampled during this elimination phase (7 days) to determine the half-life of chemical in the tissues. During each sampling interval (exposure and depuration), 5 fish were removed from each test aquarium, bottled dry, and analyzed radiometrically on a whole-fish basis.
Reliability	:	(2) valid with restrictions
Flag	:	Critical study for SIDS endpoint

10.09.2001 (46)

Species	:	Pimephales promelas (Fish, fresh water)
Exposure period	:	28 day(s) at °C
Concentration	:	
BCF	:	= 7
Elimination	:	no data
Method	:	
Year	:	1984
GLP	:	
Test substance	:	other TS
Test condition	:	Surviving fish from each test concentration were composited

into single samples for the determination of tissue residues.
Whole fish samples were homogenized with 70 g of anhydrous sodium sulfate previously cooled to about 5°C.The homogenate was transferred to a 300 ml Shell column and extracted by eluting the column with 250 ml hexane collected in a 250 ml flask.An aliquot was diluted to an appropriate volume for analysis.Analysis was performed by gas chromatography.

Test substance : purchased from Aldrich Chemical Company
purity > 95%

Reliability : (4) not assignable
12.09.2001 (47)

3.8 ADDITIONAL REMARKS

4.1 ACUTE/PROLONGED TOXICITY TO FISH

Type	:	flow through
Species	:	Pimephales promelas (Fish, fresh water)
Exposure period	:	96 hour(s)
Unit	:	mg/l
LC50	:	= 20 - 20.9 measured/nominal
LC50,24h	:	= 21.9 - 23.8 measured/nominal
LC50,48h	:	= 21.2 - 23.1 measured/nominal
LC50,72h	:	= 20 - 20.8 measured/nominal
Limit test	:	
Analytical monitoring	:	yes
Method	:	other
Year	:	1983
GLP	:	no data
Test substance	:	other TS
Method	:	U.S. EPA The committee on methods for toxicity tests with aquatic organisms: Methods for acute toxicity tests with fish, macroinvertebrates and amphibians.Ecological Research Series (EPA-660/3-75-009), 61 pp;, 1975.
Result	:	LC50 96h = 20.4 mg/l 95% confidence limit : 20-20.9
Test condition	:	Test animals: laboratory- reared fathead minnows, 30 to 35 days old. The rearing water was the same as the diluent water (temperature : 25 +-2 °C) Fish in the rearing tanks were fed live brine shrimp nauplii in excess until 12 to 24 h before testing, then not fed during the exposure period. - Unfiltered Lake Superior water was the source of dilution water. - total hardness : 45.1 (45.0 - 45.5) mg/l CaCO3 - total alkalilnity : 41.8 (35.6 - 43.4) mg/l CaCO3 - pH 6.7 - 7.6 - dissolved O2 : 8 (mean) mg/l (7.6 - 9.2) - 5 concentrations and a control, in duplicate chemical methods : The substance was analyzed by gaz chromatography with an electron capture detector. statistical method : Trimmed Spearman-Karber method for estimating median lethal concentration (Hamilton et al 1977)
Test substance	:	purchased from Aldrich Chemical Company purity > 95%
Reliability	:	(1) valid without restriction
Flag	:	Critical study for SIDS endpoint

11.09.2001 (48)

Type	:	semistatic
Species	:	Oryzias latipes (Fish, fresh water)
Exposure period	:	48 hour(s)
Unit	:	mg/l
LC50	:	= 31
Limit test	:	

Analytical monitoring	:	no data
Method	:	other
Year	:	1992
GLP	:	no data
Test substance	:	no data

Method : - Test method: In accordance with Japanese Industrial Standard (JIS K 0102-1986-71) titled "Testing methods for industrial waste water".

- Static system or semi-static system (Removal of test water at every 8-16 h)
- The 48 h LC50 value was estimated by Doudoroff method or Probit method

- Fish were reared in an acclimatization tank according to flow-trough system at temperature of 25=-2 °C for about 28 days.During the period, abnormal fish were removed.

- Dilution water : underground water pumped up from the ground of Kurume Research laboratories.
Water temperature, pH and dissolved oxygen were continuously measured.
The quality of dilution water used for the test was confirmed to meet the ministerial ordinance of Ministry of Health and Welfare (August 31, 1978) in total hardness and evaporated residue.
The other items was confirmed to meet the water quality criteria for fisheries (Shadanhozin Nihon Suisansigen Hogokyokai, March 1983).

test solution : preparation not described
no information on tested concentration
Test tank : round glass vessel
Volume of test water : 4l/level
Temperature : 25+-2 °C
Number of fish : 10 fish/level
No information on oxygen content, pH during testing
No indication on the protocol used : static or semi-static

Study considered not valid because of this lack of information.

Reliability : (1) valid without restriction
14.09.2001 (49)

Type	:	flow through
Species	:	Jordanella floridae (Fish, fresh water)
Exposure period	:	96 hour(s)
Unit	:	mg/l
LC50	:	= 18.5 measured/nominal
LC50, 24 h	:	= 21.26 measured/nominal
LC50, 48 h	:	= 18.99 measured/nominal
LC50, 72 h	:	= 18.48 measured/nominal
Limit test	:	
Analytical monitoring	:	yes
Method	:	other
Year	:	1991
GLP	:	no data
Test substance	:	no data

Method	:	- U.S.EPA: The committee on methods for toxicity tests with aquatic organisms: Methods for acute toxicity tests with fish, macroinvertebrates and amphibians.Ecological Research Series (EPA-660/3-75-009), 61 pp;, 1975. - Statistical methods : Spearman-Karber method (Hamilton et al, 1977)
Result	:	- Result of static tests (nominal concentrations) : LC50, 96h = 26.8 mg/l ; 95% CL : 21.3-33.7 - In the flow-through test, the % of measured /nominal was 81-95.
Test condition	:	- Dilution water : dechlorinated Lake Superior water - Temperature : 25+-2°C - The photoperiod consisted of 16 h of wide-spectrum lighting and 15 min of simulated dawn/dusk with low-level incandescent ligt. - Laboratory-reared juvenile (2-4 month) flagfish were used.Fish were not fed during the test. -The static-renewal tests were conducted in glass aquaria (3 l) Five or six duplicate, nominal concentrations of the test solution were prepared in a logarithmic serie and renewed every 24 h. Five juvenil flagfish were placed in each aquarium and mortality observed at 24, 48, 72 and 96 h. Flow-through tests were conducted with the apparatus described by Smith et al, 1977. Five or six duplicate, logarithmically distributed concentrations of the test solution were used in 30 l aquaria. Fresh solutions were added at a rate of 6 l/h.Each aquarium was sampled at least 3 times to determine the concentrations of the test solutions. 10 juvenile flagfish were placed in each aquarium and mortality observed at 12, 24, 48, 72 and 96 h. - Aeration was not used in either the static or flow-through tests.However, dissolved oxygen levels were measured at greater than 90% saturation. - Analytical methods : Solvent extraction followed by gas chromatography analysis.
Reliability	:	(2) valid with restrictions
Flag	:	Critical study for SIDS endpoint
11.09.2001		(50)

Type	:	semistatic
Species	:	Poecilia reticulata (Fish, fresh water)
Exposure period	:	7 day(s)
Unit	:	mg/l
LC50	:	= 36.7
Limit test	:	
Analytical monitoring	:	no
Method	:	other
Year	:	1981
GLP	:	no data
Test substance	:	no data

Test condition	:	-Test species : guppies (Poecilia reticulata) 2-3 month old. Each vessel (1.5 l) was filled with 1 l of standard water prepared according to Alabaster and Abram (1964) (Hardness: 25 mg/l CaCO3) and covered with glass. 100 µl of stock solution was added per liter. -The concentrations increased in geometrical progression with a ratio of 1.8 to 3.2. -8 guppies were tested at each concentration. The test solution was renewed daily and the guppies were fed 0.5 h before with a commercial fis food. -Dissolved Oxygen: > 5mg/l -Temperature: 22 degree C LC50's were calculated according to Litchfield and Wilcoxon (1949)
Reliability	:	(2) valid with restrictions
11.09.2001		(51)

Type	:	static
Species	:	Cyprinodon variegatus (Fish, estuary, marine)
Exposure period	:	96 hour(s)
Unit	:	mg/l
NOEC	:	< 8.8
LC50	:	= 4.7 - 32
LC50, 24h	:	= 14 - 120
LC50, 48 h	:	= 12 - 20
LC50, 72 h	:	= 5.1 - 33
Limit test	:	
Analytical monitoring	:	no
Method	:	other
Year	:	1981
GLP	:	no data
Test substance	:	other TS

Method	:	- U.S.EPA: The committee on methods for toxicity tests with aquatic organisms: Methods for acute toxicity tests with fish, macroinvertebrates and amphibians.Ecological Research Series (EPA-660/3-75-009), 61 pp;, 1975.
Remark	:	Type of water : Salt water
Result	:	LC50,96h = 12 mg/l 95% limit : 4.7 - 32 mg/l
Test condition	:	Test species : Juvenile sheepshead minnows, 8-15 mm length. Fish were maintained in laboratory in flowing, filtered seawater of ambient salinity from 10-31 0/00 and temperature from 25-31 °C. Fish were fed 24 h Artemia salina nauplii daily until there were used as test animals. Tests were conducted in either 4 l glass jars containing 3 l of test solution or 19 l glass jars containing 15 l. All dilution water was filtered (5 µm) natural seawater of ambient salinity. 10 fish were tested per container.There were no aeration. The dissolved oxygen concentration was measured in each test container at initiation of testing and daily thereafter.pH was measured in the control and low and high test concentrations at the initiation and after 96 h of testing.

control mortality < 10 %

LC 50 calculations were performed according to Stephan, C.E (1977,1978).

Test substance : purity > 80%
Reliability : (3) invalid
unmeasured concentration, open vessels.

11.09.2001 (52)

Type : static
Species : Lepomis macrochirus (Fish, fresh water)
Exposure period : 96 hour(s)
Unit : mg/l
LC50 : = 20 - 22
Limit test :
Analytical monitoring : no
Method : other
Year : 1981
GLP : no data
Test substance : other TS: >= 80%

Method : - U.S.EPA: The committee on methods for toxicity tests with aquatic organisms: Methods for acute toxicity tests with fish, macroinvertebrates and amphibians.Ecological Research Series (EPA-660/3-75-009), 61 pp;, 1975.

· Statistical methods : The LC50 and 95% confidence intervals were calculated where possible, by the moving average angle method (Harris, 1959).The nominal concentrations are transformed to logaritms and corresponding % mortalities to angles.Each group of these successive angles was then averaged and the LC50 was estimated by linear interpolation between the successive concentrations whole average angles bracketed 45°.When the test did not meet Harris' method requirements, the LC50 were calculated by the log probit method.

Test condition : Test animals were young of the year bluegill , wet weight ranging from 0.32-1.2 g.
Each test population was held in a separate tank receiving well-water at a minimum flow rate of 4 volume replacements per day.
Chemical and physical characteristics of the well-water were measured weekly:
- total hardness : 28-44 mg/l CaCO3,
- total alkalinity : 20-30 mg/l CaCO3,
- pH 6.4-7.4,
- dissolved O2 : 5.3-7.0 mg/l,
- specific conductance : 95-170 µmhos/cm,
- temperature : 20-24°C.

To control volatilization, the test jars were capped.

Dilution water used to prepare the test solutions was deionized water reconstituted according to the procedure US EPA 1975.
- Water hardness: 32-48 mg/l CaCO3
- Water alkalinity: 28-34 mg/l CaCO3
- pH: 6.7-7.8
- Dissolved oxygen: 7.0-8.8 mg/l

Ten fish were added to each test jar.
The pH and dissolved oxygen concentration of test solution were measured at 0 and 96 h.

Reliability : (3) invalid
unmeasured concentrations.
Static assay.

11.09.2001 (53)

4.2 ACUTE TOXICITY TO AQUATIC INVERTEBRATES

Type	:	static
Species	:	Daphnia magna (Crustacea)
Exposure period	:	48 hour(s)
Unit	:	mg/l
EC50	:	= 23
Analytical monitoring	:	yes
Method	:	other
Year	:	1983
GLP	:	no data
Test substance	:	other TS: Aldrich Chemical Co, purity from 95 to 99%

Remark : - Method: ASTM, (1980).Standard practice for conducting acute toxicity tests with fishes, macroinvertebrates and amphibians.ASTM Standard E 729-80, 1.Philadelphia, PA:American Society for Testing and Materials.

Result : Acute toxicity values calculated were the median effective concentration (EC) based on complete immobilization and the median lethal concentration (LC) based on death as defined by cessation of heart beat and gut movement.
Immobilization and death were determined by microscopic examination with a 30* dissection scope.

Values of EC50 (immobilization) and of LC50 (lethality) are given for fed and unfed daphnia with 95% confidence limits:

	Unfed	Fed
EC50	23.0 (16.3-34.5) mg/l	25.2 (22.2-28.2) mg/l
LC50	62.1 (55.9-70.7) mg/l	56.9 (49.9-66.3) mg/l

No mortality was observed among controls.

Test condition :

Test organisms:

Adults daphnids were obtained from laboratory stock reared at the US EPA,Duluth, MN.
Brood cultures of 25 animals in 1l beakers were maintained by renewing food (30 mg/l dry wt), a slurry of trout chow and yeast and water 3 tomes a week.

- less than 24h old daphnids collected from brood animals approximately 3 weeks old were used during the test

Test conditions

- Stock solutions were prepared by saturating Lake Superior

water with the test substance on a magnetic stirrer plate

- test temperature : 20°C +- 1°C

- exposure vessel type : 200 ml Erlenmeyer flasks filled with 200 or 160 ml for unfed and fed tests, respectively. Flasks were stoppered with foil wrapped, neoprene stoppers.

- dilution water source : Lake Superior water passed through a 5µ fiber filter, heated to 20°C and aerated with filtered air.
- Hardness: 44.7 CaCO3 mg/l
- Alkalinity: 41.5 CaCO3 mg/l
- Dissolved oxygen and pH: from 7.9 to 9.9 mg/l O2 and 7.1 to 7.7, for unfed acute tests
from 4.1 to 8.4 mg/l O2 and 7.0 to 7.5 for fed acute tests

lighting :16h light/8H dark photoperiod coupled with a 15 min. transition period.

test design :
4 replicates with 5 animals each were used for the control and 6 toxicant levels

The 48 h median effective concentration based on immobilisation and the median lethal concentration based on death were derived by the measured mean toxicant concentrations (average of initial and final test solution concentrations) and were calculated by probit (Stephan 1977)

Reliability : (1) valid without restriction
Flag : Directive 67/548/EEC, Critical study for SIDS endpoint
12.09.2001 (54)

Type : static
Species : Daphnia magna (Crustacea)
Exposure period : 48 hour(s)
Unit : mg/l
LC50 : = 6.8 - 13
LC50, 24h : = 14 - 26
LC0 : < 1.7
Analytical monitoring : no
Method : other
Year : 1980
GLP : no data
Test substance : other TS: purity >= 80 %

Remark : - Method: U.S. EPA: Methods for acute toxicity tests with fish, macroinvertebrates and amphibians.Ecological Research Series (EPA-660/3-75-009), 61 pp, 1975.
Test condition : - Daphnia magna are < 24h old
- Temperature : 22+-1°C
- Hardness: 173 mg/l CaCO3
- pH = 7.4 - 9.4
- Dissolved O2: 6.5 - 9.1 mg/l in 48h exposure period

The chemical was added to 500 ml of diluent water in 2 l jars.
The 500 ml volume of test solution was divided into three 150 ml aliquots in 250 ml beakers to provide triplicate

exposures.The remaining 50 ml of control, high, middle and low test concentrations were used to measure the 0-hour dissolved O2 concentration and pH of the solutions.
Five daphnids were placed in each 150 ml test solution within 30 minutes of the solution preparation.
15 daphnids were placed directly into the 2 l jars containing diluent water prior to addition of the test material.
The tests were also conducted in unreplicated 500 ml solutions containing 15 daphnids if dividing the solution into triplicate test vessels presented a risk of the loss of the test substance through volatilization.
In addition, these vessels were covered with plastic wrap secured with an elastic band.

A negative control consisting of the same dilution water, test conditions and test organisms, but without test substance was maintained concurrently with each test.

the dissolved oxygen concentration, pH and temperature of test solutions were mesured at the initiation and termination of the toxicity test in the high, middle and low test concentrations and controls.These parameters were only measured at the end of an exposure if a potential loss of the test substance existed due to volatilization.

Observations of test populations were made a 24 and 48 h of exposure and any mrotalities were recorded.

Mortality among water flea control populations never exceeded 10% in any test.

Reliability : (2) valid with restrictions
14.09.2001 (55)

Type : other
Species : Daphnia magna (Crustacea)
Exposure period :
Unit :
Method :
Year : 1995
GLP :
Test substance : other TS: Chemsyn, purity >86%

Remark : This study examines the hypothesis that exposure of Daphnia magna to sublethal levels of the test substance may affect subsequent sensitivity of the animals.
Prior exposure (24 h) of daphnia to sublethal level of 1,1,2,2-tetrachloroethane had no effect on their sensitivity to effective levels of this chemical.
Effective burden (24 h exposure) was independent of the sublethal body burden .

Reliability : (4) not assignable
10.09.2001 (56)

Type :
Species : Mysidopsis bahia (Crustacea)
Exposure period : 96 hour(s)
Unit : mg/l
EC50 : = 7.71 - 11
EC50,24 h : = 10.7 - 13.7

EC50,48h	:	= 9.74 - 12.4
EC50,72h	:	= 8.2 - 11.12
Analytical monitoring	:	no data
Method	:	other
Year	:	1978
GLP	:	no
Test substance	:	no data
Method	:	- Method: U.S. EPA: Methods for acute toxicity tests with fish, macroinvertebrates and amphibians.Ecological Research Series (EPA-660/3-75-009), 61 pp, 1975.
Reliability	:	(4) not assignable

10.09.2001 (57)

4.3 TOXICITY TO AQUATIC PLANTS E.G. ALGAE

Species	:	Scenedesmus subspicatus (Algae)
Endpoint	:	biomass
Exposure period	:	72 hour(s)
Unit	:	mg/l
EC50	:	= 47
Method	:	OECD Guide-line 201 "Algae, Growth Inhibition Test"
Year	:	1995
GLP	:	no data
Test substance	:	other TS: Aldrich, purity >= 98%
Result	:	The high reproducibility of the closed vessel tests were demonstrated. The cell density in the control cultures increased by a factor > 16 within 3 days. Comparison of EC50 values for 1,1,2,2-tetrachloroethane in open and closed vessels : open closed EC50 (ppm) 50 47 EC10 (ppm) 12.72 9.80
Test condition	:	The algae were cultured and the test performed according to the guidelines with some modification due to the volatility of the test substance. 500 ml flasks were fitted with cuvettes connected to glass tubes (diameter 10 mm) inserted into the flask through a silicon screw cap with teflon seal. The flasks with nutrient solution were aerated prior the test begin 10 minutes with air containing 3% CO2 as carbon source. After adding the alga solution to the various amounts of the tests compounds, the flasks were immediately closed as describes above (closed vessels) or with a screw cap (open vessels). Alga concentrations in the closed vessel were measured by turning the whole test equipment upside down and insering the cuvettes into the path of light of the

spectrophotometer.
The test flask now on top of the spectrophotometer was then covered with a black box to prevent light from entering with measurement.
Measurements from the open vessel were done using open cuvettes.
Measurements were carried out once every day at the same time.

Concentrations were measured at the beginning of the test
No measurement at the end of the test

Reliability : (2) valid with restrictions
Flag : Critical study for SIDS endpoint
11.09.2001 (58)

Species : Selenastrum capricornutum (Algae)
Endpoint :
Exposure period : 72 hour(s)
Unit : mg/l
EC50 : = 76.9
EC50,48 h : = 73.4
NOEC, 96 h : < 10
Limit test :
Analytical monitoring : no
Method :
Year : 1978
GLP : no
Test substance : no data

Remark : Publication not available.
Reliability : (4) not assignable
10.09.2001 (59)

Species : Selenastrum capricornutum (Algae)
Endpoint :
Exposure period : 96 hour(s)
Unit : mg/l
EC50 : = 136
Method :
Year : 1978
GLP : no
Test substance : no data

Method : US EPA.The selenastrum capricornutum Printz Algal Assay Bottle Test.EPA 600/9-78-018 (July 1978).
Reliability : (4) not assignable
10.09.2001 (57)

Species : Skeletonema costatum (Algae)
Endpoint :
Exposure period : 96 hour(s)
Unit : mg/l
EC50 : = 6.44
Method :
Year : 1978
GLP :
Test substance : no data

10.09.2001 (57)

4.4 TOXICITY TO MICROORGANISMS E.G. BACTERIA

Type	:	aquatic
Species	:	other bacteria
Exposure period	:	
Unit	:	
Analytical monitoring	:	no data
Method	:	other
Year	:	1991
GLP	:	no data
Test substance	:	no data

Method : All tests were carried out in sealed 125 ml serum bottles (except for Microtox test) to prevent the loss of volatile chemicals.
Experimental methods allowed the partioning of the toxicants between the gas and liquid phase.For sealed serum bottles, this partitioning could be quantified using Henry's law constants and the relative volumes of gas and liquid.
The equilibrium concentration in the liquid phase was used as the EC50.

- Nitrosomonas
  Measure of activity : Ammonia use
  Bacteria : 450 mg/l
  pH : 6.5-8.0
  Atmosphere : N2/O2 = 1.6/1
  Temperature 25°C
  Vessel : 125 ml serum bottle
  Liquid volume : 50 ml
  Shaking : yes
  Data collection times : 24 h

The seed bacteria for the nitrifying enrichment culture was obtained from the mixed liquor of an activated sludge plant.

- Methanogens
  Measure of activity : Gas production
  Bacteria : 900 mg/l
  pH : 7
  Atmosphere : N2/CO2 = 2/1
  Temperature : 35°C
  Vessel : 125 ml serum bottle
  Liquid volume : 50 ml
  Shaking : no
  Data collection times : 24, 72, 96 h

Anaerobic toxicity assays were conducted using an enrichment culture.The 400 l mix reactor was operated at 35°C.It was fed acetate (50g/l) as a sole organic carbon source in a buffered inorganic nutrient solution once per day.

- Aerobic heterotrophs
  Measure of activity : Oxygen consumption
  Bacteria : 200-1800 mg/l
  pH : 7
  Atmosphere : N2/O2 = 1/1
  Temperature : 25°C and 35°C
  Vessel : 125 ml serum bottle

Liquid volume : 25 ml
Shaking : yes
Data collection times : 15, 27, 38, 49h

Seed bacteria were obtained from the mixed liquor of an activated sludge wastewater treatment plant.

- Microtox test
Measure of activity : Bioluminescence
Bacteria : 900 mg/l
pH : 6.5-7.5
Atmosphere : atmosphere
Temperature : 15°C
Vessel : open cuvettes
Liquid volume : 1 ml
Shaking : no
Data collection times : 5 minutes

The test is based on the bioluminescence of Photobacterium phosphoreum.

Remark : - Method: described in Blum and Speece, 1991.A database of chemical toxicity to environmental bacteria and its use in interspecies comparisons and correlations.J. Water Pollut. Control Fed., 63, 198-207.

Result : - Nitrosomonas sp.
EC50, 24 h = 1.43 mg/l

- Methanogens
EC50, 24 h = 4.42 mg/l

- Aerobic heterotrophs
EC50, 24 h =127.3 mg/l

- Photobacterium phosphoreum
EC50, 5 min = 5.43 mg/l

10.09.2001 (60)

Type : aquatic
Species : Photobacterium phosphoreum (Bacteria)
Exposure period : 5 minute(s)
Unit : mg/l
EC50 : = 8.6
Analytical monitoring : yes
Method : other
Year : 1982
GLP : no data
Test substance : no data

Remark : - Method: described by: Beckman Instruments, Inc.,Operating instructions Microtox toxicity analyser model 2055.Interim manual 110679.Microbics operations, Carlsbad, Calif., 1979.

10.09.2001 (61)

4.5.1 CHRONIC TOXICITY TO FISH

Species : Jordanella floridae (Fish, fresh water)
Endpoint : other
Exposure period : 10 day(s)

Unit : mg/l
NOEC : = 4.9 calculated
LOEC : = 10.6 calculated
Analytical monitoring : yes
Method : other
Year : 1991
GLP : no data
Test substance : no data

Method : The methods employed were similar to the early life stage (ELS) toxicity test developed for the fathead minnow (Benoit et al, 1982.Environ. Pollut. , 28A, 189-197).

Result : 1,1,2,2-Tetrachloroethane (mean +- sd, mg/l)

	Control	1.807 +-0.166	3.284 +-0.387	4.931 +-2.562	10.597* +-1.256	22.016 +-2.550
Hatchability %	100	97	97	97	100	100
10-day survival %	100	86	91	86	53	4

	Control	2.241 +-0.344	3.749 +-0.755	6.147 +-1.094	11.663* +-1.630	15.819 +-4.341
28-day survival%	62	76	74	60	14	0
Weight mg	29.0 +-24.6	38.3 +-36.7	30.5 +-36.7	26.3 +-20.3	79.2 +-48.9	

* P<0.01

Hatching success and survival parameters were analyzed using Lee-Desu statistic (1972) to determine which exposure level differed significantly from control. A difference was considered statitically significant when P < 0.01.

Based on this statistical analyses, the measured NOECand LOEC for reduced 10 day larval survival are 4.9mg/l and 10.6 mg/l respectively. For 28 day juvenile survival the measured NOEC and LOEC are 6.15 and 11.7 mg/lrespectively.

The estimated maximum acceptable concentration defined as the the geometric mean of the LOEC and NOEC(4.9 mg/l) was 7.2 mg/l for reduced 10 day larval survival and 8.45 for 28 day juvenile survival.

Test condition : - Dilution water : dechlorinated Lake Superior water
- Temperature : 25+-1°C

Flow-through tests were conducted with the apparatus described by Smith et al, 1977.
Five duplicate, logarithmically distributed concentrations of the test solution were used in 30 l aquaria.
Fresh solutions were added at a rate of 6 l/h.

- Aeration was not used , however, dissolved oxygen levels were measured at greater than 90% saturation.

- Water samples were analyzed 5 days per week throughout the

28-day exposure period.

- The fish were added after stable chemical concentrations were attained (48 to 72 h after dosing commenced).
- Two age groups of flagfish were used :
embryo/larval fish, with data collected on hatching and 10-day larval survival
2 week old fry with data generated on survival and growth over 28 days.

- The embryo/larval tests began with 50 fertilized eggs (25 per duplicate) at each test concentration and the two controls.Eggs were <24 h old.
After hatching, the larvae were transferred to fry retainers and held for a 10-day, post-hatch exposure period.
Observations on both egg and fish mortality were recorded daily.

- The 28-day survival and growth test commenced with 50 fry (one week old) per test level and the controls.
Duplicate exposures were used (25 fish per duplicate).Observations on mortality were recorded daily.

- The growth parameter employed was the final weight after 28 days toxicant exposure.

- Analytical methods : Solvent extraction followed by gas chromatography analysis.

Reliability : (2) valid with restrictions
10.09.2001 (62)

Species : Pimephales promelas (Fish, fresh water)
Endpoint : weight of young fish
Exposure period : 32 day(s)
Unit : mg/l
NOEC : = 1.4
LOEC : = 4
Method : other
Year : 1985
GLP : no data
Test substance : other TS: 98-99% purity

Method : Referred to :
BENOIT, D.A. et al, 1982.A fathead minnow (Pime^hales promelas) early life stage toxicity test method evaluation and exposure to four organic chemicals.J. Environ. Pollut.

Remark : An early-life -stage test (ELST) was performed with 24-hour old fathead minnow eggs (Pimephales promelas), which extended beyond the larval stage to that of young fish.

Result :

Mean conc. (mg/l)	% survival	mean individual wet weight (mg)
0.012 (control)	95	191
1.4	100	186
4.0	95	150
6.8	95	144
13.7	12.5	25
28.4	0	0

Test condition : The early life stage (ELS) fish toxicity test was performed

in a compact continuous flow mini-diluter exposure system which delivers 3 liters of test water per hour to each of 5 concentrations plus a control.
All tests were conducted with this apparatus.

- Lake Superior water was the source of dilution water.
- total hardness : 45 mg/l CaCO3
- total alkalilnity : 42 mg/l CaCO3
- pH 7.4 (mean)
- dissolved O2 : 7 (mean) mg/l

chemical methods :
The substance was analyzed by gaz chromatography with an electron capture detector.

Reliability : (1) valid without restriction
11.09.2001 (63)

Species	:	Oryzias latipes (Fish, fresh water)
Endpoint	:	
Exposure period	:	90 day(s)
Unit	:	mg/l
Analytical monitoring	:	yes
Method	:	other
Year	:	1989
GLP	:	no
Test substance	:	no data

Method : Flow through test as described by Walker et al.(1985) :

Exposure methodology

The exposure system is schematically represented in Fig. 1, and portions are photographed as Figs 2-6. To maintain consistent concentrations of these materials successfully throughout an extended test period, a stable supply of concentrated stock was necessary for subsequent addition to exposure aquaria. The toxicant reservoir consisted of three serially connected sealed 45.41 pyrex carboys (Fig. 3). Test chemicals and test water were added to each carboy, and the contents magnetically stirred. Whereas such a system should produce a stable stock concentration at or near the saturation limit intrinsic to the test compound, an equilibrium somewhat below this theoretical maximum was typically achieved. Concentrations of all test chemicals increased as the rate of withdrawal of dissolved material decreased. To initiate a test, toxicant-laden water was withdrawn from the nearest, or dispensing, carboy in the three-carboy series by precision liquid dispensing syringe pumps (PLD-II, Hamilton Company, Reno, NV, Figs 3 and 5) and delivered through microbore tubing to each of six appropriate mixing chambers (Figs 4-6). As stock solution was removed from the dispensing carboy, an equal volume of toxicant free water from the water reservoir was added to the farthest carboy in the series. Toxicant concentration in all carboys was determined periodically throughout each 28-day exposure period and additional toxicant added as needed. Toxicant-free water entered the system by gravity .,. flow from an elevated water reservoir through a solenoid

controlled valve, filling a seven-compartment water partitioner (Fig. 4) similar to that described by Schimmel et al. (1974). Float switches within the water partitioner activated a programmable laboratory controller (Idec PLE-30R, Industrial Electric Supply Co., Birmingham, AL; Fig. 5) which in turn activated the series of PLD injectors. All injectors drew from the dispensing carboy but received different instructions from the controller regarding number of injections per cycle. The flow of diluent water into the water partitioner is variable by design to provide a range of cycling times. For these evaluations, cycling time was usually 30-40 min, providing a minimum of six volume additions per 24 h in each treatment and control aquarium.. Furthermore, syringe size and distance of plunger withdrawal can be varied, thereby facilitating introduction of a wide variety of toxicant masses and hence test concentrations. Toxicant-laden and unamended water converged in a 20.5 x 10.8 x 8.5 cm mixing chamber, shown in exploded fashion in Fig. 7. To minimize volatilization through atmospheric contact, toxicant was delivered through 1 mm 1D Teflon¿ or polyethylene tubing below the surface of the 1.5 cm residual fluid level within each mixing chamber and then mixed by the turbulence of incoming diluent water. The mixing chamber emptied by a self-starting siphon into the 12.5 x 12.0 x 22.0 cm splitter box at a rate of 500 ml/cycle (±5%), which, in turn, emptied through standpipes to four 20 x 23 x 10 cm replicate exposure aquaria. Fish were contained in meshed chambers (10 cm ID petri dishes, each with a 9 cm high nylon mesh collar; Fig. 6) within treatment aquaria. Treatment aquaria filled to a depth of 8 cm, at which time toxicant-laden water discharged through self-starting siphons to a depth of 1 cm. Contaminated effluent filtered through activated carbon (Filtersorb 400, Calgon Corp., Houston, TX) before being pumped into one of two evaporative ponds. Mixing chambers, splitter boxes, and treatment aquaria, all constructed of glass and silicone cement, were housed within a 341.6 cm long by 92.7 cm wide by 53.3 cm high resin-coated plywood exposure chamber covered with a pitched top, 343 cm high along its center (Fig. 2). Ingress and egress was accomplished through capped ports, and manipulation of materials within the chamber was through eight gloved ports along each side of the chamber. Treatment aquaria were housed within a central water bath maintained at 27 ± 1 °C in a 12 :12 h light : dark regimen. The exposure chamber was maintained at a slight negative pressure by exhaust fans which also served to draw incoming air and remove gaseous toxicants through carbon filters (BPL activated carbon, 12 x 30 mesh, Calgon Corp., Houston, TX). Fish were observed periodically each day throughout the exposure period, and dead fish were removed and recorded upon discovery. Toxicant concentrations were monitored two or three times each week throughout each exposure period.

Result : Results of histopathological examination are summarized below

Exposure group	24 wk	36 wk	52 wk
Aquarium control	0/73	1/71	NE
Flow through control	1?/72	NE	NE
Low 4 TeCE	NE	NE	NE
Intermediate 8 TeCE	0/42	NE	NE

Intermediate 13 TeCE 0/75 1/74 1*/102

* indicates a cholangiocellular lesion
NE : not examined

Because significant incidences of neoplasms were not seen in the high exposure group only one control group or group exposed to lower TeCE were examined.

TeCE is not carcinogenic to the medaka

Test condition : Three hundred 6 day old fry (medaka) were utilized.

Tests specimens were alloted to the following treatment groups:

1 - Aquarium control group (situated outside the exposure system)
2 - Flow through control group(situated inside the exposure system and thus subject to low levels of volatile test compounds)
3- Low concentration exposure group (continuous 1,1,2,2-tetrachloroethane(TeCE) exposure for 90 days)
4- Intermediate concentration exposure group (intermittent TeCE exposure administered once weekly for 24 hours throughout the 90 days exposure period)
5- high concentration exposure group (intermittent TeCE exposure administered once weekly for 24 hours throughout the 90 days exposure period)

About 100 specimens from each treatment group were sampled for histopathological examination at 24, 36 and 52 weeks post initial exposure.

TeCE concentrations were measured by electron-capture gas chromatography.

Average concentrations of TeCE in treatment groups of guppy

treatment group	TeCE concentrations mg/l
Aquarium control	not detected
Flow through control	0.024 +- 0.015
Low concentration	3.970 +- 1.350
Intermediate concentration	7.760 +- 0.350
High concentration	13.93 +- 1.260

> 92% of each species of each treatment group survived to grow out.
Histopathological examination of three whole specimens from each treatment group taken at the end of the 90-day exposure did not reveal any toxicant-related pathological effects

Attached document : Walkerfig1.doc
Walkerfig2-6.doc
Walkerfig7.doc

Reliability : (2) valid with restrictions
10.09.2001 (64)

Species : Poecilia reticulata (Fish, fresh water)
Endpoint :
Exposure period : 90 day(s)

Unit	:	mg/l
Analytical monitoring	:	yes
Method	:	other
Year	:	1989
GLP	:	no
Test substance	:	no data

Method : Flow through test as described by Walker et al.(1985) :

Exposure methodology

The exposure system is schematically represented in Fig. 1, and portions are photographed as Figs 2-6. To maintain consistent concentrations of these materials successfully throughout an extended test period, a stable supply of concentrated stock was necessary for subsequent addition to exposure aquaria. The toxicant reservoir consisted of three serially connected sealed 45.41 pyrex carboys (Fig. 3). Test chemicals and test water were added to each carboy, and the contents magnetically stirred. Whereas such a system should produce a stable stock concentration at or near the saturation limit intrinsic to the test compound, an equilibrium somewhat below this theoretical maximum was typically achieved. Concentrations of all test chemicals increased as the rate of withdrawal of dissolved material decreased. To initiate a test, toxicant-laden water was withdrawn from the nearest, or dispensing, carboy in the three-carboy series by precision liquid dispensing syringe pumps (PLD-II, Hamilton Company, Reno, NV, Figs 3 and 5) and delivered through microbore tubing to each of six appropriate mixing chambers (Figs 4-6). As stock solution was removed from the dispensing carboy, an equal volume of toxicant free water from the water reservoir was added to the farthest carboy in the series. Toxicant concentration in all carboys was determined periodically throughout each 28-day exposure period and additional toxicant added as needed. Toxicant-free water entered the system by gravity .,. flow from an elevated water reservoir through a solenoid controlled valve, filling a seven-compartment water partitioner (Fig. 4) similar to that described by Schimmel et al. (1974). Float switches within the water partitioner activated a programmable laboratory controller (Idec PLE-30R, Industrial Electric Supply Co., Birmingham, AL; Fig. 5) which in turn activated the series of PLD injectors. All injectors drew from the dispensing carboy but received different instructions from the controller regarding number of injections per cycle. The flow of diluent water into the water partitioner is variable by design to provide a range of cycling times. For these evaluations, cycling time was usually 30-40 min, providing a minimum of six volume additions per 24 h in each treatment and control aquarium.. Furthermore, syringe size and distance of plunger withdrawal can be varied, thereby facilitating introduction of a wide variety of toxicant masses and hence test concentrations. Toxicant-laden and unamended water converged in a 20.5 x 10.8 x 8.5 cm mixing chamber, shown in exploded fashion in Fig. 7. To minimize volatilization through atmospheric contact, toxicant was delivered through 1 mm 1D Teflon¿ or polyethylene tubing below the surface of the 1.5 cm residual fluid level within each mixing chamber and then mixed by the

turbulence of incoming diluent water. The mixing chamber emptied by a self-starting siphon into the 12.5 x 12.0 x 22.0 cm splitter box at a rate of 500 ml/cycle (±5%), which, in turn, emptied through standpipes to four 20 x 23 x 10 cm replicate exposure aquaria. Fish were contained in meshed chambers (10 cm ID petri dishes, each with a 9 cm high nylon mesh collar; Fig. 6) within treatment aquaria. Treatment aquaria filled to a depth of 8 cm, at which time toxicant-laden water discharged through self-starting siphons to a depth of 1 cm. Contaminated effluent filtered through activated carbon (Filtersorb 400, Calgon Corp., Houston, TX) before being pumped into one of two evaporative ponds. Mixing chambers, splitter boxes, and treatment aquaria, all constructed of glass and silicone cement, were housed within a 341.6 cm long by 92.7 cm wide by 53.3 cm high resin-coated plywood exposure chamber covered with a pitched top, 343 cm high along its center (Fig. 2). Ingress and egress was accomplished through capped ports, and manipulation of materials within the chamber was through eight gloved ports along each side of the chamber. Treatment aquaria were housed within a central water bath maintained at 27 ± 1 °C in a 12 :12 h light : dark regimen. The exposure chamber was maintained at a slight negative pressure by exhaust fans which also served to draw incoming air and remove gaseous toxicants through carbon filters (BPL activated carbon, 12 x 30 mesh, Calgon Corp., Houston, TX). Fish were observed periodically each day throughout the exposure period, and dead fish were removed and recorded upon discovery. Toxicant concentrations were monitored two or three times each week throughout each exposure period.

Result **:** Results of histopathological examination are summarized below

Exposure group	24 wk	36 wk	52 wk
Aquarium control	NE	1/74	NE
Flow through control	NE	NE	NE
Low 3.4 TeCE	NE	NE	NE
Intermediate 7 TeCE	NE	NE	NE
Intermediate 13 TeCE	0/76	0/75	2/97

NE : not examined

Because significant incidences of neoplasms were not seen in the high exposure group only one control group or group exposed to lower TeCE were examined.

TeCE is not carcinogenic to the guppies.

Test condition **:** Three hundred 2 day old fry (guppy) were used for individuel treatments except for the aquarium control group which received only 260 guppies .

Tests specimens were alloted to the following treatment groups:

1 - Aquarium control group (situated outside the exposure system)
2 - Flow through control group(situated inside the exposure system and thus subject to low levels of volatile test compounds)
3- Low concentration exposure group (continuous

1,1,2,2-tetrachloroethane(TeCE) exposure for 90 days)
4- Intermediate concentration exposure group (intermittent TeCE exposure administered once weekly for 24 hours throughout the 90 days exposure period)
5- high concentration exposure group (intermittent TeCE exposure administered once weekly for 24 hours throughout the 90 days exposure period)

About 100 specimens from each treatment group were sampled for histopathological examination at 24, 36 and 52 weeks post initial exposure.

TeCE concentrations were measured by electron-capture gas chromatography.

Average concentrations of TeCE in treatment groups of guppy

treatment group	TeCE concentrations mg/l
Aquarium control	not detected
Flow through control	0.030 +- 0.017
Low concentration	3.450 +- 1.090
Intermediate concentration	6.930 +- 0.450
High concentration	12.780 +- 1.30

> 92% of each species of each treatment group survived to grow up.
Histopathological examination of three whole specimens from each treatment group taken at the end of the 90-day exposure did not reveal any toxicant-related pathological effects

Attached document : Walkerfig1.doc
Walkerfig2-6.doc
Walkerfig7.doc

Reliability : (2) valid with restrictions
10.09.2001 (64)

4.5.2 CHRONIC TOXICITY TO AQUATIC INVERTEBRATES

Species : Daphnia magna (Crustacea)
Endpoint : reproduction rate
Exposure period : 28 day(s)
Unit : mg/l
NOEC : = 6.9
LCEC : = 14
Analytical monitoring : yes
Method : other
Year : 1983
GLP : no data
Test substance : other TS: Aldrich Chemical Co, purity from 95 to 99%

Remark : - Method: ASTM
COMOTTO, R.: ASTM (American Society for Testing and Materials) proposed standars practice for conducting renewal life cycle toxicity tests with the daphnid Daphnia magna.Draft N°4, Philadelphia, PA: American Society for Testing and Materials, 1978.

Result :
Results

chemical concentration mg/l	Number of young produced
0.0 (controls)	162 +- 49
0.42 +- 0.036	84 +- 50
0.86 +- 0.085	69 +- 39
1.7 +- 0.17	71 +- 40
3.4 +- 0.39	78 +- 37
6.9* +- 0.9	78 +- 18
14** +- 1.4	23 +- 5

* NOEC based on reproduction (P<=0.01)
**LOEC Based on reproduction (significantly different from controls, P<= 0.05)
No data on length of adult

Test condition : Test containers : 200ml erlenmeyer flasks filled to 160 ml. Each of 7-10 replicate flasks at six test concentrations (geometric series with a 0.5 dilution factor) contained 1 daphnid.
Flasks stoppered with foil wrapped neoprene stoppers
Toxicant and food solutions were renewed 3 times each week
Young daphnids were filtered fromeach flask after transfer of the adults, washed onto a watch glass and counted alive with an Artec counter.
Chronic toxicity was determined by reproductive success of animals surviving the 28 day test.

Lake superior water
hardness of water 44.7 ($CaCO_3$)
alkalinity : 41.5 ($CaCO_3$)
dissolved O_2: from 5.4 to 8.9
pH : 6.6 to 7.9

Reliability : (1) valid without restriction
11.09.2001 (54)

4.6.1 TOXICITY TO SEDIMENT DWELLING ORGANISMS

4.6.2 TOXICITY TO TERRESTRIAL PLANTS

Remark : Investigations were carried out more than 30 years ago on the effects on terrestrial plants, when 1,1,2,2-tetrachloroethane, a known insect-control fumigant, was also under consideration as a plant pesticide for fruit orchards.Studies by Gast and Early on various experimental plants (cotton, cucumbers, tomatoes, maize, beans) showed that a concentration of 0.5 % compound, applied to moist soil, had no adverse effect, except in beans, which exhibited "slight damage".Ten times that amount caused weak to moderate plant damage.The authors did not provide details on the toxic effect.

12.09.2001 (65)

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	:	mg/cm² filter paper
LC50	:	= 14
Method	:	OECD Guide-line 207 "Earthworm, Acute Toxcity Test"
Year	:	
GLP	:	no data
Test substance	:	other TS
Test condition	:	Contact test : The glass vials were completely covered with filter paper. Soluble organic chemical was applied on moist filter paper using distilled water as the solvent. One adult earthworm (300-500 mg) was added per vial and the vials were kept at 20°C in a darkened incubator for 48 h. After 48 h, mortality was determined. At least five concentrations were evaluated in the definitive test, with 10 or more replicates used for each concentration tested.Controls containing no test chemical were present in each series of experiments. The LC50 value was calculated using the method of Litchfield and Wilcoxom (1949). The LC50 values are reported as µ of test chemical per square centimeter of filter paper.
Test substance	:	From Aldrich or Eastman or Fisher Scientific Co. Chemical selected was at least 98% purity.
Reliability	:	(2) valid with restrictions

10.09.2001 (66)

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	:	= 800 mg/kg bw
Species	:	rat
Strain	:	no data
Sex	:	no data
Number of animals	:	
Vehicle	:	no data
Doses	:	no data
Method	:	other: not specified
Year	:	1982
GLP	:	no data
Test substance	:	as prescribed by 1.1 - 1.4
Remark	:	Data from handbook : No informations on symptoms . No information on number of animals used in the study.
Source	:	ATOFINA Paris la Defense EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Reliability	:	(2) valid with restrictions data from handbook or collection data (german BUA collection)
Flag	:	Critical study for SIDS endpoint

26.10.2001 (67)

Type	:	LD50
Value	:	= 250 - 430 mg/kg bw
Species	:	rat
Strain	:	other: Carworth-Wistar
Sex	:	male/female
Number of animals	:	5
Vehicle	:	other: corn oil
Doses	:	no data
Method	:	other: not specified
Year	:	1969
GLP	:	no data
Test substance	:	as prescribed by 1.1 - 1.4
Remark	:	No information on symptoms . No information on findings following the 15d observation period.
Source	:	ATOFINA Paris la Defense EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Reliability	:	(2) valid with restrictions Test procedure in accordance with national standard methods with acceptable restrictions
Flag	:	Critical study for SIDS endpoint

26.10.2001 (68)

Type	:	LD50
Value	:	= 570 mg/kg bw
Species	:	rat
Strain	:	no data
Sex	:	no data
Number of animals	:	
Vehicle	:	no data

Doses	:	no data
Method	:	other: not specified
Year	:	1972
GLP	:	no data
Test substance	:	as prescribed by 1.1 - 1.4
Remark	:	Data from handbook : No informations on symptoms . No information on number of animals used in the study.
Source	:	ATOFINA Paris La Defense, France
Reliability	:	(2) valid with restrictions data from handbook or collection data (german BUA collection)
Flag	:	Critical study for SIDS endpoint

26.10.2001 (69)

Type	:	LD50
Value	:	= 250 mg/kg bw
Species	:	rat
Strain	:	other: albino rats, strain not specified
Sex	:	no data
Number of animals	:	10
Vehicle	:	peanut oil
Doses	:	no data
Method	:	other: not specified
Year	:	1977
GLP	:	no data
Test substance	:	as prescribed by 1.1 - 1.4
Remark	:	No data were presented on acute toxicity results. Basis for the selection of 250 mg/kg called "LD50" were not presented. No reference was given for the origin of the 250 mg/kg value. In the study only the single dose of 250 mg/kg was used. No information on symptoms was presented
Source	:	ATOFINA Paris la Defense EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Reliability	:	(3) invalid significant methodological deficiencies
Flag	:	Critical study for SIDS endpoint

26.10.2001 (70)

Type	:	LDLo
Value	:	= 479 mg/kg bw
Species	:	dog
Strain	:	no data
Sex	:	no data
Number of animals	:	
Vehicle	:	no data
Doses	:	no data
Method	:	other: not specified
Year	:	1932
GLP	:	no
Test substance	:	as prescribed by 1.1 - 1.4
Remark	:	Data from handbook. No details available on the original study which was published in year1932 except the following : Liver toxicity; behavioral depressing effects.
Source	:	ATOFINA Paris la Defense, France EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Reliability	:	(2) valid with restrictions data from handbook or collection data (german BUA collection)

26.10.2001 (71)

5.1.2 ACUTE INHALATION TOXICITY

Type	:	LC50
Value	:	= 8.6 mg/l
Species	:	rat
Strain	:	no data
Sex	:	no data
Number of animals	:	
Vehicle	:	other: air
Doses	:	no data
Exposure time	:	4 hour(s)
Method	:	other: not specified
Year	:	1980
GLP	:	no data
Test substance	:	as prescribed by 1.1 - 1.4
Remark	:	Threshold for hepatotoxic effects was between 4 and 7 mg/l 8,6 mg/l = 1200 ppm
Source	:	ATOFINA Paris la Defense, France EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Reliability	:	(2) valid with restrictions data from handbook
Flag	:	Critical study for SIDS endpoint

26.10.2001 (72)

Type	:	other: single test concentration
Value	:	= 6.86 mg/l
Species	:	rat
Strain	:	Sherman
Sex	:	male/female
Number of animals	:	6
Vehicle	:	other: air
Doses	:	no data
Exposure time	:	4 hour(s)
Method	:	other: not specified
Year	:	1969
GLP	:	no
Test substance	:	as prescribed by 1.1 - 1.4
Remark	:	Single tested concentration : 1000 ppm (6,8 mg/l) exposure for 4 h incuced 3/6 death in a group of 6 rats Type: Acute Lethal Toxicity No information on symptoms
Source	:	ATOFINA Paris la Defense, France EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Test substance	:	Groups of 6 male or female albino rats were exposed for 4 hours in a 120 liter sealed chamber in a static technique to nominal concentrations not analytically verified. Exposure to the vapor was followed by a 41-day observation period. Mortality was recorded.
Reliability	:	(2) valid with restrictions study well documented, meets generally accepted scientific principles, acceptable for assessment

26.10.2001 (68)

Type	:	LC50
Value	:	= 4.5 mg/l

Species	:	mouse
Strain	:	no data
Sex	:	no data
Number of animals	:	
Vehicle	:	other: air
Doses	:	no data
Exposure time	:	8 hour(s)
Method	:	other: not specified
Year	:	1966
GLP	:	no data
Test substance	:	as prescribed by 1.1 - 1.4
Remark	:	No information on symptoms 4.5 mg/l is equivalent to 640 ppm
Source	:	ATOFINA Paris la Defense, France EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Reliability	:	(2) valid with restrictions data from handbook or collection data (german BUA collection)

26.10.2001 (73)

Type	:	other: single test concentration
Value	:	= 5900 - 6600 ppm
Species	:	mouse
Strain	:	no data
Sex	:	male
Number of animals	:	10
Vehicle	:	other: air
Doses	:	
Exposure time	:	3 hour(s)
Method	:	other
Year	:	1962
GLP	:	no data
Test substance	:	as prescribed by 1.1 - 1.4
Remark	:	Single concentration tested in a single exposure experiment. The study was repeated twice. The study was not designed for acute toxicity level determination.
Result	:	Mortality : at the end of the observation period (one week after the 3-h exposure), mortality was 4/10 for the 6600 ppm (45.3 mg/l) exposure and 3/10 for the 5900 ppm exposure (40.5 mg/l) Mortality occurred 2 to 7 days post-exposure. Irritation of mucous membranes and central nervous system depressing effects were reported. The microscopic examinations revealed slight to moderate congestion and fatty degeneration of the liver, and congestion of the other main organs (not specified).
Source	:	ATOFINA Paris la Defense,France EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Reliability	:	(2) valid with restrictions study well documented, meets generally accepted scientific principles, acceptable for assessment

26.10.2001 (74)

Type	:	LCLo
Value	:	= 19 mg/l
Species	:	cat
Strain	:	no data
Sex	:	no data
Number of animals	:	
Vehicle	:	other: air

Doses	:	no data
Exposure time	:	45 minute(s)
Method	:	other: not specified
Year	:	1936
GLP	:	no
Test substance	:	as prescribed by 1.1 - 1.4
Remark	:	Depressing effects on central nervous system, lacrimation, salivation.
Source	:	ATOFINA Paris la Defense, France EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Reliability	:	(4) not assignable data from secondary source

26.10.2001 (75)

5.1.3 ACUTE DERMAL TOXICITY

Type	:	LD50
Value	:	= 3990 mg/kg bw
Species	:	rabbit
Strain	:	no data
Sex	:	no data
Number of animals	:	10
Vehicle	:	no data
Doses	:	no data
Method	:	other (calculated)
Year	:	1979
GLP	:	no data
Test substance	:	as prescribed by 1.1 - 1.4
Source	:	ATOFINA Paris la Defense,France EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Test condition	:	Ten rabbits per group were used. Neat substace was applicated to the clipped skin of the trunk and maintained on contact with skin during 24 hours under an impervious bangage.
Reliability	:	(2) valid with restrictions study well documented, meets generally accepted scientific principles, acceptable for assessment
Flag	:	Critical study for SIDS endpoint

26.10.2001 (76)

Type	:	LD50
Value	:	= 4900 - 8200 mg/kg bw
Species	:	rabbit
Strain	:	New Zealand white
Sex	:	male
Number of animals	:	4
Vehicle	:	no data
Doses	:	
Method	:	other: not specified
Year	:	1969
GLP	:	no
Test substance	:	as prescribed by 1.1 - 1.4
Remark	:	No information on symptoms
Result	:	LD50 reported as 3.99 (3.10-5.13) ml/kg. With a density of the liquid of 1.6, these value are equivalent to 6.4 (4.9-8.2) respectively.

Source	:	ATOFINA Paris la Defense, France EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Test condition	:	The test material was maintained during 24 hours on the clipped skin of the trunk under an imprevious plastic film. Rabbits were maintained immobilized during the 24h-contact period, afeter which the animals were caged for the subsequent 14-day observation period. Four animals per group were used.
Reliability	:	(2) valid with restrictions Test procedure in accordance with national standard methods with acceptable restrictions
Flag	:	Critical study for SIDS endpoint

26.10.2001 (68)

5.1.4 ACUTE TOXICITY, OTHER ROUTES

Type	:	LC50
Value	:	= 821 mg/kg bw
Species	:	mouse
Strain	:	no data
Sex	:	no data
Number of animals	:	
Vehicle	:	no data
Doses	:	no data
Route of admin.	:	i.p.
Exposure time	:	
Method	:	no data
Year	:	1959
GLP	:	no data
Test substance	:	
Source	:	ATOFINA Paris la Defense, France EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Reliability	:	(4) not assignable data from secondary source

26.10.2001 (77)

Type	:	LC50
Value	:	= 1108 mg/kg bw
Species	:	mouse
Strain	:	
Sex	:	
Number of animals	:	
Vehicle	:	
Doses	:	
Route of admin.	:	s.c.
Exposure time	:	
Method	:	other: not specified
Year	:	1958
GLP	:	no
Test substance	:	as prescribed by 1.1 - 1.4
Remark	:	Depressing effect on central nervous system.
Source	:	ATOFINA Paris la Defense,France EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Reliability	:	(4) not assignable data from secondary source

26.10.2001 (78)

5.2.1 SKIN IRRITATION

Species	:	rabbit
Concentration	:	undiluted
Exposure	:	Open
Exposure time	:	24 hour(s)
Number of animals	:	5
Vehicle	:	
PDII	:	
Result	:	highly irritating
Classification	:	irritating
Method	:	other: not specified
Year	:	1969
GLP	:	no
Test substance	:	as prescribed by 1.1 - 1.4
Remark	:	Result: highly irritating (6/8) 0.01 ml of neat materail applicated on intact skin.
Source	:	ATOFINA Paris la Defense,France EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Reliability	:	(2) valid with restrictions study well documented, meets generally accepted scientific principles, acceptable for assessment
Flag	:	Critical study for SIDS endpoint

21.06.2001 (68)

5.2.2 EYE IRRITATION

Species	:	rabbit
Concentration	:	undiluted
Dose	:	.1 ml
Exposure time	:	
Comment	:	not rinsed
Number of animals	:	6
Vehicle	:	
Result	:	irritating
Classification	:	irritating
Method	:	other
Year	:	1974
GLP	:	no
Test substance	:	as prescribed by 1.1 - 1.4
Remark	:	Result: irritating (42.5/110) Method: FDA, 1965 0.1 ml of neat material applicated on the eye of 6 rabbits.
Source	:	ATOFINA Paris la Defense, France EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Reliability	:	(2) valid with restrictions study well documented, meets generally accepted scientific principles, acceptable for assessment
Flag	:	Critical study for SIDS endpoint

21.06.2001 (79)

5.3 SENSITIZATION

Type	:	no data

Species :

10.05.2001

5.4 REPEATED DOSE TOXICITY

Type	:	
Species	:	rat
Sex	:	male
Strain	:	Fischer 344
Route of admin.	:	gavage
Exposure period	:	3 weeks
Frequency of treatm.	:	daily
Post exposure period	:	none
Doses	:	104 and 208 mg/kg BW
Control group	:	yes
NOAEL	:	< 104 mg/kg bw
LOAEL	:	<= 104 mg/kg bw
Method	:	other
Year	:	1996
GLP	:	yes
Test substance	:	as prescribed by 1.1 - 1.4

Method : Mechanistic study with the aim of establishing if the capacity of test material to induce hyaline droplet nephropathy in mature male rats is a determining factor in the induction of renal tubul cell neoplasms.

Result : LOAEL <0.62 mmol/kg (104 mg/kg) (liver lesions)

TOXIC RESPONSE/EFFECTS BY DOSE LEVEL :

- Mortality : all rats receiving 1.24 mmol/kg (208 mg/kg) died or were killed moribund before the end of the study.
- clinical signs : rats of the 1.24 mmol/kg group were thin and lethargic ; they presented diarrhea, abnormal breathing and ruffled fur.
- Bodyweight gain : animals receiving 0.62 mmol/kg has no growth difference versus control animals.
- Urinalysis : there were no statistically significant difference in all parameters between rats receiving 0.62 mmol/kg and controls.
- Organ weight : the absolute and relative liver weight of rats receiving 0.62 mmol/kg were greater than those of the controls.
- Histopathology : No change in the kidney were attributable to the test material in animals receiving 0.62 mmol/kg including amount, size and shape of tubule hyaline droplets and PCNA labeling index of cortical tubules.

In the liver, cytoplasmic vacuolisation of hepatocytes occurred in all rats receiving 0.62 mmol/kg. The change was mild to moderate and consisted in multifocal areas of hepatocytes with clear droplets within the cytoplasm.

Source : ATOFINA Paris la Defense,France
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)

Test condition : TEST ORGANISM :
- Age : 15 weeks
- Number of animals : 5 male/group

ADMINISTRATION/EXPOSURE :

- Vehicle : corn oil
- Doses : 0.62 mmol/kg (102 mg/kg) and 1.24 mmol/kg (208 mg/kg)

CLINICAL OBSERVATIONS AND FREQUENCY :
- Clinical signs : yes, twice daily
- Mortality : yes, twice daily
- Bodyweight gain : yes, weekly
- Haematology, biochemistry : no
- Urinalysis : yes , urines of all animals collected overnight, 4 days before the end of the gavage period ; parameters examined were creatinine, glucose, tota prrotein, aspartate aminotransferase, gammaglutamyltranspeptidase, N-acetyl beta-D-glucosaminidase, volume, specific gravity.
- Organ weights : right kidney, liver, right testis of all rats at the end of the study
- Histology : right kidney, left lobe of the liver and gross lesions were examined on all animals.
- Other : cell proliferation analyses on kidney sections of all rats (S-phase analysis after proliferating cell nuclear antigen staining ; 4000 cells/per animal scored)

STATISTICS :
- Continuous variables : Dunnet test, Dunn test, Jonkheere test
- Proliferating cells : Standard Student t Test

Reliability : (2) valid with restrictions
study well documented, meets generally accepted scientific principles, acceptable for assessment

Flag : Critical study for SIDS endpoint

26.10.2001 (80)

Type	:	
Species	:	rat
Sex	:	male/female
Strain	:	Osborne-Mendel
Route of admin.	:	gavage
Exposure period	:	78 weeks
Frequency of treatm.	:	once daily 5d/wk
Post exposure period	:	32 wks
Doses	:	time-weighted average doses: 62 and 108 mg/kg/day (males); 43 and 76 mg/kg/day (females)
Control group	:	yes
NOAEL	:	< 43 - 62 mg/kg bw
LOAEL	:	<= 43 - 62 mg/kg bw
Method	:	other
Year	:	1978
GLP	:	no data
Test substance	:	as prescribed by 1.1 - 1.4

Remark : Limitations of the study : significance of bodyweight decrease not given; No hemathological and biochemical investigations ; histopathology at the end of observation period only.

Result : NOAEL : < 62 mg/kg/d (males) and < 43 mg/kg/d (females

TOXIC RESPONSE/EFFECTS BY DOSE LEVELS :
- Mortality-Time to death : increase mortality at higher dose ; survival at 105 weeks : 50% of high and low dosed males; 40% and 58% of high and low dose females

respectively.
- Clinical signs : no data
- Bodyweight gain : reversible dose-related decrease with both dose treatment
- Histopathology : No increase of incidence of non-neoplastic lesions in any of the examined organs and tissues at any dose.

Source : ATOFINA Paris la Defense,France
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)

Test condition : TEST ORGANISM :
- Age : 7 weeks
- Number of animals :2 groups of 50 males and 50 females; control groups : 40 males and 40 females

ADMINISTRATION/EXPOSURE :
- Doses : High dose animals received 100 mg/kg/d ; in males this was increased after 14 weeks to 130 mg/kg/d for 18 weeks followed by 9 cycles of 4weeks at this dose and 1 week treatment three for 45 weeks (total 78 weeks) ; in females, the dose was reduced after 25 weeks to 80 mg/kg/d for 7 weeks followed by the cyclic treatment at this dose for 45 weeks.
Low dose males received 50 mg/kg/d for 14 weeks and 65 mg/kg/d for 64 weeks ; females received 50 mg/kg/d for 25 weeks and 40 mg/kg/d for 53 weeks.
Half of the control groups received corn oil (match controls) ; the second half was not treated (untreated controls)

CLINICAL OBSERVATIONS and FREQUENCY:
- Clinical signs : yes
- Mortality : yes
- Bodyweight : yes
- Food and water consumption : not specified
- Biochemistry : no
- Urinalysis : no

ORGANS EXAMINED ATNECRPSY
- Macroscopic and Microscopic : all main organs and tissues

STATISTICAL METHOD

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

Flag : Critical study for SIDS endpoint

08.06.2001 (81)

Type	:	
Species	:	rat
Sex	:	male
Strain	:	other: albino rats, strain not specified
Route of admin.	:	gavage
Exposure period	:	6 to 27 weeks
Frequency of treatm.	:	no data
Post exposure period	:	2 weeks
Doses	:	3.2 , 8.0 and 20 mg/kg
Control group	:	yes
LOAEL	:	= 3.2 mg/kg bw
Method	:	other
Year	:	1977
GLP	:	no data

Test substance : as prescribed by 1.1 - 1.4

Remark : Limited validity study due to lack of reporting on important parameters (bodyweight, mortality, haematology...)

Result : NOAEL < 3.2 mg/kg
LOAEL = 3.2 mg/kg (27 week exposure)

- Mortality : no data
- Clinical signs : none described
- Bodyweight gain : no data
- Haemathology : no data
- Clininical biochemistry : increase of LDH and decrease of esterase activities were linked with the damage seen in the organes
- Organ weights : No data
- Histopathology :
  - At the highest doses there were damages in liver, kidney, testes and thyroid gland. These damages were not reversile in the testes and thyroid after the 2-week reversibility period in high dose groups. No damage were found in the trachea.
  - At 3.2 mg/kg there were only minor hepatic and renal effects

Source : ATOFINA Paris la Defense,France
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)

Test condition : TEST ORGANISM :
- Age : no data
- Weight at study initiation : 230-280 g
- Number of animals : 10 males/group

ADMINISTRATION/EXPOSURE :
- Vehicle : peanut oil
- Dose : 8 and 20 mg/kg (6 wk exposure) ; 3.2 and 8 mg/kg (27 wk exposure)
- Frequency of gavage not specified

CLINICAL OBSERVATIONS AND FREQUENCY :
- Clinical signs : no data
- Mortality : no data
- Bodyweight gain : no data
- Haematology: no data
- Biochemistry : SDH, LDH, G6-PDH, G6-P, AlP, unspecified esterase, Lison.
- Urinalysis : no data
- Organ weights : no data
- Histology: liver, kidney, thyroide, testes, adrenals.

STATISTICS :
- Wilcoxon rank test
- Standard Student t Test

Reliability : (3) invalid
significant methodological deficiencies

26.10.2001 (70)

Type :
Species : mouse
Sex : male/female
Strain : B6C3F1
Route of admin. : gavage
Exposure period : 78 wks

Frequency of treatm.	:	5d/wk
Post exposure period	:	12 wks
Doses	:	time-weighted average doses: 142 and 284 mg/kg/day
Control group	:	yes
NOAEL	:	< 142 mg/kg bw
LOAEL	:	< 142 mg/kg bw
Method	:	other
Year	:	1978
GLP	:	no data
Test substance	:	as prescribed by 1.1 - 1.4
Remark	:	Limitations of the study : significance of bodyweight decrease not given; No hemathological and biochemical investigations ; histopathology at the end of observation period only.
Result	:	NOAEL : < 142 mg/kg/d (males and females) TOXIC RESPONSE/EFFECTS BY DOSE LEVELS : - Mortality-Time to death : dose related increased mortality - Clinical signs : no data - Bodyweight gain : slight dose related decrease - Histopathology : No increase of incidence of non-neoplastic lesions in any of the organs and tissues examined at any dose
Source	:	ATOFINA Paris la Defense,France EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Test condition	:	TEST ORGANISM : - Age : 5 weeks - Number of animals :2 groups of 50 males and 50 females; control groups : 40 males and 40 females ADMINISTRATION/EXPOSURE : - Doses : Initially high dose and low dose animals received 200 mg/kg/d and 100 mg/kg/d respectively; thes dose were increased after 18 weeks to 300 mg/kg/d and 150 mg/kg respectively during 3 weeks. Tehse dose were further increased to 400 and 200 mg/kg during 5 weeks but returned to 300 and 150 mg/kg/d respectively during the following 52 weks (total 78 weeks). Half of the control groups received corn oil (match controls) ; the second half was not treated (untreated controls) CLINICAL OBSERVATIONS and FREQUENCY: - Clinical signs : yes - Mortality : yes - Bodyweight : yes - Food and water consumption : not specified - Biochemistry : no - Urinalysis : no ORGANS EXAMINED ATNECRPSY - Macroscopic and Microscopic : all main organs and tissues STATISTICAL METHOD
Reliability	:	(2) valid with restrictions Test procedure in accordance with national standard methods with acceptable restrictions
Flag	:	Critical study for SIDS endpoint

08.06.2001 (81)

Type	:	
Species	:	rat
Sex	:	male
Strain	:	Wistar
Route of admin.	:	inhalation
Exposure period	:	13 weeks (57 exposures)
Frequency of treatm.	:	5 h/day; 5 d/week
Post exposure period	:	none
Doses	:	single dose varying between 108 and 516 ppm
Control group	:	yes
NOAEL	:	< 516 ppm
LOAEL	:	< 516 ppm
Method	:	other: not specified
Year	:	1983
GLP	:	no data
Test substance	:	as prescribed by 1.1 - 1.4
Remark	:	Rats of Wistar and Brown Norway strains were used
Result	:	NOAEL : < 108-516 ppm (single fluctuating tested dose) Toxic response/effect : - Mortality : not specified - Clinical signs : not specified - Bodyweight gain : decreased versus control for both strains (230g versus 371g in controls and 157g versus 309g in controls, respectively for Wistar and Brown Norway) - Biochemistry : no effect on ASAT, ALAT and creatinine at any time for both strains - Urinalysis : proteinuria was lower in exposed rats of both strains versus their respective controls at the same age ($p<0.001$) : 13 versus 43 mg/24h in controls and 1.76 versus 14.87 in controls for Wistar and Bown Norway respectively. - Histopathology : Kidneys shown only minimal glumerulotoxicity in both species and only when using electronic microscopy.
Source	:	ATOFINA Paris la Defense,France EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Test condition	:	Test organism : - Strains : Wistar and Brown Norway - Age : 6 weeks - Weight at study initiation : 100-120 g - Number of animals : control groups : 10-14 males; exposed groups : 20-21 males. Administration/Exposure : - Type of exposure : Animals were exposed whole body by inhalation in 2 m3 chambers with atmospheric renewal of 2m3/hour. - Doses : each daily exposure comprised 3 periods. During the first 30 minutes, the concentration of the test material vapours increased in the chamber from zero to 466 ppm. Then, during 2h30 the concentrations fluctuated between 466 and 516 ppm. Finally the concentration decreased during 2 h progressively down to 108 ppm when the animals were removed from the chambers. So the total duration of exposure is 5 h. All concentrations were measured through a pecific analytical device. Interim sacrifice after 18, 37 and 57 exposures Clinical observations :

- Clinical signs : not specified
- Mortality : not specified
- Bodyweight : yes , followed all along the 13 week exposure
- Food and water consumption : not specified
- Biochemistry : creatinine, ASAT, ALAT
- Urinalysis : proteines

Organs examined at necropsy
- Microscopic : kidney (optical, immunofluorescence and electronic microscopy)

Statistical method : Student T test

Reliability : (2) valid with restrictions
study well documented, meets generally accepted scientific principles, acceptable for assessment

Flag : Critical study for SIDS endpoint

21.06.2001 (82)

Type	:	
Species	:	rat
Sex	:	female
Strain	:	Sprague-Dawley
Route of admin.	:	inhalation
Exposure period	:	15 weeks (78 exposures)
Frequency of treatm.	:	5-6 h/day; 5 d/week
Post exposure period	:	none
Doses	:	560 ppm
Control group	:	yes
NOAEL	:	< 560 ppm
LOAEL	:	< 560 ppm
Method	:	other: not specified
Year	:	1977
GLP	:	no data
Test substance	:	as prescribed by 1.1 - 1.4

Remark : Sub-groups sacrified after 2, 4, 9, 39 and exposures.

Result : NOAEL of 1,1,2,2-tetrachlororethane: < 560 ppm (single tested dose)

TOXIC RESPONSE/EFFECT with 1,1,2,2-tetrachlororethane:
- Mortality : not specified
- Clinical signs : transient CNS depressing effects during first exposures.
- Bodyweight gain : decreased during the last weeks of exposure
- Haemathology : slight decrease of hematocrit, red and white cells
- Organ weights : increased liver weight in each interim and final sacrifice
- Histopathology : Liver hyperplasia and hepatocellular histological lesions seen during the first weeks regressed after 19 exposure and disappeared after 39 exposures. All other organs examined appeared normal.
- Other examinations : increased DNA biosynthesis appeared after 4 exposures (313% versus controls). That effect disappeared when measured during the following weeks.

Source : ATOFINA Paris la Defense,France
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)

Test condition : Test organism :
- Age : adult

- Weight at study initiation : not stated
- Number of animals : 165 female Sprague Dawley rats were divided into one control group and 2 treated group.

Administration/Exposure :
- Type of exposure : Animals were exposed whole body by inhalation in chambers with atmospheric renewal of 2m3/hour.
- Doses : One of the two treatment groups was exposed to vapours of 1,1,2,2-tetrachloroethane at nominal concentration of 560 ppm. An unexposed group served as control. Some animals (unspecified number) were sacrificed after 2, 4, 9, 19, 39 and 63 exposures.

Clinical observations :
- Clinical signs : yes
- Mortality : yes
- Bodyweight : yes , followed all along the 15 week exposure
- Food and water consumption : not specified
- Haematology : yes, blood cytology followed
- Urinalysis : not specified

Organs examined at necropsy
- Macroscopic and microscopic : liver, kidney, adrenals, ovaries, uterus.

Other examinations :
- Hepatic DNA neosynthesis was determined 4 h after injection of 3H Thymidine.

Statistical method : not specified

Reliability : (2) valid with restrictions
study well documented, meets generally accepted scientific principles, acceptable for assessment

Flag : Critical study for SIDS endpoint

26.10.2001 (83)

Type	:	
Species	:	rat
Sex	:	no data
Strain	:	no data
Route of admin.	:	inhalation
Exposure period	:	26 days
Frequency of treatm.	:	4 h/day and 5 x 15 minutes during 4 h/day
Post exposure period	:	none
Doses	:	7 ppm (continuous exposure); 19 ppm (fluctuating exposure)
Control group	:	no data specified
NOAEL	:	< 7 ppm
LOAEL	:	< 7 ppm
Method	:	other: not specified
Year	:	1977
GLP	:	no data
Test substance	:	as prescribed by 1.1 - 1.4

Result : Increased excitability, decreased urinary protein level.
Changes persistant along the 26 days (no adaptation).

Source : ATOFINA Paris la Defense,France
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)

Reliability : (4) not assignable
abstract

08.06.2001 (84)

Type	:	
Species	:	rat
Sex	:	male
Strain	:	no data
Route of admin.	:	inhalation
Exposure period	:	9 months
Frequency of treatm.	:	4h/day, 5d/week
Post exposure period	:	none
Doses	:	single dose : 13.3 mg/m3 (1.94 ppm)
Control group	:	yes
NOAEL	:	< 13.3 mg/m³
LOAEL	:	<= 13.3 mg/m³
Method	:	other
Year	:	1972
GLP	:	no data
Test substance	:	as prescribed by 1.1 - 1.4
Remark	:	Limitations of the sudy : single dose testing ; generally poor description of effects.
Result	:	NOAEL < 13.3 mg/m3 LOAEL =or< 13.3 mg/m3 (as findings may be considered minimal at this single tested concentration) - Mortality : no significant difference between treated and control animals. - Clinical signs : none described - Bodyweight gain : At the end of 110 days, the exposed rats weighed significantly less than control (415 versus 435 g) but the difference was no longer present after 265 days due to wide individual variations). - Hematology : leucocytes were 90% higher than the controls after 110 days. No data on WBC were mentioned thereafter. - Clininical biochemistry : serum globuline were increased after 110 days and at the end of the study in treated rats; fat content of the liver was increased in treated animals after 265 days (34%); the ACTH activity in hypophyse was decreased at interim and final sacrifices (65 % to 13 %). - Organ weights : decrease relative weight of thyroide - Histopathology : mild liver changes, no testicular changes after more than 10 days exposure; follicular desquamation in thyroid ; no changes in other organs.
Source	:	ATOFINA Paris la Defense,France EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Test condition	:	TEST ORGANISM : - Age : 60 days - Weight at study initiation : 210-270 g - Number of animals : 210 males equally divided in one exposed and one control group ADMINISTRATION/EXPOSURE : - Vehicle : air - Dose : single dose tested : 13.3 +/- 0.24 mg/m3 (1.94 ppm) - Whole body exposure in 200 l chambers; dynamic flow (5000 l/h) - Interim sacrifices of 7 animals/group after 110 and 265 days of exposure CLINICAL OBSERVATIONS AND FREQUENCY : - Clinical signs : yes

- Mortality : yes,
- Bodyweight gain : yes
- Haematology: blood formula, white blood cells count.
- Biochemistry : SGOT, SGPT, BSP excretion, serum albumine, serum globuline, total fat in the liver and kidney, ACTH actibity of pituitary gland. Also SHD, alc Phosphatase and unspecified Esterases.
- Urinalysis : no
- Organ weights : hypophyse, brain, thyroide, thymus, lung, heart, liver, spleen, kidney, adrenals and testes of all rats at the end of the study
- Histology : liver, kidney, thyroide, lungs, spleen, adrenals, brain, testes of all rats

STATISTICS :
- Standard Student t Test

Reliability : (3) invalid
significant methodological deficiencies

Flag : Critical study for SIDS endpoint

29.10.2001 (85)

Type	:	
Species	:	rat
Sex	:	male
Strain	:	no data
Route of admin.	:	inhalation
Exposure period	:	4 weeks
Frequency of treatm.	:	2h/d , 2d/wk
Post exposure period	:	no
Doses	:	9000 ppm (16.8 mg/l)
Control group	:	yes
NOAEL	:	< 9000 ppm
LOAEL	:	< 9000 ppm
Method	:	other
Year	:	1962
GLP	:	no data
Test substance	:	as prescribed by 1.1 - 1.4

Result :
- Mortality : all animals survived.
- Clinical signs : hypermotility followed by CNS depression including almost complete loss of consciousness 1-1.5 hours after the 2-hour exposure.
- Bodyweight gain : no marked difference between exposed and control animals.
- Haemathology : tendency to decreased hemoglobin and red bood cell counts.
- Histopathology : congestion and fatty degeneration of the liver.Changes in the liver were qualified as "not severe" by the authors. Congestion of other main organs (no details given).

Source : ATOFINA Paris la Defense,France
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)

Test condition : TEST ORGANISM :
- Age : no data
- Weight at study initiation : 250 g
- Number of animals : 6 exposed and 2 controls male rats

ADMINISTRATION/EXPOSURE :
- Vehicle : air
- Dose : single dose tested

- Whole body exposure using a dynamic flow chamber(no details given)

CLINICAL OBSERVATIONS AND FREQUENCY :
- Clinical signs : yes
- Mortality : yes,
- Bodyweight gain : yes
- Haematology: hemoglobin, blood cells counts.
- Biochemistry : no.
- Urinalysis : no
- Organ weights : no
- Histology : liver and main organs (not specified)

STATISTICS : no

Reliability : (3) invalid
significant methodological deficiencies

08.06.2001 (74)

Type	:	
Species	:	mouse
Sex	:	male
Strain	:	no data
Route of admin.	:	inhalation
Exposure period	:	4 weeks
Frequency of treatm.	:	2 hours once a week
Post exposure period	:	no
Doses	:	7000 ppm (48100 mg/m3)
Control group	:	no
NOAEL	:	< 7000 ppm
LOAEL	:	< 7000 ppm
Method	:	other
Year	:	1962
GLP	:	no data
Test substance	:	as prescribed by 1.1 - 1.4

Result : - Mortality : All nine mice died within the 4 week test period with delayed mortality after exposure to the vapors of the test material.
- Histology : Slight to moderate congestion and fatty degeneration of the liver, and congestion of other organs (no details given) were observed.

Source : ATOFINA Paris la Defense,France
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)

Test condition : TEST ORGANISM :
- Age : no data
- Weight at study initiation : 15 g
- Number of animals : 9 exposed male mice

ADMINISTRATION/EXPOSURE :
- Vehicle : air
- Dose : single dose tested
- Whole body exposure using a dynamic flow chamber(no details given)

CLINICAL OBSERVATIONS AND FREQUENCY :
- Clinical signs : yes
- Mortality : yes
- Bodyweight gain : no
- Haematology: no.
- Biochemistry : no.

- Urinalysis : no
- Organ weights : no
- Histology : liver and main organs (not specified)

STATISTICS : no

Reliability : (3) invalid
significant methodological deficiencies

11.06.2001 (74)

Type :
Species : rabbit
Sex : no data
Strain : no data
Route of admin. : inhalation
Exposure period : 7 to 11 months
Frequency of treatm. : 3 to 4 h/day
Post exposure period : none
Doses : 15 ppm
Control group : no data specified
NOAEL : < 15 ppm
LOAEL : < 15 ppm
Method : other: not specified
Year : 1971
GLP : no
Test substance : as prescribed by 1.1 - 1.4

Result : Slight effects on liver at the test concentration (15 ppm = 100 mg/m3)
Source : ATOFINA Paris la Defense, France
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Reliability : (4) not assignable
data from secondary source

08.06.2001 (86)

Type :
Species : rabbit
Sex : no data
Strain : no data
Route of admin. : inhalation
Exposure period : 4 weeks
Frequency of treatm. : 8 to 9 hours daily
Post exposure period : no data
Doses : 100 to 160 ppm
Control group : no data specified
NOAEL : > 160 ppm
LOAEL : > 160 ppm
Method : other: not specified
Year : 1943
GLP : no
Test substance : as prescribed by 1.1 - 1.4

Remark : Result considered as surprising as experience in human indicates injury has occurred at much lower concentrations
Result : No effect ; no typical organ changes were found
Source : ATOFINA Paris la Defense,France
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Reliability : (4) not assignable
Secondary litterature

08.06.2001 (86)

Type	:	
Species	:	cat
Sex	:	no data
Strain	:	no data
Route of admin.	:	inhalation
Exposure period	:	4 weeks
Frequency of treatm.	:	8 to 9 h/day
Post exposure period	:	no data
Doses	:	100 to 160 ppm
Control group	:	no data specified
NOAEL	:	> 160 ppm
LOAEL	:	> 160 ppm
Method	:	other: not specified
Year	:	1943
GLP	:	no
Test substance	:	as prescribed by 1.1 - 1.4
Remark	:	Result considered as surprising as experience in human indicates injury has occurred at much lower concentrations
Result	:	No effect ; no typical organ changes were found
Source	:	ATOFINA Paris la Defense, France EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Reliability	:	(4) not assignable data from secondary source

08.06.2001 (87)

Type	:	
Species	:	monkey
Sex	:	male
Strain	:	other: macaca cynomolga Linné
Route of admin.	:	inhalation
Exposure period	:	9 months
Frequency of treatm.	:	2h/, 6d/wk (190 exposures)
Post exposure period	:	no
Doses	:	1000 to 4000 ppm
Control group	:	no
NOAEL	:	< 1000 ppm
LOAEL	:	< 1000 ppm
Method	:	other
Year	:	1962
GLP	:	no data
Test substance	:	as prescribed by 1.1 - 1.4
Result	:	- General condition : diarrhea, anorexia (1000 ppm = 6870 mg/m3 - up to 12 wks) ; almost complete unconsciousness (2000-4000 ppm = 13740-27480 mg/m3 from 15 wks up to end) 20 min to 1h after exposure to vapors. - Bodyweight : gradual increase from the 3rd to 5th month and decrease down to original weight at the 9th month. - Hematology: slight trend to an increase in white bood cells and a decrease of red blood cells and hemoglobin. - Urine no changes in albumin and urobilinogen - Histology : Slight to moderate congestion and fatty degeneration of the liver. Congestion of spleen. No changes in other organs.
Source	:	ATOFINA Paris la Defense,France EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Test condition	:	TEST ORGANISM : - Age : no data

- Weight at study initiation : 7 kg
- Number of animals : 1 male

ADMINISTRATION/EXPOSURE :
- Vehicle : air
- Dose : single dose tested
- Whole body exposure using a dynamic flow chamber(no details given)

CLINICAL OBSERVATIONS AND FREQUENCY :
- Clinical signs : yes
- Mortality : yes
- Bodyweight gain : yes
- Haematology: yes.
- Biochemistry : no.
- Urinalysis : yes
- Organ weights : no
- Histology : liver, heart, lung, kidney, pancreas, spleen, testis.

STATISTICS : n

Reliability : (3) invalid
significant methodological deficiencies

18.06.2001 (74)

5.5 GENETIC TOXICITY 'IN VITRO'

Type	:	Ames test
System of testing	:	Salmonella typhimurium strains TA 98, TA 100, TA 1535, TA 1537
Test concentration	:	-2.4 to -1.0 log µMole/g agar
Cycotoxic concentr.	:	no data
Metabolic activation	:	with and without
Result	:	positive
Method	:	other: plate incorporation
Year	:	1991
GLP	:	no data
Test substance	:	as prescribed by 1.1 - 1.4
Remark	:	Result: weak positive with and without metabolic activation in TA 100 strain, negative in TA 1535 strain
Source	:	ATOFINA Paris la Defense, France EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Reliability	:	(2) valid with restrictions Test procedure in accordance with national standard methods with acceptable restrictions
Flag	:	Critical study for SIDS endpoint

22.05.2001 (88)

Type	:	Ames test
System of testing	:	Salmonella typhimurium, strains TA 97, TA98, TA100 and TA102
Test concentration	:	10 µg/l to 10 g/l (Plate incorporation test) ; 100 µl/disc (spot test) ; 5µl to 100 µl in 3000µl (preincubation test)
Cycotoxic concentr.	:	no data
Metabolic activation	:	with and without
Result	:	positive
Method	:	other
Year	:	1989
GLP	:	no data
Test substance	:	as prescribed by 1.1 - 1.4

Result	:	- Without metabolic activation : the test material was active only in TA100 in the spot test. It was negative in all other strains and test conditions - With metabolic activation : the test material was only active in strains TA97 and TA98 in the plate incorporation test. It was inactive in all other strains ans test conditions.
Source	:	ATOFINA Paris la Defense,France EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Test condition	:	Metabolic Activation: Arochlor induced rat liver microsomes. Method: plate incorporation test ; spot test (48h incubation at 37°C); preincubation test (30 min. pre-incubation at 37°C).
Reliability	:	(2) valid with restrictions study well documented, meets generally accepted scientific principles, acceptable for assessment
Flag	:	Critical study for SIDS endpoint

22.05.2001 (89)

Type	:	Salmonella typhimurium reverse mutation assay
System of testing	:	strain TA 100
Test concentration	:	up to toxic concentrations
Cycotoxic concentr.	:	no data
Metabolic activation	:	with and without
Result	:	negative
Method	:	other
Year	:	1988
GLP	:	no data
Test substance	:	as prescribed by 1.1 - 1.4
Source	:	ATOFINA Paris la Defense, France EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Reliability	:	(4) not assignable abstract

03.05.2001 (90)

Type	:	Ames test
System of testing	:	Salmonella typhimurium, strains TA 1535, TA 1537, TA 98 and TA 100
Test concentration	:	not stated
Cycotoxic concentr.	:	no data
Metabolic activation	:	with and without
Result	:	negative
Method	:	other
Year	:	1984
GLP	:	no data
Test substance	:	as prescribed by 1.1 - 1.4
Remark	:	Method: plate incorporation S9 fraction of rat microsomes Arochlor induced. Bacteria were exposed to the vapors of the test material in a sealed 9-liter dessicator placed at 37°C during 8 hours. Then the bacteria were allow to incubate during 48 hours at 37°C our side of the desicator. The achived test concentration was not measured and is assumed to be the vapour saturation at 37°C.
Source	:	ATOFINA Paris la Defense, France EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Reliability	:	(2) valid with restrictions

Test procedure in accordance with national standard methods with acceptable restrictions

Flag : Critical study for SIDS endpoint
13.06.2001 (91)

Type : Ames test
System of testing : Salmonella typhimurium strains TA1535, TA1537, TA98 and TA100
Test concentration : not stated
Cycotoxic concentr. : not stated
Metabolic activation : with and without
Result : negative
Method : other
Year : 1988
GLP : no data
Test substance : as prescribed by 1.1 - 1.4

Source : ATOFINA Paris la Defense,France
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Test condition : Metabolic activation was preformed with Aroclor 1254-induced livers derived from Osborne-Mendel rats and B6C3F1 mice of both sexes.
The standard method was modified by using a 9-liter dessicator due to the volatility of the test material.
Reliability : (2) valid with restrictions
Test procedure in accordance with national standard methods with acceptable restrictions
Flag : Critical study for SIDS endpoint
26.10.2001 (92)

Type : Ames test
System of testing : Salmonella Typhimurium strains TA 97, TA98, TA100, TA104
Test concentration : 0.01, 0.025, 0.05, 0.1, 0.25, 0.5, 1.0 mg/plate
Cycotoxic concentr. : >= 1mg/plate
Metabolic activation : with and without
Result : positive
Method : other
Year : 1987
GLP : no data
Test substance : as prescribed by 1.1 - 1.4

Result : Positive in TA98, TA100 and TA97 with and without S9
Negative in TA104 with and without S9
Source : ATOFINA Paris la Defense,France
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Test condition : - Positive control : yes
- Negative control : yes
- Metabolic activation : Aroclor1254 induced rat liver microsome S9 mix
- Plate number : duplicate/triplicate
Reliability : (2) valid with restrictions
Test procedure in accordance with national standard methods with acceptable restrictions
Flag : Critical study for SIDS endpoint
26.10.2001 (93)

Type : Ames test
System of testing : Salmonella typhimurium strains TA 100, TA 98, TA 1535, TA 1537, TA 1538
Test concentration : range of concentrations up to 4 mg/plate
Cycotoxic concentr. : 4 mg/plate

Metabolic activation : with and without
Result : negative
Method : other: not specified
Year : 1980
GLP : no data
Test substance : as prescribed by 1.1 - 1.4

Remark : Metabolic Activation: S9 rat microsomes
Solvant : DMSO
Result: negative on all tested Strains at concentrations up to 4 mg/plate (which was toxic to the bacteria).
Source : ATOFINA Paris la Defense, France
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Reliability : (2) valid with restrictions
Test procedure in accordance with national standard methods with acceptable restrictions
Flag : Critical study for SIDS endpoint
03.05.2001 (94)

Type : Ames test
System of testing : Salmonella Typhimurium, STRAINS : TA1535, TA1537, TA98, TA100
Test concentration : up to 1 mg/plate in DMSO
Cycotoxic concentr. : 1 mg/plate
Metabolic activation : with and without
Result : negative
Method : other
Year : 1983
GLP : no data
Test substance : as prescribed by 1.1 - 1.4

Source : ATOFINA Paris la Defense, France
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Reliability : (2) valid with restrictions
Test procedure in accordance with national standard methods with acceptable restrictions
Flag : Critical study for SIDS endpoint
26.10.2001 (95)

Type : Ames test
System of testing : Salmonella typhimurium strains TA 1530, TA 1535, TA 1538
Test concentration : no data
Cycotoxic concentr. : no data
Metabolic activation : no data
Result : positive
Method : other: not specified
Year : 1977
GLP : no data
Test substance : as prescribed by 1.1 - 1.4

Remark : Results in this paper are imported from another previous article from the same team (see Brem et al, 1974)
Result : Positive on TA 1535, negative on TA 1538.
Source : ATOFINA Paris la Defense, France
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Reliability : (4) not assignable
Secondary litterature
13.06.2001 (96)

Type : Ames test
System of testing : Salmonella typhimurium TA 1530, TA 1535, TA 1538

Test concentration	:	5 to 23 µMol/plate
Cycotoxic concentr.	:	no data
Metabolic activation	:	without
Result	:	positive
Method	:	other: not specified
Year	:	1974
GLP	:	no
Test substance	:	as prescribed by 1.1 - 1.4
Remark	:	Result: positive on Strains TA 1530 and 1535. negative on strain TA 1538
Source	:	ATOFINA Paris la Defense, France EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Reliability	:	(2) valid with restrictions study well documented, meets generally accepted scientific principles, acceptable for assessment
Flag	:	Critical study for SIDS endpoint

03.05.2001 (97)

Type	:	Bacterial forward mutation assay
System of testing	:	L-Arabinoside resistance test of Salmonella typhimurium
Test concentration	:	0,06 to 2979 nmol/plate
Cycotoxic concentr.	:	1787 nmol/plate
Metabolic activation	:	with and without
Result	:	negative
Method	:	other
Year	:	1991
GLP	:	no data
Test substance	:	as prescribed by 1.1 - 1.4
Remark	:	Strain BAL13 was used in preincubation. Metabolic activation by rat microsomes S9 fraction induced by Arochlor1254.
Source	:	ATOFINA Paris la Defense, France EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Reliability	:	(2) valid with restrictions study well documented, meets generally accepted scientific principles, acceptable for assessment
Flag	:	Critical study for SIDS endpoint

03.05.2001 (98)

Type	:	Bacterial gene mutation assay
System of testing	:	Escherichia Coli,
Test concentration	:	10 µl/plate
Cycotoxic concentr.	:	no data
Metabolic activation	:	without
Result	:	positive
Method	:	other
Year	:	1974
GLP	:	no data
Test substance	:	as prescribed by 1.1 - 1.4
Source	:	ATOFINA Paris la Defense,France EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Test condition	:	Assay with polymerase-deficient E. coli. Test substance deposited on a sterile disc placed on the top of the surface of agar plates where the bacteria were spread. Incubation at 37°C for 8 hours. Assay carried out in duplicate on at least 3 different occasions.
Reliability	:	(2) valid with restrictions study well documented, meets generally accepted scientific

principles, acceptable for assessment
Flag : Critical study for SIDS endpoint
26.10.2001 (97)

Type : Bacillus subtilis recombination assay
System of testing : Bacillus subtilis/microsome REC-assay for the detection of DNA damaging substances.
Strains H17 and M45
Test concentration : no data
Cycotoxic concentr. : no data
Metabolic activation : with and without
Result : negative
Method : other
Year : 1989
GLP : no data
Test substance : as prescribed by 1.1 - 1.4

Source : ATOFINA Paris la Defense, France
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Reliability : (2) valid with restrictions
study well documented, meets generally accepted scientific principles, acceptable for assessment
Flag : Critical study for SIDS endpoint
09.05.2001 (99)

Type : Mitotic recombination in Saccharomyces cerevisiae
System of testing : Saccharomyces cerevisiae, strain D4 and D7
Test concentration : 3.1 to 7.3 mM
Cycotoxic concentr. : 5,2 mM
Metabolic activation : without
Result : positive
Method : other
Year : 1980
GLP : no data
Test substance : as prescribed by 1.1 - 1.4

Remark : Genetic activity of the test material was assessed through the ilv1 locus reversion frequency, the ade2 locus alteration frquency and the trp5 locus conversion frequency.
Result : Positive result found only at cytotoxic levels. Genetic effect was marginal when D4 and D7 strains were treated only during 4 h but was significant when treated during 1 h.
Source : ATOFINA Paris la Defense, France
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Reliability : (2) valid with restrictions
study well documented, meets generally accepted scientific principles, acceptable for assessment
Flag : Critical study for SIDS endpoint
09.05.2001 (100)

Type : Yeast Cytogenetic assay
System of testing : Aspergillus nidulans (strain P1). induction of chromosome malsegregation
Test concentration : 0.01 to 0.04 %v/v
Cycotoxic concentr. : 0.04 %
Metabolic activation : without
Result : positive
Method : other: not specified
Year : 1988
GLP : no data

Test substance : as prescribed by 1.1 - 1.4

Remark : Increased incidence of colonies producing euploid whole chromosome segregant was observed. However conclusive evidence for induction of aneuploidy as the primary genetic event was not provided in that study.
Source : ATOFINA Paris la Defense,France
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Reliability : (2) valid with restrictions
study well documented, meets generally accepted scientific principles, acceptable for assessment
Flag : Critical study for SIDS endpoint
09.05.2001 (101)

Type : Yeast gene mutation assay
System of testing : Saccharomyces cerevisiae, strains D7 (gene conversion) and XV185-14C (reversion)
Test concentration : 50 µl/ ml
Cycotoxic concentr. : no data
Metabolic activation : without
Result : negative
Method : other
Year : 1983
GLP : no data
Test substance : as prescribed by 1.1 - 1.4

Remark : Exposure preincubation time was 24 hours at 30°C
Source : ATOFINA Paris la Defense,France
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Reliability : (2) valid with restrictions
study well documented, meets generally accepted scientific principles, acceptable for assessment
Flag : Critical study for SIDS endpoint
26.10.2001 (102)

Type : Chromosomal aberration test
System of testing : Cloned Chinese Hamster Ovary cells (CHO-W-B1)
Test concentration : without S9 : 453-653 µl/ml
with S9 : 503-653 µl/ml
Cycotoxic concentr. : no data
Metabolic activation : with and without
Result : negative
Method : other
Year : 1987
GLP : no data
Test substance : as prescribed by 1.1 - 1.4

Source : ATOFINA Paris la Defense, France
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Test condition : Cells were harvested after 19.5 to 26 hours incubation with the test material. The test material precipatated from the culture medium at concentration higher than 653 µl/ml. Slides were stained with Giemsa an coded. One hundred cells were scored from each concentration group having sufficient metaphases. Positive control and control solvant were used.
Reliability : (2) valid with restrictions
Test procedure in accordance with national standard methods with acceptable restrictions
Flag : Critical study for SIDS endpoint
09.05.2001 (103)

Type	:	Sister chromatid exchange assay
System of testing	:	Cloned Chinese Hamster Ovary cells (CHO-W-B1)
Test concentration	:	Without S9 : 16 to 168µl/ml ; With S9 : 451-558 µl/ml
Cycotoxic concentr.	:	no data
Metabolic activation	:	with and without
Result	:	positive
Method	:	other
Year	:	1987
GLP	:	no data
Test substance	:	as prescribed by 1.1 - 1.4
Result	:	positive with and without metabolic activation
Source	:	ATOFINA Paris la Defense, France EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Test condition	:	Cells were harvested after 28.5 to 37.3 hours in BrdUrd without S9. It was 2h with S9. The test material precipatated from the culture medium at concentration higher than 558 µl/ml. Slides were stained with dilute Hoechst 33258 and examined by fluorecence microscopy. Fifty cells per dose were scored from each concentration group having sufficient M2 cells available. Positive control (MMC and CP) and control solvant were used.
Reliability	:	(2) valid with restrictions Test procedure in accordance with national standard methods with acceptable restrictions
Flag	:	Critical study for SIDS endpoint

12.06.2001 (103)

Type	:	other: SOS chromotest
System of testing	:	Escherichia Coli PQ 37
Test concentration	:	up to 500 ml/l
Cycotoxic concentr.	:	not specified
Metabolic activation	:	with and without
Result	:	negative
Method	:	other
Year	:	1989
GLP	:	no data
Test substance	:	as prescribed by 1.1 - 1.4
Remark	:	Metabolic Activation: Arochlor induced rat liver microsomes.
Source	:	ATOFINA Paris la Defense,France EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Reliability	:	(2) valid with restrictions study well documented, meets generally accepted scientific principles, acceptable for assessment
Flag	:	Critical study for SIDS endpoint

11.05.2001 (104)

Type	:	DNA damage and repair assay
System of testing	:	Escherichia Coli
Test concentration	:	no data
Cycotoxic concentr.	:	no data
Metabolic activation	:	no data
Result	:	positive
Method	:	other: not specified
Year	:	1984
GLP	:	no data
Test substance	:	as prescribed by 1.1 - 1.4

Remark	:	No detail available in the paper; result only appears in a table. Data coming from Brusik et al, 1980
Source	:	ATOFINA Paris la Defense,France EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Reliability	:	(4) not assignable data from secondary source

11.05.2001 (105)

Type	:	DNA damage and repair assay
System of testing	:	Unscheduled DNA synthesis (UDS) in rat hepatocyte primary culture
Test concentration	:	9.5 x 10-5 M
Cycotoxic concentr.	:	not specified
Metabolic activation	:	without
Result	:	negative
Method	:	other: not specified
Year	:	1989
GLP	:	no data
Test substance	:	as prescribed by 1.1 - 1.4
Source	:	ATOFINA Paris la Defense,France EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Test condition	:	Osborne-Mendel rats were used to provide the hepatocytes Monolayer cultures were simultaneously exposed to the test material and to 10 µCi [3H]thymidine. Incubation time was 18-20h. Several concentrations were tested. However only a single figure is presented in the paper which corresponds to the highest nontoxic concentration.
Reliability	:	(2) valid with restrictions study well documented, meets generally accepted scientific principles, acceptable for assessment
Flag	:	Critical study for SIDS endpoint

11.05.2001 (106)

Type	:	DNA damage and repair assay
System of testing	:	Microscreen prophage-induction assay in Escherichia coli (prophage lambda lysogen WP2s)
Test concentration	:	7.4 to 472.6 mM
Cycotoxic concentr.	:	236.3 mM (-S9) ; 472.6 mM (+S9)
Metabolic activation	:	with and without
Result	:	positive
Method	:	other
Year	:	1992
GLP	:	no data
Test substance	:	as prescribed by 1.1 - 1.4
Result	:	Positive with S9 metabolic activation. Negative without S9 metabolic activation.
Source	:	ATOFINA Paris la Defense,France EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Test condition	:	Overnight incubation at 37°C in microsuspensionin well microtiter plates. Scoring by turbidimetry.
Reliability	:	(2) valid with restrictions study well documented, meets generally accepted scientific principles, acceptable for assessment
Flag	:	Critical study for SIDS endpoint

26.10.2001 (107)

Type	:	Unscheduled DNA synthesis

System of testing	:	rat hepatocyte primary culture
Test concentration	:	from 10-7 % up to 1 % test material in DMSO
Cycotoxic concentr.	:	10-2 % to 1%
Metabolic activation	:	without
Result	:	negative
Method	:	other: not specified
Year	:	1983
GLP	:	no data
Test substance	:	as prescribed by 1.1 - 1.4
Source	:	ATOFINA Paris la Defense, France EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Test condition	:	HPC/DNA repair Assay in liquid phase. 18 h contact of the test material with the rat hepatocyte primary culture
Reliability	:	(2) valid with restrictions study well documented, meets generally accepted scientific principles, acceptable for assessment
Flag	:	Critical study for SIDS endpoint

13.06.2001 (108)

Type	:	DNA damage and repair assay
System of testing	:	Unscheduled DNA synthesis on rat and mouse hepatocytes primary cultures
Test concentration	:	not stated
Cycotoxic concentr.	:	not stated
Metabolic activation	:	without
Result	:	negative
Method	:	other
Year	:	1988
GLP	:	no data
Test substance	:	as prescribed by 1.1 - 1.4
Result	:	The test material was completely inactive both in rats and in mice hepatocyte primary cultures.
Source	:	ATOFINA Paris la Defense,France EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Test condition	:	Osborne-Mendel rats and B6C3F1 mice were used to prepare the hepatocyte cultures.
Reliability	:	(2) valid with restrictions Test procedure in accordance with national standard methods with acceptable restrictions
Flag	:	Critical study for SIDS endpoint

26.10.2001 (92)

Type	:	Unscheduled DNA synthesis
System of testing	:	mouse hepatocyte primary culture (B6C3F1)
Test concentration	:	from 10-7 % to 1 %
Cycotoxic concentr.	:	10-1 % to 1 %
Metabolic activation	:	without
Result	:	negative
Method	:	other: not specified
Year	:	1983
GLP	:	no data
Test substance	:	as prescribed by 1.1 - 1.4
Source	:	ATOFINA Paris la Defense, France EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Test condition	:	HPC/DNA repair Assay in liquid phase. 18 h contact of the test material with the rat hepatocyte primary culture
Reliability	:	(2) valid with restrictions

study well documented, meets generally accepted scientific principles, acceptable for assessment

Flag : Critical study for SIDS endpoint

21.06.2001 (109)

Type : other: in vitro DNA binding
System of testing : Covalent binding to macromolecules of rats and mouse cells from various organs
Test concentration : not stated
Cycotoxic concentr. : not stated
Metabolic activation : with
Result : positive
Method : other
Year : 1987
GLP : no data
Test substance : as prescribed by 1.1 - 1.4

Result : Only microsomal enzymes from rat and mouse liver and from mouse lung were efficient to mediate binding to DNA, to microsomal RNA and to microsomal proteins.
Cytosolic fractions from all assayed organs of mouse and from liver and lung of rat induced binding to macromolecules.
Source : ATOFINA Paris la Defense,France
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Test condition : (U- 14C)-1,1,2,2-tetrachloroethane was used.
Cell-free systems (calf thymus DNA, microsomal proteins, cytosolic proteins) were used to look for binding of the test material to exogenous DNA and the sub-cellular constituents of enzymatic fractions. The binding were studied after the test material was bioactivated by MFO and GSH-T from microsomal and cytosolic fractions of male rat and mouse liver, kidney, stomach and lung.
Reliability : (2) valid with restrictions
study well documented, meets generally accepted scientific principles, acceptable for assessment

26.10.2001 (110)

Type : other: cell transformation assay
System of testing : BALB/c 3T3 cells
Test concentration : from 1 to 250 µg/ml
Cycotoxic concentr. : LC50 = 3 mM
Metabolic activation : without
Result : negative
Method : other: not specified
Year : 1983
GLP : no data
Test substance : as prescribed by 1.1 - 1.4

Remark : 72 h exposure; positive control : 3-methylchlolanthrene.
Source : ATOFINA Paris la Defense, France
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Reliability : (2) valid with restrictions
study well documented, meets generally accepted scientific principles, acceptable for assessment
Flag : Critical study for SIDS endpoint

13.06.2001 (111) (112)

Type : other: cell transformation assay
System of testing : BALB/c-3T3 neoplastic cell transformation assay

Test concentration	:	not stated
Cycotoxic concentr.	:	not stated
Metabolic activation	:	without
Result	:	negative
Method	:	other
Year	:	1988
GLP	:	no data
Test substance	:	as prescribed by 1.1 - 1.4
Source	:	ATOFINA Paris la Defense,France EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Test condition	:	Incubation in glass chambers due to volatility. Only type III foci were scored.
Reliability	:	(2) valid with restrictions Test procedure in accordance with national standard methods with acceptable restrictions
Flag	:	Critical study for SIDS endpoint

26.10.2001 (92)

Type	:	other: cell transformation assay
System of testing	:	BALB/c3T3 cells, clone A-31, using an amplification (level II) transformation assay
Test concentration	:	10 to 1000 µg/ml
Cycotoxic concentr.	:	1000 µg/ml
Metabolic activation	:	with and without
Result	:	positive
Method	:	other: no data
Year	:	1990
GLP	:	no data
Test substance	:	as prescribed by 1.1 - 1.4
Remark	:	Rat liver microsomial S9 fraction Arochlor induced was used as metabolic activator. Amplification of the transformation was achieved by reseeding confluent cells from each treatment and allowing additional rounds of cell replication.
Result	:	The test material was not active without or with metabolic activation under the standard testing conditions (level I) Howether it was shown to be capable of inducing in vitro transformation of the cells either in the presence or in the absence of S9 activation, using an amplification-transformation assay (level II) by resseeding confluent cells from each treatment and allowing additional rounds of cell replication. In the absence of metabolic activation 1000 µg/ml was the only transforming dose. In the presence of metabolic activation lower doses were active.
Source	:	ATOFINA Paris la Defense, France EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Reliability	:	(2) valid with restrictions study well documented, meets generally accepted scientific principles, acceptable for assessment
Flag	:	Critical study for SIDS endpoint

09.05.2001 (113)

Type	:	other: cell transformation assay
System of testing	:	BALB/c3T3 cells, clone A-31,using an amplification-transformation (level II) assay.
Test concentration	:	31.25 to 500 µg/ml
Cycotoxic concentr.	:	500 µg/ml
Metabolic activation	:	without

Result	:	positive
Method	:	other: no data
Year	:	1992
GLP	:	no data
Test substance	:	as prescribed by 1.1 - 1.4
Remark	:	The objective of the study was to look for the mechanism of action of the test material in view of establishing whether it has an initiating potential to transform the BALB-c 3T3 cells. Cells were treated with sub-effective or transforming concentrations of 1,1,2,2-tetrachloroethane in the presence of an S9 metabolic activating system, followed by tetradecanoyl-phorbol acetate promoting treatment. The transforming potential of the test material which was already established by the same authors in a previous study (See Colacci et al 1990) only when using amplification (level II) conditions, was confirmed in the present study.
Result	:	The transforming activity of the test material is evident only by reseding confluent cells and allowing additional rounds of cell replications in the amplification test. Under standard conditions (level I assay) there was no evidence of transforming activity.
Source	:	ATOFINA Paris la Defense, France EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Reliability	:	(2) valid with restrictions study well documented, meets generally accepted scientific principles, acceptable for assessment

09.05.2001 (114)

Type	:	other: cell transformation assay
System of testing	:	BALB/c 3T3 cells, using an amplification (level II) transformation assay
Test concentration	:	2.9 and 5.9 mM
Cycotoxic concentr.	:	no data
Metabolic activation	:	with and without
Result	:	positive
Method	:	other: not specified
Year	:	1993
GLP	:	no data
Test substance	:	as prescribed by 1.1 - 1.4
Remark	:	Type: Cell Transformation Assay When transformed by 1,1,2,2-Tetrachloroethane the cells acquired a malignant phenotype shown by IV injection of the transformed BALB/c 3T3 cells in nude mice(athymic mice): appearing of pulmonary nodules .
Result	:	During this experiment the positive effect which was described previously by the same team (see Colacci et al, 1990) is confirmed in the amplification-level II test.
Source	:	ATOFINA Paris la Defense, France EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Reliability	:	(2) valid with restrictions study well documented, meets generally accepted scientific principles, acceptable for assessment

21.06.2001 (115)

5.6 GENETIC TOXICITY 'IN VIVO'

Type	:	Drosophila SLRL test
Species	:	Drosophila melanogaster
Sex	:	no data
Strain	:	
Route of admin.	:	other
Exposure period	:	no data
Doses	:	injection of 800 ppm; feeding of 1500 ppm
Result	:	negative
Method	:	other: not specified
Year	:	1985
GLP	:	no data
Test substance	:	as prescribed by 1.1 - 1.4
Remark	:	Route of administration: injection and feeding
Result	:	negative by feeding and injection
Source	:	ATOFINA Paris la Defense, France EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Reliability	:	(2) valid with restrictions study well documented, meets generally accepted scientific principles, acceptable for assessment
Flag	:	Critical study for SIDS endpoint

09.05.2001 (116)

Type	:	Unscheduled DNA synthesis
Species	:	mouse
Sex	:	male/female
Strain	:	B6C3F1
Route of admin.	:	gavage
Exposure period	:	single treatment
Doses	:	50, 200, 600, 1000 mg/kg
Result	:	negative
Method	:	other
Year	:	1989
GLP	:	no data
Test substance	:	as prescribed by 1.1 - 1.4
Source	:	ATOFINA Paris la Defense, France EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Test condition	:	Groups of 3 male and 3 female mice were treated orally. Hepatocytes were taken for primary culture 2 and 12 hours after gavage. Cultures were incubated with 3H-methylthymidine and UDS was quantified by autoradiography. Three slides were scored for each animal of all dose-groups for a total of 150 cells per animal.
Reliability	:	(2) valid with restrictions study well documented, meets generally accepted scientific principles, acceptable for assessment
Flag	:	Critical study for SIDS endpoint

09.05.2001 (117)

Type	:	Cytogenetic assay
Species	:	rat
Sex	:	
Strain	:	
Route of admin.	:	inhalation
Exposure period	:	5 days
Doses	:	349 mg/m3
Result	:	ambiguous
Method	:	other
Year	:	1980

GLP	:	
Test substance	:	as prescribed by 1.1 - 1.4
Source	:	ATOFINA Paris la Defense,France EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Test condition	:	bone marrow assay; the single exposure concentration used in the test did not induce cytotoxicity.
Reliability	:	(4) not assignable Secondary litterature

18.06.2001 (118)

Type	:	Dominant lethal assay
Species	:	rat
Sex	:	
Strain	:	
Route of admin.	:	inhalation
Exposure period	:	5 days
Doses	:	349 mg/m3
Result	:	negative
Method	:	other
Year	:	1980
GLP	:	
Test substance	:	as prescribed by 1.1 - 1.4
Source	:	ATOFINA Paris la Defense,France EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Reliability	:	(4) not assignable Secondary litterature

18.06.2001 (119)

Type	:	Drosophila SLRL test
Species	:	Drosophila melanogaster
Sex	:	
Strain	:	
Route of admin.	:	
Exposure period	:	
Doses	:	
Result	:	negative
Method	:	
Year	:	1980
GLP	:	no data
Test substance	:	as prescribed by 1.1 - 1.4
Source	:	ATOFINA Paris la Defense,France EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Reliability	:	(4) not assignable Secondary litterature

13.06.2001 (119)

Type	:	other: Rat liver Foci Assay
Species	:	rat
Sex	:	male
Strain	:	Osborne-Mendel
Route of admin.	:	gavage
Exposure period	:	single exposure (initiation study) ; 5d/wks, 7 wks (promotion study)
Doses	:	200 mg/kg
Result	:	positive
Method	:	other
Year	:	1988
GLP	:	no data

Test substance	:	as prescribed by 1.1 - 1.4
Result	:	When administered in the promotion protocol after initiation with DEN, the test material induced significant increase in GGT+ foci above control levels. The test material also induced significant increase in GGT+ foci when administered in the promotion protocol without DEN initiation. The test material however was inactive as an initiator when administered in the initiation protocol.
Source	:	ATOFINA Paris la Defense,France EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Test condition	:	INITIATION Protocol : 10 rats per group were given 2/3 partial hepatectomies and 24 h la ter reveived the test material at the MTD. Six days after partial hepatectomies, the animals began to receive in the diet pentobarbitone (0.05% w/w) for 7 weeks, then one week untreated, after which they were killed and the liver examined histologically. DEN (30 mg/kg ip) served as positive initiator control. PROMOTING Protocol : Ten rats per group were initiated with DEN ip (30 mg/kg) 24 h before being 2/3 partially hepatectomized. Six days later they began to receive by gavage the test material at MTD during 7 weeks and held for one more week without treatment,after which they were killed and the liver examined histologically. Gammaglutamyltranspeptidase was used as a putative preneoplastic indicator. GGT+ foci were quantified using light microscopy.
Reliability	:	(2) valid with restrictions study well documented, meets generally accepted scientific principles, acceptable for assessment

30.05.2001 (92)

Type	:	other: eye mosaic (w/w+) assay / interchromosomal mitotic recombination
Species	:	Drosophila melanogaster
Sex	:	male/female
Strain	:	other: Leiden Standard
Route of admin.	:	other: treatment of larvae by inhalation
Exposure period	:	17 hours
Doses	:	500 and 1000 ppm
Result	:	negative
Method	:	other
Year	:	1993
GLP	:	no data
Test substance	:	as prescribed by 1.1 - 1.4
Method	:	number of eyes examined : 1062 in controls , 1316 in the 500 ppm group. Inhalation exposure of 28-52 old larvae in a closed bottle maintained at 25°C during 17h. Then the larvae were removed, washed and placed in bottle with standard food.
Result	:	500 ppm was inactive in the w/w+ biassay (4.05 per 100 eyes in control versus 4.03 in treated flies per 100 eyes). 1000 ppm was lethal to the larvae.
Source	:	ATOFINA Paris la Defense,France EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)

Reliability	:	(2) valid with restrictions study well documented, meets generally accepted scientific principles, acceptable for assessment
Flag	:	Critical study for SIDS endpoint

20.07.2001 (120)

Type	:	other: in vivo DNA binding
Species	:	rodent
Sex	:	no data
Strain	:	other: Wistar rats and BALB/c mouse
Route of admin.	:	i.p.
Exposure period	:	single injection
Doses	:	127 µCi/kg
Result	:	positive
Method	:	other
Year	:	1987
GLP	:	no data
Test substance	:	as prescribed by 1.1 - 1.4
Result	:	The test material bound with DNA, RNA and proteins of all organs of both species. The covalent binding index with liver DNA was about 500 ; it is comparable to the indices of carcinogens classified as moderate initiators.
Source	:	ATOFINA Paris la Defense,France EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Test condition	:	Six rats (250 g) and 12 mice (28 g) were killed 22 h after the injection of the C14 radiolabelled test material.Their liver, kidney, lung and stomach were removed , pooled and the DNA RNA and proteins were obtained. Radioactivity was the measured by liquid scintillation.
Reliability	:	(2) valid with restrictions study well documented, meets generally accepted scientific principles, acceptable for assessment

13.06.2001 (110)

5.7 CARCINOGENICITY

Species	:	rat
Sex	:	male/female
Strain	:	Osborne-Mendel
Route of admin.	:	gavage
Exposure period	:	78 weeks
Frequency of treatm.	:	5 d/week
Post exposure period	:	32 weeks
Doses	:	time-weighted average doses: 62 and 108 mg/kg/day (males); 43 and 76 mg/kg/day (females)
Result	:	negative
Control group	:	yes
Method	:	other
Year	:	1978
GLP	:	no data
Test substance	:	as prescribed by 1.1 - 1.4
Method	:	Conventional NCI carcinogenicity protocol as used during the seventies in rats.
Result	:	NOAEL : >= 108 mg/kg/d (males) and 76 mg/kg/d (females TOXIC RESPONSE/EFFECTS BY DOSE LEVELS :

- Mortality-Time to death : increase mortality at higher dose ; survival at 105 weeks : 50% of high and low dosed males; 40% and 58% of high and low dose females respectively.
- Clinical signs : no data
- Bodyweight gain : reversible dose-related decrease
- Histopathology : No increase of incidence of non-neoplastic lesions ; No statistically dignificant incidence of neoplastic lesions was observed although 2 hepatocellular carcinomas and 1 neoplastic nodule were observed in the high dose group out of 49 males compared with 0/20 in vehicle controls.

Source : ATOFINA Paris la Defense,France
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)

Test condition : TEST ORGANISM :
- Age : 7 weeks
- Number of animals :2 groups of 50 males and 50 females; control groups : 40 males and 40 females

ADMINISTRATION/EXPOSURE :
- Doses : High dose animals received 100 mg/kg/d ; in males this was increased after 14 weeks to 130 mg/kg/d for 18 weeks followed by 9 cycles of 4weeks at this dose and 1 week treatment three for 45 weeks (total 78 weeks) ; in females, the dose was reduced after 25 weeks to 80 mg/kg/d for 7 weeks followed by the cyclic treatment at this dose for 45 weeks.
Low dose males received 50 mg/kg/d for 14 weeks and 65 mg/kg/d for 64 weeks ; females received 50 mg/kg/d for 25 weeks and 40 mg/kg/d for 53 weeks.
Half of the control groups received corn oil (match controls) ; the second half was not treated (untreated controls)

CLINICAL OBSERVATIONS and FREQUENCY:
- Clinical signs : yes
- Mortality : yes
- Bodyweight : yes
- Food and water consumption : not specified
- Biochemistry : no
- Urinalysis : no

ORGANS EXAMINED ATNECRPSY
- Macroscopic and Microscopic : all main organs and tissues

STATISTICAL METHOD

Reliability : (2) valid with restrictions
study well documented, meets generally accepted scientific principles, acceptable for assessment

Flag : Critical study for SIDS endpoint
11.05.2001 (81)

Species : mouse
Sex : male/female
Strain : B6C3F1
Route of admin. : gavage
Exposure period : 78 weeks
Frequency of treatm. : 5 d/week
Post exposure period : 12 weeks
Doses : time-weighted average doses: 142 and 284 mg/kg/day
Result : positive

Control group	:	yes
Method	:	other
Year	:	1978
GLP	:	no data
Test substance	:	as prescribed by 1.1 - 1.4
Method	:	Conventional NCI carcinogenicity protocol as used during the seventies in rats. NOAEL : >= 108 mg/kg/d (males) and 76 mg/kg/d (females TOXIC RESPONSE/EFFECTS BY DOSE LEVELS : - Mortality-Time to death : increase mortality at higher dose ; survival at 105 weeks : 50% of high and low dosed males; 40% and 58% of high and low dose females respectively. - Clinical signs : no data - Bodyweight gain : reversible dose-related decrease - Histopathology : No increase of incidence of non-neoplastic lesions ; No statistically dignificant incidence of neoplastic lesions was observed although 2 hepatocellular carcinomas and 1 neoplastic nodule were observed in the high dose group out of 49 males compared with 0/20 in vehicle controls.
Result	:	NOAEL : < 142 mg/kg/d (males and females) TOXIC RESPONSE/EFFECTS BY DOSE LEVELS : - Mortality-Time to death : dose related increased mortality - Clinical signs : no data - Bodyweight gain : slight dose related decrease - Histopathology : No increase of incidence of non-neoplastic lesions ; statistically significant excess of hepatocellular carcinomas were found in males (6%, 26% and 90% in control, low and high dose group respectively) and in females (0%, 63% and 91% in control, low and high dose group respectively). These tumours appeared earlier in mice administred the higher dose.
Source	:	ATOFINA Paris la Defense,France EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Test condition	:	TEST ORGANISM : - Age : 5 weeks - Number of animals :2 groups of 50 males and 50 females; control groups : 40 males and 40 females ADMINISTRATION/EXPOSURE : - Doses : Initially high dose and low dose animals received 200 mg/kg/d and 100 mg/kg/d respectively; thes dose were increased after 18 weeks to 300 mg/kg/d and 150 mg/kg respectively during 3 weeks. Tehse dose were further increased to 400 and 200 mg/kg during 5 weeks but returned to 300 and 150 mg/kg/d respectively during the following 52 weks (total 78 weeks). Half of the control groups received corn oil (match controls) ; the second half was not treated (untreated controls) CLINICAL OBSERVATIONS and FREQUENCY: - Clinical signs : yes - Mortality : yes - Bodyweight : yes

- Food and water consumption : not specified
- Biochemistry : no
- Urinalysis : no

ORGANS EXAMINED ATNECRPSY
- Macroscopic and Microscopic : all main organs and tissues

STATISTICAL METHOD

Reliability : (2) valid with restrictions
Flag : Critical study for SIDS endpoint
17.05.2001 (81)

Species : mouse
Sex : male
Strain : Strain A
Route of admin. : i.p.
Exposure period : 3 to 9 weeks
Frequency of treatm. : 2/week
Post exposure period : 15 to 21 weeks
Doses : 80 mg/kg (5 inj.); 200 mg/kg (18 inj.) and 400 mg/kg (16 inj.)
Result : negative
Control group : yes
Method : other: Pulmonary Tumor Response Bioassay
Year : 1977
GLP : no data
Test substance : as prescribed by 1.1 - 1.4

Method : Strain: A/St
Route of Administration: intra-peritoneal injections of the test material ; vehicle : tricaprylin

Result : LUNG TUMOR FREQUENCY :
Lung tumor incidences were increased in treated groups versus control the differences were not statistically significant. Although the highest dose group reached nearly statistical significance (p = 0.059), the biological significance of this result is limited due to poor survival (5/20 versus 15/20 in controls).

Source : ATOFINA Paris la Defense,France
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)

Test condition : TEST ORGANISM :
- Age : 6-8 weeks
- Number of animals : 20/group

ADMINISTRATION/EXPOSURE :
- Vehicle : tricaprylin

CLINICAL OBSERVATIONS : None

ORGANS EXAMINED :
- Lungs : examined under dissecting microscope and the number of surface adenomas was counted. A few surface nodules were examines hitologically to confirm the typical morphological appearence of the adenoma.

STATISTICAL METHODS :
- Standard Student t test : the frequency of lung adenomas in each treated group was compared with that in the control group.

Reliability : (2) valid with restrictions
study well documented, meets generally accepted scientific

principles, acceptable for assessment

11.05.2001 (121)

5.8.1 TOXICITY TO FERTILITY

Type	:	One generation study
Species	:	rat
Sex	:	male
Strain	:	no data
Route of admin.	:	inhalation
Exposure period	:	9 months
Frequency of treatm.	:	4h/d, 5d/wk
Premating exposure period		
Male	:	9 months
Female	:	none
Duration of test	:	up to sexual maturation of F1
No. of generation studies	:	
Doses	:	13.3 mg/m3 (1.94 ppm)
Control group	:	yes
NOAEL parental	:	< 13.3 mg/m³
NOAEL F1 offspring	:	> 13.3 mg/m³
Method	:	other
Year	:	1972
GLP	:	no data
Test substance	:	as prescribed by 1.1 - 1.4

Method : Only male were exposed . There fertility was checked by mating them with untreated females that were allowed to produce a F1 generation.

Result : TOXIC RESPONSE/EFFECTS BY DOSE LEVEL :

- Systemic toxicity data on male parents :
NOAEL < 13.3 mg/m3
  - Mortality : no significant difference between treated and control animals.
  - Clinical signs : none described
  - Bodyweight gain : At the end of 110 days, the exposed rats weighed significantly less than control (415 versus 435 g) but the difference was no longer present after 265 days due to wide individual variations).
  - Hematology : leucocytes were 90% higher than the controls after 110 days. No data on WBC were mentioned thereafter.
  - Clininical biochemistry : serum globuline were increased after 110 days and at the end of the study in treated rats; fat containt of the liver was increased in treated animals after 265 days (34%); the ACTH activity in hypophyse was decreased at interim and final sacrifices (65 % to 13 %).
  - Organ weights : No data reported
  - Histopathology : No data reported

- FERTILITY AND GESTATIONAL DATA :
  - NOAEL : > 13.3 mg/m3
  - There was no statistical difference between females sired by exposed males and females sired by control males on number of gravid females and any of the gestational parameters measured

- DATA ON OFFSPRINGS:
  - NOAEL : > 13.3 mg/m3
  - There was no statistically significant difference between results of offsprings from the exposed father group and offsprings from the control father group on any of the measured parameter.
  - There was no gross malformations.

Source : ATOFINA Paris la Defense,France
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)

Test condition : PROTOCOLE:
One week before the end of the 9th month of inhalation exposure, the male rats were mated with untreated virgin females.

TEST ORGANISM:
- Number : 7 control and 7 exposed male rats were mated each one with 5 virgin females
- Weight at start of mating : females : 250-300 g

PARAMETERS ASSED DURING STUDY P AND F1:
- Clinical observations : no data
- Estrous cycle : not appropriate
- Sperm examination : no

PARAMETERS ASSED DURING STUDY F1:
- Number and % pregnant females
- Number of offsprings delivered
- Number of offsprings per litter

OFFSPRING :
- Mean neo-natal offspring weight per litter
- survival at days 1, 2 7 14 21 and 84 after birth
- Weight and sex/ration at day 84
- gross external malformations

ORGANS EXAMINED AT NECROPSY : none

STATISTICAL METHOD :
- Standard Student t-Testt

Reliability : (2) valid with restrictions
significant methodological deficiencies
Study limited due to non examination of sperm and no histological data on testes of males of parent generation.

Flag : Critical study for SIDS endpoint
09.08.2002 (85)

Type : other: examination of male fertility
Species : rat
Sex : male
Strain : no data
Route of admin. : inhalation
Exposure period : 5 days
Frequency of treatm. : dominant lethal assay
Premating exposure period
Male : 5 days
Female :
Duration of test :
No. of generation studies :
Doses : 349 mg/m3

Control group :
Method : other
Year : 1980
GLP : no data
Test substance : as prescribed by 1.1 - 1.4

Remark : Abstract only available from the CICAD document. We did not have access to the original NTP report.
Result : WHO, CICAD, 1998 reported the following :
Small but statistically significant, increase in one type of sperm abnormality were observed in rats exposed to 349 mg/m3 for 5 days, although the authors considered this effect to be of questionable biological significance.
Source : Atofina Paris la Defense
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Reliability : (4) not assignable
Secondary litterature
18.06.2001 (119)

Type : other: examination of sexual organs during a sub-chronic toxicity study
Species : rat
Sex : male
Strain :
Route of admin. : gavage
Exposure period : 120 days (82 times)
Frequency of treatm. : 5d/wk
Premating exposure period
Male :
Female :
Duration of test :
No. of generation studies :
Doses :
Control group :
NOAEL parental : < 3.2 mg/kg bw
Method : other
Year : 1977
GLP : no data
Test substance : as prescribed by 1.1 - 1.4

Result : - High incidence of interstitial edema in the testes
Clumped sperm
Epithelial cells present in the tubular lumen
Partial necrosis and totally atrophied tubules , giant cells two-row germinal epithelial cells
Disturbed spermatogenesis
Some of these changes persisted during the follow-up observation period.
- In parallel at the highest doses there were damages in liver, kidney and thyroid gland. These damages in thyroid after the 2-week reversibility period in high dose groups.
Minor liver changes occured at 3.2 mg/kg.
- NOAEL for testicular effects : 3.2 mg/kg
Source : Atofina Paris la Defense
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Reliability : (3) invalid
significant methodological deficiencies
19.06.2001 (122)

Type : other: sexual organ examination during a chronic toxicity study

Species	:	monkey
Sex	:	male
Strain	:	
Route of admin.	:	inhalation
Exposure period	:	9 months
Frequency of treatm.	:	2h/d, 6d/wk (190 exposures)
Premating exposure period		
Male	:	
Female	:	
Duration of test	:	
No. of generation studies	:	
Doses	:	1000-4000 ppm
Control group	:	
NOAEL parental	:	> 1000 - 4000 ppm
Method	:	other
Year	:	1962
GLP	:	no data
Test substance	:	as prescribed by 1.1 - 1.4

Result : Exposure of one male monkey (macaca cynomolga Linné) for 9 months to 1000-4000 ppm (= 13740-27480 mg/m3) produced no pathology in the testes.

Source : ATOFINA Paris la Defense,France
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)

Reliability : (3) invalid
significant methodological deficiencies

09.08.2002 (123)

Type	:	other: sexual organ examination during sub-chronic toxicity study
Species	:	rat
Sex	:	female
Strain	:	Sprague-Dawley
Route of admin.	:	inhalation
Exposure period	:	15 weeks (78 exposures)
Frequency of treatm.	:	5-6 h/d ; 5d/wk
Premating exposure period		
Male	:	
Female	:	
Duration of test	:	
No. of generation studies	:	
Doses	:	560 ppm (3850 mg/m3)
Control group	:	yes
NOAEL parental	:	> 560 ppm
Method	:	other
Year	:	1977
GLP	:	no data
Test substance	:	as prescribed by 1.1 - 1.4

Method : Sub-chronic toxicity study on female rats including necropsies and histopathological analysis of ovaries and uterus.

Result :

Toxic response/effect : general systemic effects

- Mortality : not specified
- Clinical signs : transient CNS depressing effects during first exposures.
- Bodyweight gain : decreased during the last weeks of

exposure
- Hematology : slight decrease of hematocrit, red and white cells
- Organ weights : increased liver weight in each interim and final sacrifice
- Histopathology : Liver hyperplasia and hepatocellular histological lesions seen during the first weeks regressed after 19 exposure and disappeared after 39 exposures.
- Other examinations : increased DNA biosynthesis appeared after 4 exposures (313% versus controls). That effect disappeared when measured during the following weeks.

EFFECTS ON REPRODUCTIVE ORGANS :
- ovaries and uterus : histological examinations did not show any abnormalities on all animals necropsied at interim intervals or at final sacrifice.
- NOAEL for female reproductive organs : >560 ppm

Source : ATOFINA Paris la Defense,France
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)

Test condition : TEST ORGANISM :
- Age : adult
- Weight at study initiation : not stated
- Number of animals : 165 female Sprague Dawley rats were divided into one control group and 2 treated groups.

ADMINISTRATION/EXPOSURE:
- Type of exposure : Animals were exposed whole body by inhalation in chambers with atmospheric renewal of 2m3/hour.
- Doses : One group was exposed to vapours of 1,1,1-trichloroethane and the other to 1,1,2,2-tetrachloroethane at nominal concentration of 1100 and 560 ppm respectively. A third unexposed group served as control. Some animals (unspecified number) were sacrificed after 2, 4, 9, 19, 39 and 63 exposures.

CLINICAL OBSERVATIONS:
- Clinical signs : yes
- Mortality : yes
- Bodyweight : yes , followed all along the 15 week exposure
- Food and water consumption : not specified
- Haematology : yes, blood cytology followed
- Urinalysis : not specified

ORGANS EXAMINED AT NECROPSY:
- Macroscopic and microscopic : liver, kidney, adrenals, ovaries, uterus.

OTHER EXAMINATIONS:
- Hepatic DNA neosynthesis was determined 4 h after injection of 3H Thymidine.

STATISTICAL METHOD: not specified

Reliability : (2) valid with restrictions
study well documented, meets generally accepted scientific principles, acceptable for assessment

Flag : Critical study for SIDS endpoint
26.10.2001 (83)

Type : other: sexual organs examination during a chronic toxicity study
Species : rat
Sex : male/female

Strain	:	Osborne-Mendel
Route of admin.	:	oral feed
Exposure period	:	78 weeks
Frequency of treatm.	:	
Premating exposure period		
Male	:	
Female	:	
Duration of test	:	
No. of generation studies	:	
Doses	:	time-weighted average doses: 62 and 108 mg/kg/day (males); 43 and 76 mg/kg/day (females)
Control group	:	
NOAEL parental	:	> 108 mg/kg bw
Method	:	other
Year	:	1978
GLP	:	no data
Test substance	:	as prescribed by 1.1 - 1.4
Result	:	

TOXIC RESPONSE/EFFECTS BY DOSE LEVELS :
NOAEL : >= 108 mg/kg/d (males) and 76 mg/kg/d (females

- Mortality-Time to death : increase mortality at higher dose ; survival at 105 weeks : 50% of high and low dosed males; 40% and 58% of high and low dose females respectively.
- Clinical signs : no data
- Bodyweight gain : reversible dose-related decrease
- Histopathology : No increase of incidence of non-neoplastic lesions ; No statistically dignificant incidence of neoplastic lesions was observed although 2 hepatocellular carcinomas and 1 neoplastic nodule were observed in the high dose group out of 49 males compared with 0/20 in vehicle controls.

- HISTOPATHOLOGY OF SEXUAL ORGANS :
NOAEL : >108 mg/kg/d (males) and 76 mg/kg/d (females
no changes in male and in female organs examined on animals dead during the exposure period or at final necrops

Source	:	ATOFINA Paris la Defense,France EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Test condition	:	TEST ORGANISM : - Age : 7 weeks - Number of animals :2 groups of 50 males and 50 females; control groups : 40 males and 40 females ADMINISTRATION/EXPOSURE : - Doses : High dose animals received 100 mg/kg/d ; in males this was increased after 14 weeks to 130 mg/kg/d for 18 weeks followed by 9 cycles of 4weeks at this dose and 1 week treatment three for 45 weeks (total 78 weeks) ; in females, the dose was reduced after 25 weeks to 80 mg/kg/d for 7 weeks followed by the cyclic treatment at this dose for 45 weeks. Low dose males received 50 mg/kg/d for 14 weeks and 65 mg/kg/d for 64 weeks ; females received 50 mg/kg/d for 25 weeks and 40 mg/kg/d for 53 weeks. Half of the control groups received corn oil (match

controls) ; the second half was not treated (untreated controls)

CLINICAL OBSERVATIONS and FREQUENCY:
- Clinical signs : yes
- Mortality : yes
- Bodyweight : yes
- Food and water consumption : not specified
- Biochemistry : no
- Urinalysis : no

ORGANS EXAMINED ATNECRPSY
- Macroscopic and Microscopic : all main organs and tissues

STATISTICAL METHOD

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

Flag : Critical study for SIDS endpoint

18.06.2001 (81)

Type	:	other: sexual organs examination during a chronic toxicity study
Species	:	mouse
Sex	:	male/female
Strain	:	B6C3F1
Route of admin.	:	oral feed
Exposure period	:	78 weeks
Frequency of treatm.	:	
Premating exposure period		
Male	:	
Female	:	
Duration of test	:	
No. of generation studies	:	
Doses	:	time-weighted average doses: 142 and 284 mg/kg/day
Control group	:	
NOAEL parental	:	> 284 mg/kg bw
Method	:	other
Year	:	1978
GLP	:	no data
Test substance	:	as prescribed by 1.1 - 1.4

Result :

TOXIC RESPONSE/EFFECTS BY DOSE LEVELS
NOAEL : < 142 mg/kg/d (males and females)

- Mortality-Time to death : dose related increased mortality
- Clinical signs : no data
- Bodyweight gain : slight dose related decrease
- Histopathology : No increase of incidence of non-neoplastic lesions ; statistically significant excess of hepatocellular carcinomas were found in males (6%, 26% and 90% in control, low and high dose group respectively) and in females (0%, 63% and 91% in control, low and high dose group respectively).

- HISTOPATHOLOGY OF SEXUAL ORGANS :
NOAEL > 284 mg/kg
no changes in male and in female organs examined on animals

dead during the exposure period or at final necropsy

Source : ATOFINA Paris la Defense,France
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)

Test condition : TEST ORGANISM :
- Age : 5 weeks
- Number of animals :2 groups of 50 males and 50 females; control groups : 40 males and 40 females

ADMINISTRATION/EXPOSURE :
- Doses : Initially high dose and low dose animals received 200 mg/kg/d and 100 mg/kg/d respectively; thes dose were increased after 18 weeks to 300 mg/kg/d and 150 mg/kg respectively during 3 weeks. Tehse dose were further increased to 400 and 200 mg/kg during 5 weeks but returned to 300 and 150 mg/kg/d respectively during the following 52 weks (total 78 weeks).
Half of the control groups received corn oil (match controls) ; the second half was not treated (untreated controls)

CLINICAL OBSERVATIONS and FREQUENCY:
- Clinical signs : yes
- Mortality : yes
- Bodyweight : yes
- Food and water consumption : not specified
- Biochemistry : no
- Urinalysis : no

ORGANS EXAMINED ATNECRPSY
- Macroscopic and Microscopic : all main organs and tissues

STATISTICAL METHOD

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

Flag : Critical study for SIDS endpoint

18.06.2001 (81)

Type : other: sexual organs examined during a sub-acute toxicity study
Species : rat
Sex : male
Strain :
Route of admin. : inhalation
Exposure period : 4-10 days
Frequency of treatm. :
Premating exposure period
Male :
Female :
Duration of test :
No. of generation studies :
Doses : 2 ppm
Control group : yes
NOAEL parental : < 2 ppm
Method : other
Year : 1972
GLP : no data
Test substance : as prescribed by 1.1 - 1.4

Result : Seminal vesicles and sperm production :

due to inconsitent results the validity of the data is questionable :
- 4-day treatment : some atrophy of seminal vesicles and decreased spermatogenesis on 5/7 rats
- 10-day treatment : no damage to seminal vesicles or sperm production.

Source : Atofina Paris la Defense
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)

Reliability : (3) invalid
significant methodological deficiencies

06.02.2002 (124)

Type	:	other: sperm motility and vaginal cytology evaluation
Species	:	rat
Sex	:	male/female
Strain	:	Fischer 344
Route of admin.	:	other: oral feed (microencapsulated)
Exposure period	:	13 weeks
Frequency of treatm.	:	ad libitum
Premating exposure period		
Male	:	
Female	:	
Duration of test	:	
No. of generation studies	:	
Doses	:	37, 75, 150 mg/kg feed
Control group	:	yes, concurrent vehicle
other: NOAEL male rats	:	< 37 ppm
other: NOAEL female rats	:	= 37 ppm
Method	:	other: NTP, sperm motility and vaginal cytology evaluation
Year	:	
GLP	:	yes
Test substance	:	as prescribed by 1.1 - 1.4

Method : In a subchronic study, F344 rats were exposed to 1,1,2,2-tetrachloroethane via dosed feed. This study describes the "Sperm Motility Vaginal Cytology Evaluation" (SMVCE) portion of the subchronic study. For male rats, the reproductive endpoints evaluated are caudal, epididymal, and testicular weights, sperm motility, sperm count per 'g' caudal tissue, and testicular spermatid head count. For female rats, the parameters evaluated are terminal body weight, relative frequency of different estrous phases and the estrous cycle length.

STATISTICAL ANALYSIS: For male and female terminal body weights and male reproductive parameters, the significance of differences between control and dosed group response is as-sessed using the parametric multiple comparisons procedures of Williams and Dunnett. Jonckheere's test was used to assess the significance of dose-response trends. Trend sensitive tests were used when Jonckheere's test was significant at $p<0.01$. If the p-value from Jonckheere's test for a dose-related trend is greater than or equal to 0.10, Dunn's test is used. If the p-value is less than 0.10, Shirley's test is more appropriate.

The outlier test of Dixon and Massey was employed to detect extreme values. Implausible values, extreme values from ani-mals that were suspected of being sick due to causes other than treatment and values that were indicated to be inadequate due to measurement problems were

eliminated from analysis.

Treatment effects on vaginal cytology data are investigated by applying a multivariate analysis of variance (using Wilk's Criterion as the test statistic) to test for the simultaneous equality of measurements across dose levels. Since the data are proportions (the proportion of the observation period that an animal was in a given estrous phase), an arcsine transformation was used to bring the data into closer conformance with the normality assumptions required for the multivariate analysis of variance.

Remark : The decrase of the reproductive organ weights was secondary to the body weight decrease as demontrated by the absence of effect on the organ to body weight ratio.

Result : MALE RATS: There was a dose-related decrease in terminal body weights and the differences were significant at the 75 and 150 mg/kg dose levels. There was a significant decrease in left caudal absolute weights at the 150 mg/kg dose level and in left epididymal absolute weights at the 75 and 150 mg/kg dose levels. Epididymal sperm motility was significantly decreased for all three dose levels tested ($p<0.01$). Left testicular weights, epididymal sperm count per 'g' caudal tissue, total spermatid heads per testis and total spermatid heads per 'g' testis were not affected ($p>0.05$).

FEMALE RATS: There was a dose-related decrease in terminal body weights and the differences were significant at the 75 and 150 mg/kg dose levels ($p<0.01$). There was a significant difference with respect to the amount of time spent in estrous phases between controls and rats treated with 150 mg/kg 1,1,2,2-tetrachloroethane. This appeared to be primarily an increase in time spent in the diestrus phase. The average estrous cycle length was not affected ($p>0.05$).

Source : Atofina, Paris-la-Défense, France.

Conclusion : For male and female rats, terminal body weights were significantly decreased at the 75 and 150 mg/kg dose levels. There was a significant decrease in left caudal absolute weights at the 150 mg/kg level, in left epididymal absolute weights at the 75 and 150 mg/kg levels and in epididymal sperm motility at the 37, 75 and 150 mg/kg levels. For female rats, there was a significant difference with respect to the amount of time spent in estrous stages at the 150 mg/kg dose level when compared to the controls.

Reliability : (2) valid with restrictions

Flag : Critical study for SIDS endpoint

06.02.2002 (125)

Type : other: sperm motility and vaginal cytology evaluation
Species : mouse
Sex : male/female
Strain : B6C3F1
Route of admin. : other: oral feed (microencapsulated)
Exposure period : 13 weeks
Frequency of treatm. : ad libitum
Premating exposure period
Male :
Female :
Duration of test :
No. of generation studies :
Doses : 175, 700, 1400 mg/kg feed
Control group : yes, concurrent vehicle
NOAEL parental : = 175 ppm
Method : other: NTP, sperm motility and vaginal cytology evaluation
Year :
GLP :
Test substance :

Method : In a subchronic study, B6C3F1 mice were exposed to 1,1,2,2-tetrachloroethane via dosed feed. This report describes the "Sperm Motility Vaginal Cytology Evaluation" (SMVCE) portion of the subchronic study. For male mice, the reproductive endpoints evaluated are caudal, epididymal, and testicular weights, sperm motility, sperm count per 'g' caudal tissue, and testicular spermatid head count. For female mice, the parameters evaluated are terminal body weight, relative frequency of different estrous phases and the estrous cycle length.

STATISTICAL ANALYSIS: For male and female terminal body weights and male reproductive parameters, the significance of differences between control and dosed group response is as-sessed using the parametric multiple comparisons procedures of Williams and Dunnett. Jonckheere's test was used to assess the significance of dose-response trends. Trend sensitive tests were used when Jonckheere's test was significant at $p<0.01$. If the p-value from Jonckheere's test for a dose-related trend is greater than or equal to 0.10, Dunn's test is used. If the p-value is less than 0.10, Shirley's test is more appropriate.

The outlier test of Dixon and Massey was employed to detect extreme values. Implausible values, extreme values from ani-mals that were suspected of being sick due to causes other than treatment and values that were indicated to be inadequate due to measurement problems were eliminated from analysis.

Treatment effects on vaginal cytology data are investigated by applying a multivariate analysis of variance (using Wilk's Criterion as the test statistic) to test for the simultaneous equality of measurements across dose levels. Since the data are proportions (the proportion of the observation period that an animal was in a given estrous phase), an arcsine transformation was used to bring the data into closer conformance with the normality assumptions required for the multivariate analysis of variance.

Remark : The decrase of the reproductive organ weights was secondary to the body weight decrease as demontrated by the absence of effect on the organ to body weight ratio.

Result : MALE MICE: Terminal body weights were significantly decreased at the 700 and 1400 mg/kg dose levels ($p<0.01$). Left caudal and epididymal absolute weights were significantly decreased at the 1400 mg/kg dose level while left testicular absolute weights were significantly decreased at the 700 mg/kg dose level ($p<0.05$). The mean value for left testicular absolute weights at the 1400 mg/kg dose level was also decreased but was not statistically significant. Epididymal sperm motility was slightly decreased compared to controls and other dosed animals but this difference was found significantly different at the 1400 mg/kg dose level ($p<0.05$). Epididymal sperm count per 'g' caudal tissue was decreased in a dose-related manner for treated animals but these differences were not statistically significant. Total spermatid heads per testis and total spermatid heads per 'g' testis were not affected ($p>0.05$).

FEMALE MICE: Terminal body weights were significantly decreased at the 700 and 1400 mg/kg dose levels ($p<0.01$: Table 3). While the average estrous cycle length was significantly increased at the 1400 mg/kg dose level ($p<0.05$), estrual cyclicity was not affected ($p>0.05$).

Source : Atofina, Paris-la-Défense, France.

Conclusion : Terminal body weights were significantly decreased for both male and female mice at the 700 and 1400 mg/kg dose levels. Left caudal and epididymal absolute weights and epididymal sperm motility were significantly decreased at the 1400 mg/kg level and left testicular absolute weights were significantly decreased at the 700 mg/kg level. For female

mice, the average estrous cycle length was significantly increased at the 1400 mg/kg dose level.

Reliability : (2) valid with restrictions
Flag : Critical study for SIDS endpoint
06.02.2002 (125)

5.8.2 DEVELOPMENTAL TOXICITY/TERATOGENICITY

Species : rat
Sex : female
Strain : Sprague-Dawley
Route of admin. : oral feed
Exposure period : from gestation day 6 to 15
Frequency of treatm. : ad libitum
Duration of test : Sacrifice on gestation day 20
Doses : 0.045, 0.135, 0.270, 0.405 and 0.540% (equivalent to a daily intake of 34, 98, 180, 278 and 330 mg/kg bw/d, respectively)
Control group : yes, concurrent vehicle
NOAEL maternal tox. : < 34 mg/kg bw
NOAEL Fetotoxicity : = 34 mg/kg bw
Method : other: range finding developmental toxicity study
Year :
GLP : yes
Test substance : other TS: 1,1,2,2-tetrachloroethane, 98% purity

Method : Formulation

The microencapsulated test chemical was formulated according to procedures specified in the "Microencapsulation Report" of August 1989 by NIEHS for the 1,2-dichloroethylene feed studies. Meal feed was formulated at 105% of the desired dose levels due to a predicted loss of chemical when mixed. The microcapsules were 54% TCE which was taken into account during dosing formulations

Reference Analyses of Dosing Samples:

Dose group	Theoretical Concentration (percent)	Found Concentration (percent)	Percent of Theoretical
Control	0.0	0.0	---
0.0473%	0.473	0.473	100
0.142%	1.420	1.480	104
0.284%	2.840	2.880	101
0.425%	4.250	4.290	101
0.567%	5.670	5.770	102

Analyses were performed via a packed column gas chromatographic method by Research Triangle Institute, Research Triangle Park, NC.

Observations:

A. In-life

- bw on gd 4, 6, 9, 11, 14, and 16
- feed consumption gd 6-11 and gd 11-16
- overt signs of toxicity or mortality, twice daily

B. At Cesarean Section

- terminal body weight (gd 20)
- number of implantation sites
- number of resorptions
- number of dead fetuses
- number of live fetuses
- gravid uterine weight

Statistical Analysis:

Data were analyzed using nonparametric statistical methods to identify dose response trends among treatment groups, and differences between control and treated groups. Whenever possible the data are presented as mean t standard error. Kruskal-Wallis one-way analysis of variance by ranks was used to test for differences among dose groups for all parameters except gd 4 to gd 20 body weights and consumption data. Whenever the result of a Kruskal-Wallis test was significant ($p<0.05$), the Mann-Whitney Wilcoxan U test vas used to make individual comparisons between control and treated groups for the measure: a one-tailed test was used for all parameters except that maternal and fetal body weight parameters were examined in a two-tailed test. Jonckheere's test for k independent samples was employed to identify significant dose-response trends for gd 4 to gd 20 body weight data and consumption data. If no trend was found, Dunn's test was used for differences among dose groups. If a trend was detected, Shirley's test was applied.

Body weight data from non-pregnant animals were not included. Rats that were visibly pregnant only by ammonium sulfide staining were included only in the body weight and consumption data calculations.

Result : A. Maternal Toxicity

Signs of systemic toxicity were noted in the 0.540% and 0.405% dose groups. Maternal body weights were decreased in an almost dose-related manner beginning gd 9 and the differences were significant at 0.135% and higher levels ($p<0.05$) In the 0.045% group, the average body weight on gd 16 was significantly lower than the control group ($p<0.05$).

Maternal weight gain expressed as weight gain during treatment, and corrected weight gain decreased significantly ($p<0.05$) in all dose groups except the 0.045% group. Maternal weight gain during gestation decreased ($p<0.05$) in all dose groups with the exception of the 0.135% group.

Daily consumption values were significantly lower ($p<0.05$) in all dose groups. The reduced intake of feed in the 0.135% and higher dose groups ($p<0.05$), particularly for days 6-11, may have contributed to the decrease in body weights in these groups.

B. Developmental Toxicity

At scheduled sacrifice on gd 20, average fetal weight in all dose groups except the 0.045% group was decreased significantly relative to the control group ($p<0.05$). Gravid uterus weight was adversely affected ($p<0.05$) in the 0.540% dose group. One out of nine animals in the 0.135% group and four out of nine in the 0.540% group completely resorbed their litters.

Source : Atofina, Paris-la-Défense, France.

Conclusion : TCE treatment caused maternal toxicity at almost all dose levels tested. Maternal body weights were adversely affected in an almost dose-related manner beginning gd 9. Developmental toxicity in the form of decreased average fetal weight was noted at all dose levels except the 0.045% group. Also, an increase in totally resorbed litters was noted at the 0.54% dose level.

Reliability : (2) valid with restrictions

Flag : Critical study for SIDS endpoint
06.02.2002 (126)

Species : mouse
Sex : female
Strain : Swiss
Route of admin. : oral feed
Exposure period : from gestation day 6 to 15
Frequency of treatm. : ab libitum
Duration of test : Sacrifice on gestation day 20
Doses : First study: 4.0, 7.5 and 10.0%
Second study: 0.5, 1.0, 1.5, 2.0, 3.0% (equivalent to a daily intake of 987, 2120, 2216 and 4575 mg/kg bw/d, respectively)

Control group : yes, concurrent vehicle
NOAEL maternal tox. : = 987 mg/kg bw
NOAEL Fetotoxicity : = 987 mg/kg bw
Method : other: range finding developmental toxicity study
Year : 1991
GLP : no data
Test substance : other TS: 1,1,2,2-tetrachloroethane, 98% purity

Method : Dose Selection/Formulation

In an earlier study, TCE was tested at 0.0125, 0.05, 0.10, 0.20, and 0.30% levels. Due to a low rate of pregnancy (63% of experimental animals were not pregnant) and the lack of signs of maternal and/or developmental toxicity, TCE was retested. Dose levels selected for the repeat study were 1.5, 5.0 and 10.0%. The dosed feed was mistakenly formulated at levels of 4.0, 7.5, and 10.0% and the study initiated prior to detection of this error. All animals in these three groups died by gd 13. Based on these data, dose levels for the second repeat study were 0.5, 1.0, 1.5, 2.0, and 3.0%. Results of both repeat studies are described in this report.

The microencapsulated test chemical was formulated according to procedures specified in the "Microencapsulation Report" of August 1989 by NIEHS for the 1,2-dichloroethylene feed studies. Meal feed was formulated at 105% of the desired dose levels due to a predicted loss of chemical when mixed. The microcapsules were 54% TCE which was taken into account during dosing formulations.

REFERENCE ANALYSES OF DOSING SAMPLES:

Dose Group	Theoretical Concentration (mg/g)	Found Concentration (mg/g)	Percent of Theoretical
Control	0.0	0.0	----
0.50 %	5.00	5.45	109
1.00 %	10.00	11.30	113
1.50 %	15.00	18.10	121
2.00 %	20.00	23.60	118
3.00 %	30.00	36.90	123

Analyses were performed by a packed column gas chromatographic method by Research Triangle Institute, Research Triangle Park, NC.

OBSERVATIONS:

A. In-life

- bw on gd 4, 6, 9, 11, 14, and 16
- feed consumption gd 6-11 and gd 11-16
- overt signs of toxicity or mortality, twice daily

B. At Cesarean Section

- terminal body weight (gd 17)
- number of implantation sites
- number of resorptions
- number of dead fetuses
- number of live fetuses
- gravid uterine weight

STATISTICAL ANALYSIS:

Data were analyzed using nonparametric statistical methods to identify dose response trends among treatment groups, and differences between control and treated groups. Whenever possible the data are presented as mean ± standard error. Kruskal-Wallis one-way analysis of variance by ranks was used to test for differences among dose groups for all parameters except gd 4 to gd 17 body weights and consumption data. Whenever the result of a Kruskal-Wallis test was significant ($p<0.05$), the Mann-Whitney Wilcoxan U test was used to make individual comparisons between control and treated groups for the measure: a one-tailed test was used for all parameters except that maternal and fetal body weight parameters were examined in a two-tailed test. Jonckheere's test for k independent samples was employed to identify significant dose-response trends for gd 4 to gd 17 body weight data and consumption data. If no trend was found, Dunn's test was used for differences among dose groups. If a trend was detected, Shirley's test was applied. Data were analyzed, using the methods noted above, separately for each study. For example, the data for the animals in the 4.0, 7.5, and 10.0% groups were analyzed using the control animals from the same batch only.

Body weight data from non-pregnant animals were not included. Mice that were visibly pregnant by ammonium sulfide staining were included in the body weight calculations.

Result : A. Maternal Toxicity

All animals in the 4.0, 7.5, and 10.0% groups were found dead or were sacrificed for humane reasons by gd 13.

As previously mentioned, TCE was retested at 0.5 to 3.0% levels. Signs of systemic toxicity were noted in some animals in the 1.0% group and all animals in the 1.5% and higher groups during the twice daily health surveillances. At necropsy, abnormal livers were noted in females from the 0.5, 1.0, and 1.5% groups.

Maternal body weights at 0.5% and higher levels were decreased beginning gd 9 in a generally dose-related manner. Body weights were significantly decreased ($p<0.05$) in the 1.0% group gd 9 to 16, in the 1.5% groups on gd 11 and 14 and in the 2.0% group from gd 9 to gd 16. Two out of ten animals were sacrificed for humane reasons in the 1.0% group. Four out of five animals in the 1.5% group and five out of seven animals in the 2.0% group were found dead or were sacrificed for humane reasons. All nine animals in the 3.0% group were sacrificed for humane reasons by gd 12.

Maternal weight gain expressed as weight gain during gestation, weight gain during treatment, and corrected weight gain were statistically decreased ($p<0.05$) at the 1.0% level. Weight gain during treatment also

decreased (p<0.05) at the 2.0% dose level. The presence of only one animal at necropsy at the 1.5% level precluded statistical analysis.

B. Developmental Toxicity

As previously mentioned, all experimental animals in the 4.0, 7.5, and 10.0% groups died prior to the scheduled necropsy on gd 17.

At scheduled necropsy in the second repeat study, one out of eleven animals in the control group, two out of eight animals in the 1.0% group, the only pregnant animal in the 1.5% dose group and one out of the two animals in the 2.0% dose group had completely resorbed their litters. The other animal in the 2.0% group had fewer live fetuses per litter, and increased resorptions and non-live implants per litter when compared to the control values. However, these parameters were not statistically analyzed due to the presence of the one animal. All other endpoints were similar to control values.

C. Feed Consumption

The average daily feed consumption was adversely affected (p<0.05) in almost all dose groups except the 0.5% level.

Source : Atofina, Paris-la-Défense, France.
Conclusion : TCE treatment caused significant maternal toxicity in the form of maternal deaths and decreased (p<0.05) body weights at all levels 1.0% and higher. Indeed an MTD for TCE could not be reached due to the decreased feed consumption which compromised the study. Mortality was 100% at the 3.0% and higher levels. Developmental toxicity was evident in the form of completely resorbed litters at the 1.0% and 2.0% levels.
Reliability : (2) valid with restrictions
Flag : Critical study for SIDS endpoint
06.02.2002 (127)

Species : mouse
Sex : female
Strain : other: AB-Jena and DBA
Route of admin. : i.p.
Exposure period : 1-14 days of gestation
Frequency of treatm. : single daily injections on day 1-14 or day 7-14 or day 9 of gestation
Duration of test : mouse gestation period
Doses : 300, 400 and 700 mg/kg/day
Control group : yes
NOAEL teratogen. : >= 300 mg/kg bw
Method : other: not specified
Year : 1976
GLP : no data
Test substance : as prescribed by 1.1 - 1.4

Remark : The study suffers from several important limitations :
- Maternal effects were not described, allowing no judgment on potential maternal toxicity interference on the developmental toxic findings while high doses were used;
- Data on foetuses were poorly reported (only bodyweight given); no details on malformations observed in each group (only number and % shown in tabular form.
- There is no statistical evaluation ;
- Non-pertinent route of administration was used ;
- Dose-relationship cannot be established as each dose was allocated to a different timing of treatment during pregnancy: 300 mg/kg on day 1-14 ; 400 mg/kg on day 7-14 ;

and 700 mg/kg on day 9.

Result : NOAEL maternal toxicity : there was no maternal data
NOAEL embryofetal toxicity : 300 mg/kg
NOAEL teratogenicity : 300 mg/kg

Some embryotoxic effects (increased postimplantation lost versus controls) was found in the AB-Jena strain in the 400 and 700 mg/kg groups ; no effects were seen in the DBA strain.
Fetal bodyweight were similar in control and all treatment groups.

Teratogenic data were as lollowing :

STRAIN AB-Jena :

Days of gestation	ip dose(mg/kg/day)	% malformations
-	Controls	0.67
1-14	Placebo-controls	2.40
1-14	300	0.50
7-14	400	1.72
9	700	9.39

STRAIN DBA :

Days of gestation	ip dose(mg/kg/day)	% malformations
-	Controls	0.47
1-14	Placebo-controls	2.20
1-14	300	3.25
7-14	400	4.82
9	700	2.59

Based on these data the authors concluded that the test material is a faintly teratogenic compound.

Source : ATOFINA Paris la Defense,France
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)

Test condition : TEST ORGANISM :
- Age : 10-12 weeks virgin females
- Number of animals : 25-30 females/treatment groups ; 37-78 / control groups

ADMINISTRATION/EXPOSURE :
- Vehicle : olive oil

MATING PROCEDURE :
- Vaginal proof method

PARAMETERS ASSED DURING STUDY :
- Bodyweight/ Clinical signs/ food consumption: no data
- Examination of uterine content : number of implantations ; pre and post implantation lost ; early, medium and late resorption
- Examination of fetuses : bodyweight ; gross and skeletal malformations

ORGANS EXAMINED AT NECROPSY : none

STATISTICAL METHOD : none

Reliability : (3) invalid

significant methodological deficiencies

Flag : Critical study for SIDS endpoint
19.06.2001 (128)

Species	:	rat
Sex	:	male
Strain	:	no data
Route of admin.	:	inhalation
Exposure period	:	9 months before mating
Frequency of treatm.	:	4h/d ; 5d/wk
Duration of test	:	
Doses	:	13.3 mg/m3 (1.94 ppm)
Control group	:	yes
NOAEL teratogen.	:	> 13.3 mg/m³
Method	:	other
Year	:	1972
GLP	:	no data
Test substance	:	as prescribed by 1.1 - 1.4

Method : Males exposed during 9 months were mated with untreated females. Gravid females were allowed to deliver and F1 offsprings were followed up to sexual maturation.

Result : NOAEL : > 13.3 mg/m3
- Maternal data :
There was no statistical difference between females sired by exposed males and females sired by control males on number of gravid females and any of the gestational parameters measured

-Offspring data :
There was no statistically significant difference between results of offsprings from the exposed father group and offsprings from the control father group on any of the measured parameter.
There was no gross malformations.

Source : ATOFINA Paris la Defense,France
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)

Test condition : PROTOCOLE:
One week before the end of the 9th month of inhalation exposure, the male rats were mated with untreated virgin females.

TEST ORGANISM:
- Number : 7 control and 7 exposed male rats were mated each one with 5 virgin females
- Weight at start of mating : females : 250-300 g

PARAMETERS ASSED DURING STUDY:
- Number and % pregnant females
- Number of offsprings delivered
- Number of offsprings per litter
- Mean neo-natal offspring weight per litter
- survival at days 1, 2 7 14 21 and 84 after birth
- Weight and sex/ration at day 84
- gross external malformations

ORGANS EXAMINED AT NECROPSY : none

STATISTICAL METHOD :
- Standard Student t-Test

Reliability : (3) invalid
significant methodological deficiencies (dams no treated during pregnancy)
Flag : Critical study for SIDS endpoint
19.06.2001 (85)

5.8.3 TOXICITY TO REPRODUCTION, OTHER STUDIES

5.9 SPECIFIC INVESTIGATIONS

5.10 EXPOSURE EXPERIENCE

Remark : Experience in human was reported from numerous cases of suicidal or accidental poisonings mainly by oral and inhalation exposures, and from cases of chronic intoxications in workers or studies on volunteers exposed by inhalation and dermal contacts. Limited epidemiological surveys in workers are available. Many reviews of this large human experience on 1,1,2,2-tetrachloroethane are available (BUA, 1989 ; Lauweris, 1990 ; ACGIH, 1991 ; ATSDR, 1995 ; INRS, 1997 ; IARC, 1999). They can be summarised as following :

ACUTE/SUB-ACUTE INTOXICATION :
Acute intoxication by 1,1,2,2-tetrachloroethane may combine the following :
- Signs of mucosae irritation : digestive signs if ingested ; respiratory and ocular signs if inhaled.
- Signs of depression of the central nervous system: confusion, loss of equilibrium, drowsiness, then coma, sometimes with convulsions..
- Liver cytolysis with, occasionally, renal tubular damages.
- Contacts with skin induces orthoergic irritation.

CHRONIC TOXICITY :
The initial phase may include : fatigue, sweating, anorexia, digestive troubles.
After a latency period of several days/weeks the following damages occur :
- liver : hepatitis, often icteric and initially apyretic, cirrhosis.
- kidney : nephritis
- nervous system (less frequently): central effects (tremor, headache, asthenia, mood troubles) and peripheral effects (tip polynevritis, cranial nerves damages)
- hematological effects (less frequently and sometimes late): hyperleucocytosis, mononucleosis, lymphocytosis, thrombocytosis, anemia.

EPIDEMIOLOGY :
No excess of cardiovascular lesions were observed in a study on 75 workers exposed in a plant production (mean exposure : 2.5 to 22 mg/m3 ; peaks of 275 mg/m3). Neurological signs (mainly tremor) and epigastric symptoms but not jaundice were seen in a survey of 380 workers exposed to

1,1,2,2-tetrachloroethane in pearl manufacturing plants (exposures from 63 to 686 mg/m3). There was no significant excess of cancer mortality in a cohort of 3859 army personel exposed to 1,1,2,2-tetrachloroethane (exposure not measured) used as a clothing impregnation solvent during World war II. Due to confounding factors the small excess of genital cancer and leukemia could not be confidently associated with the use of 1,1,2,2-tetrachloroethane.

QUANTITATIVE DATA :
Oral : fatalities from 285 to 6000 mg/kg ; LOAEL : 100 mg/kg
Inhalation : odor detected at 20 mg/m3 ; NOAEL /10 minutes : 90 mg/m3 ; LOAEL /30 minutes : 1000 mg/m3
ACUTE, SUB-ACUTE, CHRONIC TOXICITY, EPIDEMIOLOGY, QUANTITATIVE DATA

Source : Atofina Paris la Defense
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
20.06.2001 (129) (130) (131) (86)

5.11 ADDITIONAL REMARKS

Type : adsorption

Remark : 1,1,2,2-Tetrachloroethane is readily adsorbed by all routes of exposure: inhalation, dermal and oral

Source : ATOFINA Paris la Defense,France
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
21.06.2001 (132) (133) (86) (134)

Type : Excretion

Remark : Respiration is the route of excretion for non-transformed 1,1,2,2-tetrachlororethane, volatile metabolites and terminal metabolite CO2. Most of the metabolites are excreted by the urinary route. In mice, urinary metabolites represent about 1/3 of the absorbed dose.

Source : ATOFINA Paris la Defense,France
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
21.06.2001 (135) (132) (133) (86)

Type : Metabolism

Remark : Minute amount of tri- and tetrachloroethylen are formed. Trichloroethanol, trichloroacetic and dichloroacetic acids are the next step metabolites. Then oxalic and glyoxilic acids are the last step before urea and CO2. Part of metabolism occurs in liver via cytochrome P450 enzymatic processes.

Source : ATOFINA Paris la Defense,France
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
21.06.2001 (136) (137) (138) (86)

Type : Neurotoxicity

Remark : Humans exposed to high levels of 1,1,2,2-tetrachloroethane vapours or who have accidentally ingested it get effects including : tremors, headache, numbness, drowsiness,dizziness or even loss of consciousness.

Specific exposure levels and length of exposure were not measured, but air concentrations were measured between 9 an 98 ppm (60 to 700 mg/m3).
Inhalation or oral exposure of animals has resulted similarly in effects including narcosis, decrease of motor activity or ataxia, and learning ability inhibition.

Source : ATOFINA Paris la Defense,France
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