FOREWORD INTRODUCTION

2-CHLOROTOLUENE

CAS N°: 95-49-8

SIDS Initial Assessment Report for 11th SIAM

(Orlando, USA, 23-26 January 2001)

Chemical Name : 2-Chlorotoluene

CAS No : 95-49-8

Sponsor Country : Germany

National SIDS Contact Point in Sponsor Country
Lead Organization:

Name of lead organization: BMU (Bundesministerium für Umwelt, Naturschutz und Reaktorsicherheit)

Contact person: Prof. Dr. Ulrich Schlottmann
Address: Postfach 12 06 29
D- 53048 Bonn- Bad Godesberg

History: see next page;

Testing: No new SIDS testing (X)

New SIDS testing ( )

Comments:

Deadline for circulation: 10 November 2000

Date of Circulation: 10. November 2000

SIDS INITIAL ASSESSMENT PROFILE

CAS No.	95-49-8
Chemical Name	2-Chlorotoluene
Structural Formula	

RECOMMENDATIONS

Human Health: If substantial exposure cannot be ruled out, there is need for further work.

Environment: The substance is a candidate for further work.

SUMMARY CONCLUSIONS OF THE SIAR

Human Health

The acute oral toxicity: LD_{50} (Rat, male): 3227 mg/kg bw; LD_{50} (Rat, female): 3860 mg/kg bw
The acute inhalation toxicity: LC_{50} (Rat): 37517 mg/m^3 (4 h)
The acute dermal toxicity: LD_{50} (Rat): > 1083 mg/kg bw; LD_{50} (Rabbit): > 2165 mg/kg bw
2-Chlorotoluene, tested according to OECD Guideline 404, is slightly irritating to the skin. However, when tested under occlusive conditions, the substance is corrosive.
2-Chlorotoluene, tested according to OECD Guideline 405, was irritating to the eye in 1 out of 3 animals.
2-Chlorotoluene, tested according to OECD Guideline 406, is not sensitizing to the skin of guinea pigs.

The NOEL for repeated dosing (3 months) by gavage in rats is 20 mg/kg bw. In higher dosage (80 or 320 mg/kg bw) unspecific signs of toxicity were observed, e.g. reduced body weight gain in male animals, elevated BUN, elevated WBC count, reduced prothrombin time.

The NOEL for repeated dosing via capsule (3 months) in dogs is 20 mg/kg bw. In higher dosage (80 mg/kg bw) one animal showed vomiting, and red blood was detected in faeces, which might be due to the slightly irritating property of 2-chlorotoluene.

In range finding study tests, the LOAELs after inhalation were 4 mg/l (approx. 4000 mg/m^3, 14 d) in rats and 8 mg/l (approx. 8000 mg/m^3, 23 d) in rabbits. There is no NOEL from these data.

2-Chlorotoluene showed no mutagenic activity in bacterial and in mammalian cell test systems *in vitro*.
2-Chlorotoluene showed no clastogenic activity *in vitro* and *in vivo*.

Regarding reproductive toxicity there are 3 months-studies on rats and dogs which evaluated also the reproductive organs.

In the rat study, males and females received 2-chlorotoluene 0, 20, 80, or 320 mg/kg bw solution by gavage for 103-104 days. Gross and histological evaluation revealed that the administration of 2-chlorotoluene to rats did not produce any treatment-related pathology in these organs. Histopathologic examination of the reproductive organs showed that in 1/20 male rats and in 3/20 female rats in the lowest dose group testicular atrophy or hydrometra occurred.

In the dog study, males and females received 0, 5, 20, or 80 mg/kgbw as via capsule for 95-96 days.

Also in this study, there were no treatment related changes regarding gross examination of the organs, and the histological examination showed no pathological alteration.

However, there are data from structurally related compounds showing effects on fertility.

Developmental toxic effects in rats and rabbits occur in the presence of maternal toxicity and without a clear dose-response relationship, however as a specific malformation, brachydactyly.

Rats: NOAEL: 1.0 mg/l (maternal toxicity) and no NOAEL, LOAEL 1.1 mg/l (developmental toxicity)
Rabbit: NOAEL: 1.0 mg/l (maternal toxicity) and 4 mg/l (developmental toxicity)

Environment

2-Chlorotoluene is a colourless liquid, with a solubility in water of 47 mg/l and with a vapour pressure of 360 Pa at 20 °C. The log Kow was measured to 3.42.

The favourite target compartment for 2-chlorotoluene is air with 98.8 % according to Mackay I. In air 2-chlorotoluene is indirectly photodegradable with $t_{1/2}$ = 8.8 d. The substance is not readily biodegradable. Nevertheless under the conditions of sewage treatment plants the substance will be eliminated by stripping and adsorption. Hydrolysis is not expected to occur under environmental conditions. The bioconcentration factor in fish was measured to 20-112.

2-Chlorotoluene has to be classified as toxic to aquatic organisms. In short-term tests the most sensitive organism was Oncorhynchus mykiss with a 96 h-LC_{50} of 2.3 mg/l. In long-term ecotoxicity tests with aquatic organisms the following effect values were found:

- *Pimephales promelas*: 30d-NOEC = 1.4 – 2.9 mg/l
- *Daphnia magna*: 21d-NOEC = 0.14 mg/l
- *Scenedesmus subspicatus*: 72h-EbC50 > 100 mg/l; 72h-EbC10 = 60 mg/l

The result from the long-term daphnia study is based on measured concentrations.

With an assessment factor of 10 a PNECaqua of 0.014 mg/l was derived.

From ecotoxicity tests with terrestrial plants a PNECsoil of 89 µg/kg can be derived.

Exposure

130,000 t/a chlorotoluenes are produced worldwide, about 60,000 to 70,000 t/a o-chlorotoluene.

In Germany, Bayer AG is the only producer of 2-chlorotoluene. 10,000 to 50,000 t/a chlorotoluene isomer mixture is produced at Bayer AG. More than 50 % of the produced isomer mixture is processed on-site to cresoles. About 5,000 t/a 2-chlorotoluene are separated from the isomer mixture for serving as basic chemical in the chemical industry for producing intermediates. 2-chlorotoluene is also directly used as a solvent for chemical processing as well as a solvent for the formulation of agricultural pesticides.

NATURE OF FURTHER WORK RECOMMENDED

Human Health: The route and level of possible exposure has to be clarified. Depending on the level of exposure further data on toxicity to reproduction are necessary.

Environment: The relevance of the releases to the terrestrial compartment due to the use as solvent in agricultural pesticides should be clarified.

FULL SIDS SUMMARY

CAS NO: 95-49-8		SPECIES	PROTOCOL	RESULTS
PHYSICAL-CHEMICAL				
2.1	Melting Point			- 36.5 °C
2.2	Boiling Point			159.3 °C (at 101.3 kPa)
2.3	Density			1.08 g/cm^3 (20 °C)
2.4	Vapour Pressure			0.36 kPa at 20 °C
2.5	Partition Coefficient (Log Pow)			3.42 (exp.)
	BCF	Cyprinus carpio	Meth. corr. to OECD 305 C	20 – 112
2.6 A.	Water Solubility			47 mg/l at 20 °C
B.	pH			
	pKa			
2.12	Oxidation: Reduction potential			
ENVIRONMENTAL FATE AND PATHWAY				
3.1.1	Photodegradation		Calculated (acc. to Atkinson)	In air $T_{1/2}$ = 8.83 d * (24 hr-day; 0.5 * 10^6 OH/cm^3) * under the conditions in Western Europe
3.1.2	Stability in Water			
3.2	Monitoring Data			In air = mg/m^3 In surface water = < 0.02 and < 0.1 µg/l In soil/sediment = mg/g In biota = mg/g
3.3	Transport and Distribution		Henry-constant (Bond Contribution method)	4.47*10^{+02} (Pa*m^3/mol)
			(Group Contribution method)	4.94*10^{+02} (Pa*m^3/mol)
			Calculated (Fugacity Level 1 type acc. to Mackay)	In Air 98.8 % In Water 0.8 % In Sediment 0.2 % In Soil 0.2 % In Biota < 0.1 %
3.5	Biodegradation	Predominantly domestic sewage, adapted	Dir. EEC 79/831 Respirometer-test, corr. OECD 301 F	0 % after 28 d
		Predominantly domestic sewage, adapted	OECD 302 B "Mod. Zahn-Wellens-Test"	82 % after 7 d 86 % after 28 d

CAS NO: 95-49-8		SPECIES	PROTOCOL	RESULTS
ECOTOXICOLOGY				
4.1	Acute/Prolonged Toxicity to Fish	Oncorhynchus mykiss	Flow through; US-EPA approved protocol	LC_{50} (96 hr) = 2.3 mg/l
		Oryzias latipes	Japan. JIS K 0102-1986-71	LC_{50} (48 hr) = 9.6 mg/l
		Alburnus alburnus (fish, astuary)	no test method specified	LC_{50} (96 hr) = 6.7 - 9.1 mg/l
4.2	Acute Toxicity to Aquatic Invertebrates	Daphnia magna	DIN 38 412 Part 11	EC_{50} (24 hr) = 20 mg/l, EC_0 (24 hr) = 9 mg/l
		Nitocra spinipes	no test method specified	EC_{50} (96 hr) = 40 - 50 mg/l
4.3	Toxicity to Aquatic Plants e.g. Algae	Scenedesmus subspicatus	DIN 38 412 Part 9	E_bC_{50} (72 hr) => 100 mg/l
4.5.1	Chronic Toxicity to Fish	Pimephales promelas	ELS; US-EPA approved protocol	NOEC (30 d) = 1.4 - 2.9 mg/l
4.5.2	Chronic Toxicity to Aquatic Invertebrates	Daphnia magna	UBA-Verf.-vorschlag 1984: Prolonged toxicity test on D. magna	Reproduction: NOEC (21 d) = 0.14 to 0.27 mg/l LOEC (21 d) = 0.27 to 0.55 mg/l
			US-EPA approved protocol, 1984	NOEC (21 d) survival = 0.08 mg/l NOEC (21 d) reprod. = 0.21mg/l
4.6.1	Toxicity to Soil Dwelling Organisms			No data available
4.6.2	Toxicity to Terrestrial Plants	Avena sativa	Guideline of German Biologische Bundesanstalt	EC_{50} (14 d) = 89 mg/kg soil dw
		Brassica rapa	Guideline of German Biologische Bundesanstalt	EC_{50} (14 d) > 1000 mg/kg soil dw
4.6.3	Toxicity to Other Non-Mammalian Terrestrial Species (Including Birds)	Gallus domesticus		LC_0 (14 d) = 2710 mg/kg bw (male) LC_0 (14 d) = 2710 mg/kg bw (female) LC_{50} (14 d) = 5410 mg/kg bw (male) LC_{60} (14 d) = 5410 mg/kg bw (female)
		Anas platyrhynchos		LC_0 (14 d) = 5410 mg/kg bw (male) LC_0 (14 d) = 5410 mg/kg bw (female)
		Colinus virginianus		LC_0 (14 d) = 5410 mg/kg bw (male) LC_0 (14 d) = 5410 mg/kg bw (female)

TOXICOLOGY				
5.1.1	Acute Oral Toxicity	Rat male Rat female		LD_{50} = 3227 mg/kg LD_{50} = 3860 mg/kg
5.1.2	Acute Inhalation Toxicity	Rat	Exposure time: 4 h	LC_{50} = 37517 mg/m^3
5.1.3	Acute Dermal Toxicity	Rat Rabbit	Exposure time: 24 h Exposure time: 24 h	LD_{50} = > 1083 mg/kg LD_{50} = > 2165 mg/kg
5.2	Corrosiveness and Irritation			
5.2.1.	Skin Irritation	Rabbit	OECD 404	slightly irritating
		Rabbit	Patch-Test occlusive Exposure time: 24 h	Moderately irritating
5.2.2.	Eye Irritation	Rabbit	OECD 405	slightly irritating in 1/3 animals
5.3.	Sensitization	Guinea pig	OECD 406	not sensitizing
5.4	Repeated Dose Toxicity	Rat	Gavage, 3 months (103-104 d)	NOEL = 20 mg/kg
		Dog	Capsule, 3 months (96 rsp. 95 d)	NOEL = 20 mg/Kg
		Rat	Inhalation, 14 d	LOAEL = 4000 mg/m^3
		Rabbit	Inhalation, 23 d	LOAEL = 8000 mg/m^3
5.5	Genetic Toxicity In Vitro			
A.	Bacterial Test (Gene mutation)	Salmonella typhimurium TA98, 100, 1537, 1538, 1535	Ames test	- (with metabolic activation) - (without metabolic activation)
B.	Non-Bacterial In Vitro Test (Chromosomal aberrations)	Chinese Hamster Ovary cells		- (with metabolic activation) - (without metabolic activation)
	Non-Bacterial In Vitro Test	Mouse Lymphoma L5178Y TK +/- cells		- (with metabolic activation) - (without metabolic activation)
5.6	Genetic Toxicity In Vivo			
	Cytogenetic assay	Mouse bone marrow cells	single application by gavage	-
	Cytogenetic assay	Mouse bone marrow cells	5 applications by gavage	-
5.8	Toxicity to Reproduction	no data	see: Additional information	
5.9	Developmental Toxicity/ Teratogenicity	Rat, female	Inhalation, d 6 – 19 of gestation	NOAEL = 1.1 mg/l (maternal toxicity) LOAEL = 1.1 mg/l (foetal toxicity)
		Rabbit, female	Inhalation, d 6 - 28 of gestation	NOAEL = 1.5 mg/l (maternal toxicity) NOAEL = 4 mg/l (foetal toxicity)
5.11	Experience with Human Exposure			

Additional Information

Toxicity to Reproduction

There are no specific studies on toxicity to reproduction.

There are carefully performed 3 months-studies on rats and dogs which evaluated also the reproductive organs.

In the rat study, males and females received 2-chlorotoluene 0, 20, 80, or 320 mg/kg bw as a 5 % acacia solution by gavage for 103-104 days. Examination of the means of the absolute organ weights of the reproductive organs for rats showed that none of these weights differ significantly from the controls. Gross and histologic evaluation revealed that the administration of 2-chlorotoluene to rats did not produced any treatment-related pathology in these organs. Histopathologic examination of the reproductive organs (testes or uterus and ovaries) showed that in 1/20 male rats and 3/20 female rats in the lowest dose group, given doses of 20 mg/kg bw, testicular atrophy or hydrometra occurred.
In the dog study, males and females received 0, 5, 20, or 80 mg/kg bw as a 5 % acacia solution via capsule for 95-96 days. Also in this study, there were no treatment related changes on reproductive organ weights of the dogs. The gross examination of the organs and the histological examination showed no pathological alteration induced by 2-chlorotoluene.
In an acute oral toxicity study report with rats, given doses of 2700-10800 mg/kg bw reduced spermatogenesis was mentioned. This observation is regarded to be due to the systemic toxicity of these extremely high doses.

Based on the observations in the 3-month-studies on rat and dog, there is no indication that 2-chlorotoluene affects the reproductive organs. However, since there is no additional supporting information and higher chlorinated benzene derivatives have shown effects on fertility without histopathological correlate, further data are necessary if substantial exposure cannot be ruled out.

OECD/ICCA - The BUA* Peer Review Process

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

- a full (or update) literature search to verify completeness of data provided by industry in the IUCLID/HEDSET
- Review of data and assessment of the quality of data
- Review of data evaluation
- Check of adequacy of selection process for key studies for OECD endpoints, and, where relevant, for non-OECD endpoints by checking original reports/publications
- Review of key study description according robust summaries requirements; completeness and correctness is checked against original reports/publications (if original reports are missing: reliability (4) not assignable)
- Review o f validity of structure-activity relationships
- Review of full SIDS dossier (including SIAR, SIAP and proposal for conclusion and recommendation for further work)

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

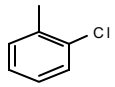
* BUA (GDCh-Beratergremium für Altstoffe): Advisory Committee on Existing Chemicals of the Association of German Chemists (GDCh)

SIDS INITIAL ASSESSMENT REPORT

1. IDENTITY

CAS Number	95-49-8
Name	2-Chlorotoluene
Molecular formula	C_7H_7Cl

Structure:



Physico-chemical properties:

2-Chlorotoluene is a colourless liquid with a melting point of -36.5 °C and a boiling point of 159.3 °C. With a density of 1.08 g/cm³ 2-chlorotoluene is heavier than water (Ullmann 1986). The solubility of the substance in water was experimentally detected with 47 mg/l (Bayer AG 1987). The vapour pressure of the substance is 360 Pa (Verschueren 1996). The measured log K_{ow} is 3.42 (Leo et al. 1971). These data relate to 20 °C.

The purity of the substance is given with > 99 % w/w.

2. GENERAL INFORMATION ON EXPOSURE

130,000 t/a chlorotoluenes are produced worldwide, about 60,000 – 70,000 t/a o-chlorotoluene.

In Germany Bayer AG is the only producer of 2-chlorotoluene.

There, 2-chlorotoluene is produced continuously by converting toluene with chlorine under moderate temperature and normal pressure in the presence of a catalyst. This gives a crude product with the isomeric ratio of chlorotoluenes depending on temperature and the catalyst. A part of this isomer mixture is processed directly, the other part is used for gaining the isomers by fractional distillation.

10,000 to 50,000 t/a chlorotoluenes isomer mixture is produced at Bayer AG. More than 50 % of the produced isomer mixture is processed on-site to cresoles. Production and processing takes place in closed systems. Cresoles are further used for the production of flame retardants, plasticizers, agrochemicals, material preservatives, thermal oils, fragrances, condenser fluids, and anti-aging agents.

About 5,000 t/a 2-chlorotoluene are separated from the isomer mixture at Bayer AG for serving as a basic chemical in the chemical industry for producing intermediates. The West European market of 2-chlorotoluene breaks down to intermediates such as cresols (about 50 %), 2-chlorobenzaldehyde (about 30 %), mixed dichlorotoluenes (about 15 %), 2-chlorobenzoic acid (about 2 %), 2-chlorobenzonitrile (about 2 %), and 2-chlorobenzylchloride (about 1 %). These intermediates are further used i.e. in the production of coloring agents, agrochemicals, and pharmaceuticals. 2-Chlorotoluene can be used as a solvent for chemical processing as well as a solvent for the formulation of agricultural pesticides (Federal Register 1982). A mixture of isomeric chlorotoluenes is used as a solvent in “SPLENDOR”, a formulation of the herbicide tralkoxydime.

In older japanese patent literature (1971 and 1979) it is reported that 2-chlorotoluene could be used as a desinfecting agent for coccidomycosis disease in fowls and as an insecticide for application to latrine and sewage treatment plants. Because of the restricted information on human exposure it should be clarified whether the products are still on the market in Japan.

Furthermore, during the period for commenting it should be clarified whether human exposure and, in particular, consumer exposure results from the use in Switzerland and Japan. Dependent on the outcome of exposure assessment, it should be considered whether the statement under chapter 3.2.10 “Toxicity on Reproduction” is still appropriate.

2.1 Environmental Exposure and Fate

Environmental Exposure

In Germany, there are two Bayer AG sites involved in production and processing of chlorotoluenes.

Weekly monitoring data at the release of the industrial sewage treatment plant into the receiving river Rhein showed no emission of 2-chlorotoluene from production and processing in 1999 through July 2000 on the basis of the determination limit of 2 µg/l. On the second processing site daily monitoring data at the release of the industrial sewage treatment plant into the receiving river Rhein showed no emission of 2-chlorotoluene in 1998 and 1999 on the basis of the determination limit of 1 µg/l.

The exhaust from production and processing of chlorotoluenes at the Bayer AG sites are connected to a thermal exhaust purification plant (TAR). Thus during normal operation of the TAR no 2-chlorotoluene is emitted. In 1998 to July 2000 less than 25 kg/a 2-chlorotoluene were emitted into the atmosphere. This amount is the limit in Germany above which emissions into the atmosphere have to be notified to the local authorities.

In Germany the river Rhein and its tributary Neckar has been monitored at different places for 2-chlorotoluene with determination limits of 0.02 and 0.1 µg/l depending on the state institute where the analysis was carried out. No 2-chlorotoluene has been found in 1996 through 1998. Alike no 2-chlorotoluene has been found in the Donau with a determination limit of 0.02 µg/l.

In France, in the Picardie region the effluents of industrial sites were monitored for several chemical substances (DRIRE Picardie, 1998). A single 24 h mixing sample was taken at each site. The results are summarized in the following table:

Industrial activity	**Conc. in effluent [µg/l]**	**Daily release [g/d]**
Chemical industry	1 (date: 24/09/96)	0.21
Paint manufacturing	40 (date: 14/09/95)	2.92

Exposure to the terrestrial compartment may occur due to the use of 2-chlorotoluene as solvent in agricultural pesticides. However, as neither the volume used as solvents for herbicides is known nor information on the applied dosages of the herbicides that contain 2-chlorotoluene is available, no estimation of soil exposure is possible at present.

Environmental Distribution and Fate

With regard to its chemical structure 2-chlorotoluene is not expected to hydrolyse under environmental conditions.

According to Mackay Level I, the favourite target compartment for 2-chlorotoluene is air with 98.8 %. A high volatility from water to air is also indicated by the Henry constant of 447 and 494 Pa m^3 mol^{-1} (depending on the calculation method; Bayer AG 1999).

The indirect photodegradation of 2-chlorotoluene in air is calculated according to Atkinson with $t_{1/2}$ = 8.8°d (Bayer AG 1999). Long-range distribution via the atmosphere is therefore possible.

2-Chlorotoluene has to be classified as not readily biodegradable. In a respirometer test corresponding to OECD 301 F with adapted inoculum 0 % biodegradation was observed after 28 days (Bayer AG 1991a).

In a Zahn-Wellens test (OECD 302B) the substance was eliminated to 86 % within 28 days. Due to the rapid elimination (64 % after 3 hours) it can be assumed that elimination took place through stripping and adsorption effects, however no further information is given in the study (Bayer AG 1991b).

According to the model Simpletreat 89 % of 2-chlorotoluene will be eliminated in sewage treatment plants by stripping and adsorption.

The soil sorption tendency was determined in a test according to OECD 106. The adsorption constant K_{oc} was determined to be 346 - 397. The soil samples (sand, sandy loam and loamy sand) showed a content of organic carbon from 0.7 to 2.29 % (Bayer AG 1992). Banerjee et al. (1985) determined an average K_{OC} value of 370 for the sorption of 2-chlorotoluene to a low carbon subsurface core. In soil it is supposed that 2-chlorotoluene would be moderately mobile. Regarding sewage, suspended solids, and sediment in water it is supposed that

2-chlorotoluene would adsorb moderately, too.

An experimental bioconcentration factor on fish (Cyprinus carpio) of 20 - 112 is given (MITI 1992).

2.2 Human Exposure

In Germany/Europe no workplace limit concentration is laid down. At Bayer AG the exposure is well below the value of 50 ppm (= 259 mg/m³) which is in consistency with the US TLV/TWA value. Measurements within the scope of the monitoring duty according to the Gefahrstoff-Verordnung (German Dangerous Substances Regulations) were below 1 mg/m³ for production and processing in 1995 to 1999.

3. HUMAN HEALTH HAZARDS

3.1 Hazard Assessment Experience with Human Exposure

3.1.1 Experience with human exposure

An earlier occupational health study reported that 60 minutes of workplace exposure to 400 ml of a mixture of 2- and 4-chlorotoluene/m^3 (2100 mg/m^3) caused severe symptoms of poisoning. Short-term exposure to a concentration of 200 ml/m^3 (1050 mg/m^3) resulted in symptoms of illness (no further details) (Goldblatt 1955).

3.2 Effects on Human Health

3.2.1 Acute oral toxicity

There is no study according to the current OECD Test Guideline, but there is an earlier study which is carefully performed and gives sufficient information to evaluate this end-point (Bayer AG 1976): LD_{50} (male rat): 3227 mg/kg; LD_{50} (female rat): 3860 mg/kg bw. Until the 10th day post application the animals showed poor general condition which was for at least 3 days accompanied by difficulties in breathing and sedation. At necropsy, 14 days post application, the following effects were observed: the abdominal organs showed reduced size, especially the liver. The mucous membrane of the stomach showed focus of inflammation and the stomach content appeared to be bloody.

Conclusion: The acute oral toxicity is low.

3.2.2 Acute inhalation toxicity

There is no study according to the current OECD Test guideline, but there is a study report which give sufficient information to evaluate this endpoint (Hazleton 1972): LC_{50} (male rat): 7119 ppm or 37.517 mg/l. During exposure and until 24 days post exposure the animals showed hypoactivity, dyspnea, abdominal respiration, exsudation from eyes and nose, tremor and prostration. An uneven coloration on the surface of the lungs and liver and foci of red and black discoloration on the surface of the lungs was found at necropsy.

Conclusion: The acute toxicity via inhalation is low. In the EU, labelling and classification in the Dangerous Substance Regulation is Xn (harmful) and R 20 (harmful to health when inhaled).

3.2.3 Acute dermal toxicity

The LD_{50} values were > 1083 mg/kg bw for rat and rabbit; in the two available studies there is a discrepancy regarding clinical signs of toxicity:

Applying 2-chlorotoluene to the back of rats, pain, difficulties in breathing and reduced general condition were observed (Bayer AG 1976); applying 2-chlorotoluene to the back of rabbits, no signs of systemic toxicity were observed (Arthur et al. 1974).

Conclusion: The acute toxicity via dermal exposure is low.

3.2.4 Skin irritation

In one patch test according to OECD Guideline No. 404 2-chlorotoluene (purity 99,8%) caused slight irritation to rabbit skin after a 4-hour semiocclusive exposure. During the observation time no oedema but slight erythema occurred (3/3 at 48 hour; 2/3 at 72 hour; 0/3 at 7 day) (Bayer AG 1988).

The acute skin irritation was also examined in earlier studies. Pads (1.5 x 1.5 cm) soaked with 0.5 ml 2-chlorotoluene (technically pure) were applied to the ear of rabbits (n = 2 per exposure time), fixed and covered by cotton patches (semiocclusive application). The exposure times were 1, 2 and 24 hours. After 1-hour exposure, slight erythema was observed lasting for up to 2 days; after a 2-hour exposure, the animals showed slight erythema and superficial erosions during the whole observation period of 7 days. The 24-hour exposure caused strong erythema and severe skin erosions of the ear which were, after 6 days, still observed as slight erythema and superficial erosions (Bayer AG 1976). The study is less valid compared to Bayer AG 1988 because of the unknown purity of the test compound, the prolonged exposure-time (24 hours) and application to rabbit ear which is not in accordance with the current OECD Guideline.

0.5 ml 2-chlorotoluene per patch (test substance was considered free of impurities, no further information) was occlusive applied to abraded (n=3) and intact (n=3) rabbit skin for 24 hours. At 24 hours post exposure all intact and abraded sites were blanched and showed slight or moderate oedema. At 72 hours blanching was still present in all of the abraded and in 2 of the intact sites and slight to moderate oedema was still present on all sites. One week after application, the animals showed moderate desquamation; the application sites appeared thickened, denuded and scarified. In the authors opinion 2-Chlorotoluene is moderately irritating to the rabbit skin (Hazleton Laboratories Inc. 1966). The study is only poorly reported individual animal data are not available. Thus, the strong effect can only be explained by the occlusive application and the prolonged exposure-time (24 hours) which is, however, not in accordance with the current OECD Guideline.

Data on guinea pigs show comparable results (Ely 1986). In rats there was no irritation after an occlusive application with an exposure time of 24 hours lasting but the animals (5/sex) showed excitation obviously induced by severe pain (Bayer AG 1976).

Conclusion: 2-Chlorotoluene has a potential for skin irritation. The intensity of the irritating effect depends on the mode of application, the exposure-time and the possibility of evaporating. In a study according OECD Guideline No. 404, the substance was slightly

irritating; when tested under occlusive conditions and with prolonged exposure-times, the substance is evaluated as moderately irritating to rabbit skin.

3.2.5 Eye irritation

In a study according to OECD Guideline No. 405, 0.1 ml 2-chlorotoluene (purity 99,8%) caused 1 hour after instillation into the conjunctival sac diffuse crimson colour of the conjunctivae with individual vessels not easily to discern (score 2), slight conjunctival swelling (score 1) and slight increase in lacrimation (score 1) in all three rabbits. 24 hours post application the eyes were rinsed. At this time, 2/3 rabbits showed some blood vessels definitely hyperaemic (score 1), which was seen only in 1/3 rabbits until 72 hours post application. At the end of the observation period (7 days) all signs of irritation had disappeared (Bayer AG 1988). Due to the slight effects and their reversibility, 2-chlorotoluene can be regarded as slightly irritating.

In an earlier study, application of 0.1 ml technical pure 2-Chlorotoluene into the conjunctival sac of rabbits (n = 2) caused slight to moderate redness of the conjunctiva for up to 24 h post application. After that the signs were reversible. The compound was regarded as slightly irritating. No individual animal data were included in the report and there is no chemical analysis (Bayer AG 1976).

0.1 ml 2-chlorotoluene were instilled into one eye in each of 3 male and 3 female rabbits without subsequent rinsing, Draize scores were recorded 1 hour, 1, 2, 3 and 7 days post-treatment but not included in the report. On post-treatment day 1, sodium fluorescein was placed into the eyes for estimating corneal injuries. Ten percent of the corneal surface of the eye of one rabbit was stained with sodium fluorescein 24 hours after treatment; there were no positive staining areas at 72 hours; all animals had slight conjunctival inflammation that cleared by day 7. No individual animal data were reported. According to the author 2-chlorotoluene was evaluated as slightly irritating (Arthur et al. 1974).

A short report (no details were given) describes the results of the single application of 0.1 ml into one eye of 3 rabbits (no rinsing). The animals showed moderate conjunctival irritation which disappeared by the fifth day; fluorescein staining on the seventh day revealed no evidence of corneal damage (Hazleton Laboratories Inc. 1966).

24 hours after application of approximately 0.1 ml 2-chlorotoluene into one eye in each of 3 rabbits there was slight mucopurulent discharge in two animals and redness round the rim of one eye of the third animal; 24 hours later the eyes were normal. No detailed information was given. According to the author 2-chlorotoluene was evaluated as irritating (Barry 1970)

Conclusion: 2-Chlorotoluene is only slightly irritating when tested according to OECD Guideline 405 in 1/3 rabbits. Earlier studies which don't meet the criteria of today and which are poorly reported yielded comparable results.

3.2.6 Skin sensitization

The guinea pig maximisation test was performed on male guinea pigs using the OECD Guideline No. 406 (Bayer AG 1991c). The doses for the induction and challenge treatments were selected on the basis of the results of the dose range-finding studies:

Dose-range finding for intradermal induction:

One guinea pig was given intradermal injections twice, in each case, with 0.1 ml of the following test item concentration: 0, 1, 2.5 and 5 %. The injection sites were evaluated after 24 and 48 hours: 0 %: no reaction; 1-5 % grey wheal with red surrounding.

Dose range-finding study for topical induction

Four different concentrations (12, 25, 50, 100 %) were tested in each case on four guinea pigs using occlusive conditions for 24 hours. Skin reactions were evaluated 48 and 72 hours after the start of the application: no erythema or oedema were observed.

Dose range-finding study for challenge

One week prior to challenge, the challenge concentration was determined on 5 guinea pigs (12, 25, 50, 100 %) using occlusive conditions for 24 hours. Skin reactions were evaluated 48 and 72 hours after the start of the application: no erythema or oedema were observed.

Thus the study was performed with the following test item concentrations:

Intradermal induction:	*5%*
Topical induction:	100%
Challenge	100%

Due to the lack of skin irritation sodium laurylsulfate (10%) was applied before the topical induction. The challenge using a 100 % test item formulation led to no skin effects in the animals in the treatment group.

There are additional studies which do not meet the criteria of today and which are poorly reported, but yielded the same results.

Conclusion: 2-Chlorotoluene is not sensitizing to the skin in guinea pigs when tested according to the OECD Guideline 406.

3.2.7 Repeated dose toxicity

The repeated dose toxicity was examined in male and female Harlan rats for a period of 3 months and application of the substance via gavage in doses of 0, 20, 80 and 320 mg/kg bw and day (20 animals/sex and group). In all dose groups there were no treatment-related changes in behaviour, survival, clinical biochemistry or histopathology (Gibson et al. 1974a, Hill 1981). There were no treatment related effects in females reported. Except for a slight increase in the white blood cell count and a decrease in the prothrombin time of the male rats treated with the high dose there were no significant changes in the hematology profiles. Only one significant change appeared in the clinical biochemistry, i.e., an increase in the blood urea nitrogen of rats treated with the mid dose. Males of the intermediate and high dose group showed depressed growth. Relative adrenals weights

increased in males given mid and high dose, relative heart and testes weights were increased in males treated with the high dose. The mean absolute weights of these organs were similar to the controls. The NOEL was 20 mg/kg bw.

In dogs (4 dogs/sex and group), oral application of 2-chlorotoluene in doses of 0, 20, 80 and 320 mg/kg bw and day by capsule for 3 months resulted in a NOEL of 20 mg/kg bw and day (Gibson et al. 1974b, Hill 1981). In all dose groups there were no treatment-related effects on behaviour, survival, hematology, clinical chemistry, histopathology, eyes and bone marrow. Occasional episodes of vomiting in 1/4 females and red blood in the feces of this animal given 80 mg/kg bw is regarded to be the physiological response to the treatment with the slightly irritating compound.

There are additional 90-day-oral studies in rats (Industrial Bio-Test Laboratories Inc. 1977) and dogs (Industrial Bio-Test Laboratories Inc. 1976) using a mixture containing of 51% 2-chlorotoluene und 49% 4-chlorotoluene. Therefore these studies were not taken into account.

Slight damage to the liver and the kidneys as well as inflammation and oedema of the stomach were observed in the subacute oral test on rats (7 per sex) given a dosage of 270 mg 2-chlorotoluene/kg bw by gavage (duration 14 d) (Barry 1970).

In range study tests for reproductive toxicity, 10 male and 10 female (nonpregnant) rats per dose group were exposed for 6 hours daily on 14 consecutive days to analyzed 2-chlorotoluene concentrations of 4.0; 7.7; 11.4 and 15.3 mg/l, and 6 female (nonpregnant) rabbits per dose group were exposed for 6 hours a day on 23 consecutive days to analyzed 2-chlorotoluene concentrations of 4.0; 7.8; 11.5 and 15.6 mg/l (whole-body exposure). No NOAEL could be determined. The LOAEL were 4 mg/l in rats and approx. 8.0 mg/l in rabbits (Huntington Research Centre 1983a).

In rats, dose-related suppression of bodyweight gain and increase in water consumption was noted in all dose groups. 1/10 female rats died at 11.4 mg/l, at 15.3 mg/l 1/10 female and 1/10 male rats died. Animals exposed at 4.0 mg/l showed slight signs of irritation and CNS depression, at higher concentrations dose-related salivation, lacrimation, CNS depression, ataxia, and with a dose-related incidence alopecia and brown staining of fur; male rats showed a decrease in food consumption. There was an increase of liver and kidney weights of males in all dose groups and of females in the 3 highest dose groups. The effect was dose-related for liver, for kidney in females only. The spleen weights of males in the 3 highest dose groups and of females in the 2 highest dose groups were significant lower. The effect was dose-related. Exposure to 15.3 mg/l resulted in histopathological changes in the liver of 6/9 females; they showed apparent centrilobular hepatocyte enlargement. Haematologic analysis revealed an increase of the haemoglobin level in male rats exposed to 4.0 and 15.3 mg/l and increased PVC at 15.3 mg/l. In female rats of the high dose group there was a decrease of the sodium and chloride levels in blood. Urinalysis revealed an increase in the volume of urine (except females at 4.0 mg/l) and an lowered pH in the examined dose groups 4.0 and 15.3 mg/l.

1/6 rabbits of the control and 1/6 rabbits of the 11.5 mg/l group died. Increased respiration and dose-related suppression of bodyweight gain was noted in all dose groups. At the highest dose group the loss of bodyweight was significant. Dose-related decrease in food consumption was found, statistically significant at the highest dose group. Animals exposed at 7.8 mg/l showed slight salivation, at higher doses salivation and lacrimation. At 11.5 mg/l 1/6 rabbits was sacrificed because of its debilitated condition. Macroscopic post mortem findings being consistent with the presence of severe respiratory disease.

4 rats/sex and dose were exposed daily, 6 h/d, 5 d/w, for 3 weeks against 0, 500, 1000 and 40,000 ppm: While the lowest concentration was tolerated by all animals without any symptoms, all animals which received the highest concentration died within 3 minutes. Animals in the 1000 ppm group exhibited lethargy, decreased sensitivity to noise, bloody snouts, and reduced body weight gain. Normal results were obtained from both the hematological investigation 24 hours after the last exposure and the analysis of the last 24-hour urine. At necropsy there were no findings in animals from the 1000 ppm group, sacrificed at the end of the experiment. Histological investigation revealed only a few isolated macrophages in the alveoli (Barry 1970). There is only an abstract available, the method is not described in full detail, control groups are not specified and there is no statistical evaluation mentioned. Thus the study cannot be evaluated adequately.

4 rabbits/sex and group were treated daily, 5 days/week, 4 weeks followed by a 2-week of recovery and observation, by dermal application of 2-chlorotoluene. The doses used were 0, 0.1, 0.3 or 1.0 ml/kg bw and day (approximate 108, 324 or 1081 mg/kg bw and day). The only toxicity that was directly related to the daily topical applications was moderate to severe dermal irritation at the sites of application. The death of one control and 2 middle dose animals during the study were related to intestinal disturbances which is according to the authors not uncommon to laboratory rabbits. One high dose male showed low erythrocyte and high leukocyte count, enlarged kidneys and adrenals and multiple abscess of the lungs, kidneys, and subcutaneuous tissues, which probably resulted from the massive infection that occurred during the second week of treatment (Arthur and Harris 1974). Conclusion on the absorption rate cannot be drawn. Because of the non-treatment related deaths and impairments the number of animals is too small for adequate evaluation. In addition, the purity of the test substance is not given and the method used is not carefully described. Therefore the study is not suitable to assess dermal toxicity.

Conclusion: The NOEL for repeated dosing by gavage to rats and dogs (3 months) is 20 mg/kg bw. In higher dosage (80 or 320 mg/kg bw) unspecific signs of toxicity were observed in rats. In dogs given a dosage of 80 mg/kg bw one animal showed effects, which might be due to the slightly irritating property of 2-chlorotoluene. In inhalation studies no NOAEL was determined. LOAELs being 4 mg/l (6 hrs/d, daily, 14 d) in rats and approx. 8 mg/l (6 hrs/d, daily, 23 d) in rabbits. In rats, the effects at the lowest level were CNS depression and slight signs of irritation; in rabbits increased respiration and suppression of bodyweight gain was noted at the lowest dose.

3.2.8 Genotoxicity

In vitro

(A) Gene mutation

An Ames test with Salmonella typhimurium strains TA 98, TA 100, TA 1535, TA 1537 and TA 1538 gave no indication on gene mutation with and without metabolic activation (Litton Bionetics Inc. 1982a). The highest dosage used (1.17 µl/plate) exhibits 100 % toxicity. The available umu test using Salmonella typhimurium TA 1535/pSK 1002 and a concentration of 100 µg/ml of 2-Chlorotoluene with unknown purity in the presence and in the absence of metabolic activation yielded a negative result (Ono et al. 1992)

Also the mouse lymphoma assay (7.5 – 40 nl/ml assay medium without metabolic activation, 60 nl/ml cytotoxic; 10-60 nl/ml assay medium in the presence of metabolic activation; 80 nl/ml cytotoxic) does not show any mutagenic activity (Litton Bionetics Inc. 1982b).

Conclusion: 2-Chlorotoluene showed no mutagenic activity in bacterial and in mammalian cell test systems in vitro.

(B) Cytogenicity

There is a study on cytogenicity (chromosome aberration) using Chinese Hamster ovary cells in vitro: 0.83-250 n/ml (250 nl/ml cytotoxic), with and without metabolic activation (Litton Bionetics Inc. 1982c). The study gave no indication on clastogenic activity of the substance.

Conclusion: 2-Chlorotoluene showed no clastogenic activity in vitro.

In vivo

Cytogenicity

There is a study on cytogenicity (chromosome aberration) using bone marrow cells of Sprague-Dawley rats following single oral treatment (0, 30, 100, 300 mg/kg bw) and repeated (0, 30, 100, 300 mg/kg bw, 5 applications) oral treatment. In none of these tests 2-chlorotoluene revealed clastogenic activity. The mitotic index was comparable to the control (Litton Bionetics Inc. 1982d).
Conclusion: 2-Chlorotoluene showed no clastogenic activity in vivo.

3.2.9 Carcinogenicity

2-Chlorotoluene did not induce transformation in the mouse BALB/3T3 cell test in vitro using 27.7 to 110.8 nl/ml compared to the concurrent control (Litton Bionetics Inc. 1982e).

3.2.10 Toxicity to Reproduction

There are no specific studies on toxicity to reproduction.

There are carefully performed 3 months-studies on rats and dogs which evaluated also the reproductive organs.
In the rat study (Gibson et al. 1974a, no GLP), males and females received 2-chlorotoluene 0, 20, 80, or 320 mg/kg bw as a 5 % acacia solution by gavage for 103-104 d. Examination of the means of the absolute organ weights of the reproductive organs showed that none of these weights differ significantly from the controls. Gross and histologic evaluation revealed that the administration of 2-chlorotoluene to rats did not produced any treatment-related pathology in these organs. Histopathological examination of the reproductive organs (testes or uterus and ovaries) showed the occurence of testicular atrophy in 1/20 male rats and hydrometra in 3/20 female rats in the lowest dose group, given 20 mg/kg bw. At 80 or 320 mg/kg bw there were no such findings.

In the dog study (Gibson et al. 1974b, no GLP), males and females received 0, 5, 20, or 80 mg/kg bw as a 5 % acacia solution via capsule for 3 months. Also in this study, there were no treatment related changes on reproductive organ weights of the dogs. The gross examination of the organs and the histological examination showed no pathological alteration induced by 2-chlorotoluene.

In an acute oral toxicity study report with rats (n = 3 per group), given the doses of 2700, 5420 and 10800 mg/kg bw, reduced spermatogenesis was mentioned without giving further details (Barry 1970). This observation is regarded to be due to the systemic toxicity of these extremely high doses.

Experiments were carried out on the embryotoxic, teratogenic, and chromosome-damaging effects of 4-chlorotoluene in 83 sexually mature female rats and 357 fetuses. The following dose plan was used (while the mode of application is not specified, it was probably intragastric): a single dose of 1,100 of 1,833 mg/kg bw (= 1/5 or 1/3 LD_{50}); 55 or 550 mg/kg bw (1/100 or 1/10 LD_{50}) for 2 months; 0.01, 0.1 or 1.0 mg/kg bw for 6 months. To investigate reproduction toxicity, the animals were sacrificed on the twentieth day of pregnancy and the numbers of corpora lutea, implantations, and malformed fetuses were determined, as was the number of intra-uterine and postnatal deaths. The course of the newborn animals' body development was also monitored, along with organogenesis and ossification. Only the 2-month study showed a statistically significant increase in embryonic mortality in animals in the 550 mg/kg group, caused by preimplantation losses. In addition, 12.7% of the fetuses in this dose group exhibited liver hypertrophy, while 47% displayed hypotrophy. 4-Chlorotoluene did not show a teratogenic or cytogenetic effect. Only after the single dose of 1,833 mg/kg bw was a slight tendency towards chromosome fragmentation observed (BUA 1989).

To assess fertility 12 male and female rats per dose group were gavaged with 0, 12.5, 79 or 500 mg/kg bw, 7 d/w (males: 46 days including 14 days prior to mating, females: from 14 days prior to mating up to day 3 of lactation). At 12.5 and 79 mg/kg bw no effects on

reproductivity were observed. In the 500 mg/kg group 12 pairs showed evidence of copulation with a sperm positive vaginal smear, but only 5 pairs out of them achieved pregnancy. No effects were observed in delivery or lactating behavior of all treated mothers. Litter and pup body weights were decreased on day 1 and 4 of lactation. At necropsy, paternal organs, such as testes, epididymis and endocrine organs, showed no histological changes. Thus, the NOEL parental and F1 offspring is 79 mg/kg bw (SIDS Initial Assessment Report, 2,4-Dichlorotoluene (CAS-No. 95-73-8) unpublished report).

Conclusion: Based on the observations in the 3-month-studies on rat and dog, there is no indication that 2-chlorotoluene affects the reproductive organs. However, since there is no additional supporting information and higher chlorinated benzene derivatives have shown effects on fertility without histopathological correlate, further data are necessary if substantial exposure cannot be ruled out (see Chapter 2).

3.2.11 Developmental toxicity / Teratogenicity

The developmental toxicity was examined in CrL:COBS CD (SD)BR rats (Huntingdon Research Centre 1983b) and New Zealand white rabbits (Huntingdon Research Centre 1983c) using inhalational exposure.

Female rats were exposed to 0, 1.1, 3.1 and 9.0 mg/l 6 h/d from days 6 to 19 of gestation. The NOAEL for maternal toxicity is 1.1 mg/l. Animals in the 3.1 mg/l group exhibited slight ataxia during exposure. Animals in the 9.0 mg/l group displayed ataxia, lacrimation and/or salivation, as well as a brownish discoloration of the fur. Beginning at 3.1 mg/l, a dose-dependent reduction in feed intake and body weight gain was observed, as well as a dose-dependent increase in drinking water consumption. At 3.1 mg/l there were no significant deviation from control values in litter parameters and among incidences of malformations, anomalies and skeletal variants of the offspring. At 1.1 mg/l one fetus with a specific malformation (brachydactyly and brachymelia of all four limbs) and at 9.0 mg/l six fetuses from 4 litters showed brachydactyly of a single fore- or hindpaw. In addition, in the highest dose (9.0 mg/l), the mean values for litter and fetal weight are significantly reduced. The fetuses of the 3.1 mg/l exposure group had no notable adverse effects at all. Historical control data for developmental toxicity studies by the same laboratory show that the brachydactyly malformation does occur spontaneously, but with a very low incidence (2189 litters: 12.209 fetuses: 3 with brachydactyly (one of them additional with brachymelia), 3 with oligodactyly (one of them additional with brachymelia), and one only with brachymelia). Therefore, a NOAEL for developmental toxicity cannot be derived, the LOAEL is 1.1 mg/l.

Female rabbits were exposed to 0, 1.5, 4.0 and 10.0 mg/l 6 h/d from days 6 to 28 of gestation. The NOAEL for maternal toxicity is 1.5 mg/l. During the first days of exposure, animals in the 4.0 mg/l group showed partial ptosis, while those in the 10.0 mg/l group exhibited lacrimation, salivation, and ptosis. Immediately after each exposure, animals in both of these dose groups exhibited an increased breathing rate. At 4.0 mg/l and above, a

dose-related reduction in feed intake and body weight gain was determined during the initial experimental period. In all exposure groups no significant effect on litter size, pre- and post implantation loss or litter and mean fetal weight occurred. In 10.0 mg/l dose group a specific fetal malformation (brachydactyly) was observed in one animal. Historical control data for developmental toxicity studies by the same laboratory show that the brachydactyly malformation does occur spontaneously, but with a very low incidence (1058 litters: 8646 fetuses, 2 with brachydactyly and 1 with oligodactyly). Therefore, 4.0 mg/l can be regarded as the NOAEL for developmental toxicity.

Conclusion: Developmental toxic effects in rats and rabbits occur mostly in the presence of maternal toxicity and without a clear dose-relationship, however as a specific malformation, brachydactyly.

Rat:	NOAEL maternal = 1.1 mg/l	LOEAL foetal = 1.1 mg/l
Rabbit:	NOAEL maternal = 1.5 mg/l	NOAEL foetal = 4 mg/l

3.2.12 Toxicokinetics

When male and female Sprague-Dawley rats were given a single oral dose of 2-chlorotoluene at 1 mg/kg bw by gavage, 85-92% of the applied dose was eliminated in urine, 5-8% was excreted in feces and 1-4% of the applied dose was exhaled as volatile ^{14}C; at least 84% of the volatile ^{14}C was identified as unmetabolized 2-chlorotoluene whereas ^{14}C-carbon dioxide was an insignificant metabolite (< 1% applied dose); a similar distribution of radioactivity was also seen in female rats given single oral doses of 91 or 102 mg/kg bw. The major urinary and fecal metabolites were 2-chlorohippurate, a beta-glucuronide of 2-chlorobenzyl alcohol and mercapturic acid. No significant sex-related metabolic difference were noticed between males and females and the same qualitative and quantitative distribution of metabolites was found for doses of 1-102 mg/kg bw. 2-Chlorotoluene is quickly absorbed from the gastrointestinal tract into blood as evidenced by exhalation of 2-chlorotoluene and the rapid peak in ^{14}C residues at approx. 2 h in blood plasma. Analysis of the ^{14}C residues in plasma showed that the two major radioactive components were mercapturic acid and the beta-glucuronide of 2-chlorobenzyl alcohol (38 and 25% of plasma ^{14}C, respectively), while trace levels of 2-chlorotoluene, 2-chlorobenzoic acid, 2-chlorobenzyl alcohol and 2-chlorohippurate were detectable also. Virtually all of the administered 2-chlorotoluene was eliminated within 4 d with < 1% remaining in the carcass (Quistad et al. 1983).

4. HAZARDS TO THE ENVIRONMENT

4.1 Aquatic Effects

According to the test results 2-chlorotoluene has to be classified as toxic to aquatic organisms.

The lowest acute toxicity data are of fish with 96h-LC_{50} = 2.3 mg/l (*Oncorhynchus mykiss*) (EG & G, 1982a) and 48h–LC_{50} = 9.6 mg/l (*Oryzias latipes*) (MITI 1992). The test with *Oncorhynchus mykiss* was conducted according to an US-EPA protocol in a flow through test. The effect value is based on measured concentration. The less extended test with *Oryzias latipes* was conducted according to the Japanese Standard JIS K 0102-1986-71. In this test no information is available on analytical monitoring of the test concentration. A test with the brackish water fish species *Alburnus alburnus* showed a 96h-EC_{50} of 6.7 – 9.1mg/l, related to nominal concentrations.

A short-term test on *Daphnia magna* showed a 24h-EC_{50} = 20 mg/l. It was conducted according to the German DIN 38 412 Part 11 as a pre-test to the reproduction test specified below. No information is available on analytical monitoring of the test concentration or whether open or closed vessels were used. As the reproduction test was performed in closed vessels it is assumed that also for the short-term test closed vessels were used (Kühn and Pattard 1988). Six years in advance 2-chlorotoluene had been tested in open vessels with a 24h-EC_{50} = 41 mg/l in the same laboratory. This test with the open vessels is regarded invalid. QSAR estimations using ECOSAR gives a 48h-EC_{50} of 5.1 mg/l showing that the available short-term tests with *Daphnia magna* significantly underestimate the toxicity of 2-chlorotoluene. However, as long-term test with daphnids are available in which the NOECs are based on measured concentrations and these long-term tests have a higher relevance for assessment purposes than short-term tests, the performance of acute tests with daphnids is not regarded as highly relevant.

A test with the green algae *Scenedesmus subspicatus* showed a 72h-$EC_{50} \geq 100$ mg/l on biomass and growth and a 72 h-EC_{10} of 60 mg/l related to biomass. The effect values are given as nominal concentrations. The test was conducted according to the German DIN 38412 Part 9. The test vessels had a gas space and were loosely capped (Kühn and Pattard 1990). QSAR estimation using ECOSAR gives a 96h-EC_{50} of 3.5 mg/l for green algae showing that the available test with *Scenedesmus subspicatus* significantly underestimates the toxicity of 2-chlorotoluene.

An early life stage test with *Pimephales promelas* showed a 30d-NOEC for embryo hatchability, survival and growth of 1.4 mg/l. At the next highest test concentration of 2.9 mg/l 81 % of the fish were dead. This test was also conducted according to an US-EPA protocol (EG & G, 1982b). More sensitiveness to 2-chlorotoluene in long-term tests was shown with *Daphnia magna*. In one test the 21d – NOEC and LOEC on reproduction is given by the authors with nominal 0.27 and 0.55 mg/l respectively. Due to analytical

problems at that time a determination limit of 10 mg/l could only be achieved. With a 48 hour aged test solution of 80 mg/l a recovery rate of 50 % was determined by the authors. Thus a minimal 21d-NOEC and LOEC of 0.14 and 0.27 mg/l are given. The 48 hour aging is in conformance with the semi static test system prescribing a water change after 48 hours. The test was performed in accordance with the proposed preliminary testing method recommended by the German Umweltbundesamt in 1984 (Kühn and Pattard 1988). A further 21d-reproduction test with *Daphnia magna* confirms the high sensitivity of this species to 2-chlorotoluene. In this study the daphnids were continuously exposed in a flow-through system. The NOEC for reproduction was 0.21 mg/l while the NOEC for survival was 0.08 mg/l. Both values are based on measured concentrations (Springborn Bionomics, 1986).

The lowest available effect value, the NOEC of 0.08 mg/l found in a long-term test with *Daphnia magna* and related to measured concentrations, is used as basic value for the derivation of the PNECaqua. Long-term test with species from three trophic levels are available. It is assumed that the EC_{50} found in the test with *Scenedesmus subspicatus* significantly underestimates the toxicity of 2-chlorotoluene to green algae. However, as the QSAR estimation shows that the sensitivity of algae, daphnids and fish in acute tests is in the same order of magnitude, it is not assumed that the NOEC from an algae test using measured concentrations is lower than the NOECs found in the long-term tests with *Daphnia magna* and *Pimephales promelas* and the application of an assessment factor of 10 according to the TGD is proposed.

Therefore: PNECaqua = 0.08 mg/l / 10 = 0.008 mg/l.

4.2 Terrestrial Effects

Growth inhibition of terrestrial plants was tested with 2-chlorotoluene and showed 14d-EC_{50} of 89 mg/kg soil dw for *Avena sativa* and 14d-EC_{50} > 1000 mg/kg soil dw for *Brassica rapa*. Both effect values are related to nominal concentrations (Bayer AG 1986). As no analytical monitoring was performed in these studies the results are likely to be underestimated.

From these effect values a provisional PNECsoil can be derived according to the TGD by the application of an assessment factor of 1000 on the lowest value.

Therefore: PNECsoil = 89 mg/kg / 1000 = 89 µg/kg

It has to be regarded that only short-term tests with plants are available and that the effect values are related to nominal concentrations. Therefore, for comparison, an additional PNECsoil is derived from the PNECaqua using the equilibrium partitioning method:

$$PNECsoil = \frac{K_{soil-water}}{RHO_{soil}} \cdot PNEC_{aqua} \cdot 1000\ l/m^3$$

With a $K_{soil\text{-}water}$ of 10.6 (derived from the measured Koc of 346) and a RHO_{soil} of 1700 kg/m^3, a PNECsoil of 50 µg/kg can be derived from the PNECaqua of 8 µg/l. This value is in the same order of magnitude with the PNECsoil derived from experimental data.

4.3 Other Environmental Effects

With a single dose application by gavage *Gallus domesticus* showed mortality at 5410 mg/kg bw 14 days after application (female: 3/5 , male 2/4) but no mortality at 2710 mg/kg bw. *Anas platyrhynchos* and *Colinus virginianus* showed no mortality in a parallel test up to 5410 mg/kg bw (Arthur et al. 1974).

5. CONCLUSIONS AND RECOMMENDATIONS

5.1 Conclusions

130,000 t/a chlorotoluenes are produced worldwide, about 60,000 – 70,000 t/a 2-chlorotoluene. In Germany, Bayer AG is the only producer of 2-chlorotoluene. 10,000 to 50,000 t/a chlorotoluene isomer mixture is produced at Bayer AG. More than 50 % of the produced isomer mixture is processed on-site to cresoles. About 5,000 t/a 2-chlorotoluene are separated from the isomer mixture for serving as basic chemical in the chemical industry for producing intermediates. The intermediates are further used i.e. in the production of coloring agents, agrochemicals and pharmaceuticals. 2-Chlorotoluene is directly used as a solvent for chemical processing as well as a solvent for the formulation of agricultural pesticides.
Monitoring data showed no emission of 2-chlorotoluene into the hydrosphere during production and processing at Bayer AG on the basis of the detection limit of 2 µg/l resp. 1 µg/l. Emissions into the atmosphere are <25 kg/a. Emission into the terrestrial compartment due to the use of 2-chlorotoluene as solvent in agricultural pesticides may occur but cannot be quantified at present.

The favourite target compartment for 2-chlorotoluene is air with 98.8 % according to Mackay I. In air, the substance is indirectly photodegradable with $t_{1/2}$ = 8.8 days. 2-Chlorotoluene can be classified as inherently biodegradable. Under conditions of sewage treatment plants the substance will be eliminated by stripping and adsorption. The bioconcentration factor in fish was measured to 20-112.
The most sensitive aquatic organism in long-term ecotoxicity test was *Daphnia magna* (21d-NOEC = 0.08 mg/l). With an assessment factor of 10 a PNECaqua of 0.008 mg/l was derived.

From ecotoxicity tests with terrestrial plants a PNECsoil of 50 µg/kg can be derived.
2-Chlorotoluene caused acute toxic effects in mammals: LD_{50} rat (oral) male: 3227 mg/kg bw, LD_{50} rat (oral) female: 3860 mg/kg bw, LC_{50} rat (inhalative, 4 h): 37517 mg/m^3 (4 h), LD_{50} rat (dermal): > 1083 mg/kg bw, LD_{50} Rabbit (dermal): > 2165 mg/kg bw.

2-Chlorotoluene, tested according to OECD Guideline 404, is slightly irritating to the skin. However, when tested under occlusive conditions and with prolonged exposure-time, the substance is moderately irritating to rabbit skin. 2-Chlorotoluene, tested according to OECD Guideline 405, is slightly irritating to the eye in 1 out of 3 rabbits. 2-Chlorotoluene, tested according to OECD Guideline 406, is not sensitizing to the skin of guinea pigs.
The NOEL for repeated dosing (3 months) by gavage in rats is 20 mg/kg bw. In higher dosage (80 or 320 mg/kg bw) unspecific signs of toxicity were observed, e.g. reduced body weight gain in male animals, elevated BUN, elevated WBC count, reduced prothrombin time.
The NOEL for repeated dosing via capsule (3 months) in dogs is 20 mg/kg bw. In higher dosage (80 mg/kg bw) one female animal showed vomiting, and red blood was detected in feces, which might be due to the slightly irritating property of 2-chlorotoluene.
In range finding study tests, the LOAELs after inhalation were 4 mg/l (approx. 4000 mg/m^3, 14 d) in rats and 8 mg/l (approx. 8000 mg/m^3, 23 d) in rabbits. There is no NOEL from these data.

2-Chlorotoluene showed no mutagenic activity in bacterial and in mammalian cell test systems in vitro and it showed no clastogenic activity in vitro (CHO-cells) and in vivo (rats).
Regarding reproductive toxicity there are 3 months-studies on rats and dogs which evaluated also the reproductive organs. In the rat study, males and females received 2-chlorotoluene 0, 20, 80 of 320 mg/kg bw solution by gavage for 103-104 days. Examination of the means of the absolute organ weights of the reproductive organs showed that none of these weights differ significantly from the controls. Gross and histological evaluation revealed that the administration of 2-chlorotoluene to rats did not produce any treatment-related pathology in these organs. Histopathologic examination of the reproductive organs showed that in 1/20 male rats and in 3/20 female rats in the lowest dose group testicular atrophy of hydrometra occurred. At 80 or 320 mg/kg bw there were no such findings.
In the dog study, males and females received 0, 5, 20, or 80 mg/kg bw as via capsule for 95-96 days. Also in this study, there were no treatment related changes regarding gross examination of the organs, and the histological examination showed no pathological alteration. However, there are data from structurally related compounds showing effects on fertility.

Developmental toxic effects in rats and rabbits occur mostly only in the presence of maternal toxicity and without a clear dose-response relationship. However, as a specific malformation, brachydactyly was observed.

Rat:	NOAEL maternal = 1.1 mg/l	LOEAL foetal = 1.1 mg/l
Rabbit:	NOAEL maternal = 1.5 mg/l	NOAEL foetal = 4 mg/l

5.2 Recommendations

Concerning environment, the relevance of the releases to the terrestrial compartment due to the use of 2-chlorotoluene as solvent in agricultural pesticides should be clarified.

Concerning human health, if substantial exposure cannot be ruled out, further data on toxicity to reproduction are necessary.

6. REFERENCES

Arthur BH and Harris PN (1974) Subacute dermal toxicity of o-chlorotoluene to rabbits, unpublished report. Toxicology Division, Lilly Research Laboratories

Arthur BH, Gibson WR, Griffing WJ, Kehr CC (1974) The effects on laboratory animals from single exposure to 2-chlorotoluene, unpublished report. Toxicology Division, Lilly Research Laboratories

Banerjee P, Piwoni MD and Ebeid K (1985) Sorption of organic contaminants to a low carbon subsurface core. Chemosphere 14, 1057 - 1067

Barry ES (1970) Toxicological report o-chlorotoluene. Report Number HO/IH/T/768, ICI-Ltd., unpublished report, July 10

Bayer AG (1976) Report No. 5799, Test on acute toxicity of 2-chlorotoluene and skin and eye irritation

Bayer AG (1986), Test on Phytotoxicity of o– chlorotoluene, unpublished

Bayer AG (1987), Test on water solubility of 2-chlorotoluene, unpublished

Bayer AG (1988), Report No. 16899, Test on skin and eye irritation (rabbit) according to OECD 404 and 405

Bayer AG (1991a), Biodegradation Test (Respiration Test)

Bayer AG (1991b), Biodegradation Test (Zahn Wellens Test)

Bayer AG (1991c), Report No. 20859, Test on skin sensitization on guinea pig, according to OECD 406

Bayer AG (1992), Test on soil sorption of 2-chlorotoluene, according to OECD 106, unpublished test

Bayer AG (1999), Calculation SCR– AOP / AOPWIN 1994

BUA (1989) Chlortoluole (Methylchlorbenzole). Beratergremium für umweltrelevante Altstoffe (BUA). BUA-Stoffberichte 38. Gesellschaft Deutscher Chemiker. VCH Verlagsgesellschaft Weinheim, April 1989. ISBN 3-527-28048-0. English translation (1992). Chlorotoluenes (Methylchlorobenzenes). GDCh-Advisory Committee on Existing Chemicals of Environmental Relevance. ISBN 3-527-28466-4

DRIRE Picardie (1998), Monitoring data from the Picardie region, France

EG & G, Bionomics (1982a): Acute toxicity of o-chlorotoluene to rainbow trout (Salmo gairdneri). Toxicity test report submitted to Hooker Chemicals & Plastics Corporation, Niagara Falls, New York. Report #BW-82-6-1204. EG & G, Bionomics, Wareham, Massachusetts, June 1982.

EG & G, Bionomics (1982b):The toxicity of o-chlorotoluene to fathead minnow (Pimephales promelas) embryos and larvae. Toxicity test report submitted to Hooker Chemicals & Plastics Corporation, Niagara Falls, New York. Report #BW-82-7-1235. EG & G, Bionomics, Wareham, Massachusetts, July 1982.

Ely TS (1986), Personal Communication, cited in ACGIH Documentation of TLV's, 5th edition, p. 137

Federal Register, Office of Federal Register 47, 231, 54160 - 54161 (1982), Ed.: National Archives and Records Administration, Washington DC 20408

Gibson WR, Gossett FO, Koenig GR, Marroquin F (1974a) The toxicity of daily oral doses of o-chlorotoluene in the rat. Lilly Research Laboratories, Toxicology Division. OTS 0507456

Gibson WR, Gossett FO, Koenig GR, Marroquin F (1974b) The toxicity of daily oral doses of o-chlorotoluene in the dog. Lilly Research Laboratories, Toxicology Division. OTS 0507456

Goldblatt MW (1955) Research in industrial health in the chemical industry. Br J Ind Med 12, 1-20

Hazleton Laboratories Inc. (1966) o-Chlorotoluene, Acute Inhalation Exposure - rats, mice, guinea pigs; primary skin irritation-rabbits; acute eye irritation- rabbits, at the request of Hooker Chemical Corporation, EPA OTS206449

Hazleton Laboratories Inc. (1972) Acute Vapor Inhalation Toxicity (LC50) of Orthochlorotoluene and Orthodichlorobenzene in Rats, unpublished report. Cited in: Hooker Chemicals and Plastics Corporation: 2-Chlorotoluene proposal for voluntary testing program, unpublished report, December 22, 1981

Hill RM (1981) The safety evaluation of o-chlorotoluene. Elanco Products Company. OTS 0507354

Huntingdon Research Centre (1983a) 2-Chlorotoluene, a preliminary inhalation study in the rat and rabbit, HRC Report No. HKR 5/82802. OTS 0557419

Huntingdon Research Centre (1983b) Effect of 2-chlorortoluene vapour on pregnancy of the rat, Final Report HKR 8/821122. OTS 0507458, 0557419, 0507453, 0537014, 0557418, 0507455

Huntingdon Research Centre (1983c) Effect of 2-chlorortoluene vapour on pregnancy of the New Zealand white rabbit, Final Report HKR 8/821122. OTS 0507457, 0557419, 0507453, 0557416

Industrial Bio-Test Laboratories Inc. (1976) 90-day subacute oral toxicity study with monochlorotoluene isomeres in beagle dogs, Unpublished report IBT No. 8531-08284 to Hooker Chemicals & Plastics Corporation, date of report: october 15, 1976, cited also in Mf-No.: OTS0507456 and Mf No.: OTS0507442

Industrial Bio-Test Laboratories Inc. (1977) 90-day subacute oral toxicity study with monochlorotoluene isomeres in albino rats, Unpublished report IBT No. 8532-08283 to Hooker Chemicals & Plastics Corporation, date of report: january 4, 1977, cited in Mf-No.:OTS0513166

Kühn R and Pattard M (1988) Damaging effects of environmental chemicals in the Daphnia reproduction test as a basis for evaluation of the environmental hazard in aquatic system, report of Umweltbundesamt, Berlin (UFOPLAN–Nr. 10603052)
Kühn R and Pattard M (1990) Results of the harmful effects of water pollutants to green algae (*Scenedesmus subspicatus*) in the cell multiplication inhibition test. Water Research 24 (1), 31–38

Leo A, Hansch C, Elkins D (1971) Partition coefficients and their uses. Chemical Reviews 71(6)

Litton Bionetics Inc. (1982a) Mutagenicity evaluation of ortho-chlorotoluene in the Ames Salmonella/microsome plate test, Final Report, LBI Project No. 20988 (at the request of Hooker Chemical and Plastics Corporation). OTS 0507442

Litton Bionetics Inc. (1982b) Mutagenicity evaluation of ortho-chlorotoluene in the mouse lymphoma forward mutation assay, Final Report, LBI Project No. 20989 (at the request of Hooker Chemical and Plastics Corporation). OTS 0507444

Litton Bionetics Inc. (1982c) Mutagenicity evaluation of ortho-chlorotoluene in the in vitro cytogenetic assay measuring chromosome aberration frequencies in Chinese hamster ovary (CHO) cells, Final Report, LBI Project No. 20990 (at the request of Hooker Chemical and Plastics Corporation). OTS 0507446

Litton Bionetics Inc. (1982d) Mutagenicity evaluation of ortho-chlorotoluene in the rat bone marrow cytogenetic assay, Final Report, unpublished report.

Litton Bionetics Inc (1982e) Evaluation of orthochlorotoluene in the in vitro transformation of BALB/3T3 cells assay with microsomal enzyme-mediated metabolic activation, Final Report, LBI Project No. 20992 (at the request of Hooker Chemical and Plastics Corporation). OTS 0507443

MITI (1992), Biodegradation and Bioaccumulation Data of Existing Chemicals Based on the CSCL Japan, Compiled under the Supervision of Chemical Products Safety Division, Basic Industries Bureau MITI, Ed. by CITI, October 1992. Published by Japan Chemical Industry Ecology–Toxicology & Information Center

Ono Y et al. (1992) Genotoxic evaluation on aromatic organochlorine compounds by using umu test. Water Sci Technol 26, 61--69

Quistad GB, Mulholland KM, Jamieson GC (1983) 2-Chlorotoluene metabolism by rats. J Agric Food Chem 31, 1158-1162

SIDS Initial Assessment Report: 2,4-Dichlorotoluene (CAS No. 95-73-8) unpublished

Springborn Bionomics, Inc. (1986): The chronic toxicity of o-chlorotoluene to Daphnia magna under flow-through conditions. Research report submitted to Occidental Chemical Corp., Niagara Falls, New York. Report #BW-86-9-2121; Study #10826.0885.6100. Springborn Bionomics, Inc., Wareham, Massachusetts, August 1986

Ullmann (1986), Ullmann's Encyclopedia of Industrial Chemistry, 5th edition, Vol. A6, Weinheim: VCH (1986), p.340

Verschueren (1996), Handbook of Environmental Data on Organic Chemicals, Ed. : Karel Verschueren. 3rd ed. (1996), S. 519

SIDS Dossier including Robust Study Summaries

Existing Chemical	:	ID: 95-49-8
CAS No.	:	95-49-8
EINECS Name	:	2-chlorotoluene
EC No.	:	202-424-3
TSCA Name	:	Benzene, 1-chloro-2-methyl-
Molecular Formula	:	C7H7Cl

Producer related part

Company	:	Bayer AG
Creation date	:	13.12.1993

Substance related part

Company	:	Bayer AG
Creation date	:	13.12.1993
Status	:	
Memo	:	
Printing date	:	27.02.2002
Revision date	:	02.06.1994
Date of last update	:	06.02.2002
Number of pages	:	71
Chapter (profile)	:	Chapter: 1, 2, 3, 4, 5, 6, 7, 8, 10
Reliability (profile)	:	Reliability: without reliability, 1, 2, 3, 4
Flags (profile)	:	Flags: SIDS

1.0.1 APPLICANT AND COMPANY INFORMATION

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	:	> 99 % w/w
Colour	:	
Odour	:	
Remark	:	cooperating company for the Existing Chemicals Regulation: EniChem Synthesis SpA; Italy
Flag	:	Critical study for SIDS endpoint

20.07.2000

1.1.2 SPECTRA

1.2 SYNONYMS AND TRADENAMES

1-CHLOR-2-METHYLBENZOL

Flag : Critical study for SIDS endpoint

1-CHLORO-2-METHYLBENZENE

Flag : Critical study for SIDS endpoint

1-METHYL-2-CHLORBENZOL

Flag : Critical study for SIDS endpoint

1-METHYL-2-CHLOROBENZENE

Flag : Critical study for SIDS endpoint

2-CHLOR-1-METHYLBENZOL

Flag : Critical study for SIDS endpoint

2-CHLORO-1-METHYLBENZENE

Flag : Critical study for SIDS endpoint

2-CHLOROTOLUENE

Flag : Critical study for SIDS endpoint

2-METHYLCHLOROBENZENE

Flag : Critical study for SIDS endpoint

BENZENE, 1-CHLORO-2-METHYL-

Flag : Critical study for SIDS endpoint

O-CHLOROTOLUENE

Flag : Critical study for SIDS endpoint

O-CHLORTOLUOL

Flag : Critical study for SIDS endpoint

O-TOLYL CHLORIDE

Flag : Critical study for SIDS endpoint

TOLUENE, O-CHLORO-

Flag : Critical study for SIDS endpoint

1.3 IMPURITIES

1.4 ADDITIVES

1.5 TOTAL QUANTITY

Quantity : 5000 - 10000 tonnes produced in 1998

Flag : Critical study for SIDS endpoint
24.08.2000

Remark : no change of production volume range in 1999
Flag : Critical study for SIDS endpoint
24.08.2000

1.6.1 LABELLING

Labelling	:	as in Directive 67/548/EEC
Specific limits	:	
Symbols	:	Xn, N, ,
Nota	:	, ,
R-Phrases	:	(20) Harmful by inhalation (51/53) Toxic to aquatic organisms, may cause long-term adverse effects in the aquatic environment
S-Phrases	:	(24/25) Avoid contact with skin and eyes (61) Avoid release to the environment. Refer to special instructions/Safety data sets
Remark	:	EG-No. 602-040-00-X
Flag	:	Critical study for SIDS endpoint

28.03.2000

1.6.2 CLASSIFICATION

Classified	:	as in Directive 67/548/EEC
Class of danger	:	dangerous for the environment
R-Phrases	:	(51/53) Toxic to aquatic organisms, may cause long-term adverse effects in the aquatic environment
Specific limits	:	
Flag	:	Critical study for SIDS endpoint

26.08.1999

Classified	:	as in Directive 67/548/EEC
Class of danger	:	harmful
R-Phrases	:	(20) Harmful by inhalation
Specific limits	:	
Remark	:	EG-No. 602-040-00-X
Flag	:	Critical study for SIDS endpoint

26.08.1999

1.6.3 PACKAGING

1.7 USE PATTERN

Type of use	:	type
Category	:	Use in closed system
Flag	:	Critical study for SIDS endpoint

29.09.2000

Type of use	:	type
Category	:	Wide dispersive use
Flag	:	Critical study for SIDS endpoint

29.09.2000

Type of use : industrial
Category : Agricultural industry

Flag : Critical study for SIDS endpoint
29.09.2000

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

Flag : Critical study for SIDS endpoint
29.09.2000

Type of use : use
Category : Intermediates

Flag : Critical study for SIDS endpoint
29.09.2000

Type of use : use
Category : Pesticides

Remark : used as solvent in pesticides formulations
Flag : Critical study for SIDS endpoint
29.09.2000

1.7.1 DETAILED USE PATTERN

1.7.2 METHODS OF MANUFACTURE

1.8 REGULATORY MEASURES

1.8.1 OCCUPATIONAL EXPOSURE LIMIT VALUES

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

1.11 ADDITIONAL REMARKS

1.12 LAST LITERATURE SEARCH

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

Remark : Last literature search: August 1999
Flag : Critical study for SIDS endpoint
10.07.2000

1.13 REVIEWS

Memo : BUA Report No. 38 (Chlorotoluenes), April 1989

Flag : Critical study for SIDS endpoint
24.08.2000 (1)

2.1 MELTING POINT

Value : -36.5 °C

Flag : Critical study for SIDS endpoint
22.11.1999 (2)

2.2 BOILING POINT

Value : 159.3 °C at 1013 hPa

Flag : Critical study for SIDS endpoint
22.11.1999 (2)

2.3 DENSITY

Type : density
Value : 1.08 g/cm³ at 20 °C
Method : other: DIN 51757
Year :
GLP :
Test substance :

Flag : Critical study for SIDS endpoint
02.09.1999 (3) (2)

2.3.1 GRANULOMETRY

2.4 VAPOUR PRESSURE

Value : 3.6 hPa at 20 °C

Flag : Critical study for SIDS endpoint
29.09.2000 (4)

2.5 PARTITION COEFFICIENT

Partition coefficient :
Log pow : 3.42 at °C
pH value :
Method : other (measured): shaking method
Year :
GLP :
Test substance :

Flag : Critical study for SIDS endpoint
11.10.2000 (5)

2.6.1 SOLUBILITY IN DIFFERENT MEDIA

Solubility in	:	Water
Value	:	.047 g/l at 20 °C
pH value	:	
concentration	:	at °C
Temperature effects	:	
Examine different pol.	:	
pKa	:	at 25 °C
Description	:	
Stable	:	

Flag : Critical study for SIDS endpoint
24.08.2000 (6)

2.6.2 SURFACE TENSION

2.7 FLASH POINT

Value	:	49 °C
Type	:	
Method	:	other: DIN 51755
Year	:	
GLP	:	
Test substance	:	

Flag : Critical study for SIDS endpoint
02.09.1999 (3) (2)

2.8 AUTO FLAMMABILITY

2.9 FLAMMABILITY

Method	:	other: DIN 51794
Year	:	
GLP	:	
Test substance	:	

Result : Ignition temperature: not below 600 degree C
The substance forms inflammable mixtures with air
Flag : Critical study for SIDS endpoint
29.09.2000 (3)

2.10 EXPLOSIVE PROPERTIES

Result : Explosive limits: lower: approx. 1.0 % by vol.
upper: approx. 12.6 % by vol.
Flag : Critical study for SIDS endpoint
29.09.2000 (3)

2.11 OXIDIZING PROPERTIES

2.12 DISSOCIATION CONSTANT

2.13 VISCOSITY

2.14 ADDITIONAL REMARKS

3.1.1 PHOTODEGRADATION

Type	:	other: Calculation according to Atkinson
Light source	:	
Light spectrum	:	nm
Relative intensity	:	based on intensity of sunlight
Deg. product	:	
Method	:	
Year	:	1999
GLP	:	
Test substance	:	
Remark	:	* under the conditions of Western Europe
Result	:	calculated half life: t1/2 = 8.83 days (0.5 E6 OH/cm3) *, kOH = 1.81 E -12 cm3/molecule*s
Reliability	:	(2) valid with restrictions accepted calculation method
Flag	:	Critical study for SIDS endpoint

29.09.2000 (7)

3.1.2 STABILITY IN WATER

Remark	:	Based on the chemical structure of the compound hydrolysis is not expected under temperatures and pH values occuring in the environment
Flag	:	Critical study for SIDS endpoint

09.11.1999

3.1.3 STABILITY IN SOIL

3.2.1 MONITORING DATA

Type of measurement	:	background concentration
Media	:	surface water
Concentration	:	
Method	:	
Remark	:	In Germany the river Rhein and its tributary Neckar has been monitored at different places for 2-chlorotoluene with determination limits of 0.02 and 0.1 ug/l depending on the state institute where the analysis was carried out. No 2-chlorotoluene has been found in 1996 through 1998. Alike no 2-chlorotoluene has been found in the Donau with a determination limit of 0.02 ug/l.
Flag	:	Critical study for SIDS endpoint

24.08.2000 (8)

3.2.2 FIELD STUDIES

3.3.1 TRANSPORT BETWEEN ENVIRONMENTAL COMPARTMENTS

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: Estimation of the Henry Constant (25°C) EPIWIN 2.30
Year : 1999

Result : Bond Contribution Method: 447 Pa x m3 / mol
Group Method: 494 Pa x m3 / mol
Reliability : (1) valid without restriction
Flag : Critical study for SIDS endpoint
29.09.2000 (9)

Type : adsorption
Media : water - soil
Air : % (Fugacity Model Level I)
Water : % (Fugacity Model Level I)
Soil : % (Fugacity Model Level I)
Biota : % (Fugacity Model Level II/III)
Soil : % (Fugacity Model Level II/III)
Method : other: OECD 106 "Adsorption-Desorption Using a Batch Equilibrium Method"
Year : 1992

Result : Adsorption coefficient Koc 346 to 397 for sand, sandy loam and loamy sand with an organic carbon content of 0.7 to 2,29 %
Reliability : (1) valid without restriction
Flag : Critical study for SIDS endpoint
31.08.2000 (10)

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: estimation of the Henry constant (20°C)
Year : 1987

Remark : calculation based on vapour pressure and water solubility
Result : 970 Pa x m³/mol
Reliability : (2) valid with restrictions
Flag : Critical study for SIDS endpoint
11.10.2000 (11)

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

Result	:	Determination of an average Koc value of 370 to a low carbon subsurface core.
Reliability	:	(2) valid with restrictions
Flag	:	Critical study for SIDS endpoint

06.02.2002 (12)

3.3.2 DISTRIBUTION

Media	:	air - biota - sediment(s) - soil - water
Method	:	other (calculation): Calculation according Mackay, Level I (AOPWIN 1994)
Year	:	1999
Result	:	Distribution air: 98,8 %
Reliability	:	(1) valid without restriction
Flag	:	Critical study for SIDS endpoint

29.09.2000 (7)

3.4 MODE OF DEGRADATION IN ACTUAL USE

3.5 BIODEGRADATION

Type	:	aerobic
Inoculum	:	predominantly domestic sewage, adapted
Contact time	:	
Degradation	:	0 (±) % after 28 day(s)
Result	:	under test conditions no biodegradation observed
Deg. product	:	
Method	:	other: Directive EEC 79/831 corresponding to OECD Guide-line 301 F
Year	:	1991
GLP	:	yes
Test substance	:	
Remark	:	Inoculum (30 mg/l dry weight) taken from Zahn-Wellens-test, substance concentration 100 mg/l
Reliability	:	(1) valid without restriction
Flag	:	Critical study for SIDS endpoint

31.08.2000 (13)

Type	:	aerobic
Inoculum	:	predominantly domestic sewage, adapted
Concentration	:	23 mg/l related to DOC (Dissolved Organic Carbon) related to
Kinetic of testsubst.	:	3 hour(s) 64 % 7 day(s) 82 % 28 day(s) 86 % % %
Deg. product	:	
Method	:	OECD Guide-line 302 B "Inherent biodegradability: Modified Zahn-Wellens Test"
Year	:	1991
GLP	:	yes
Test substance	:	
Remark	:	Due to the low water solubility the initial DOC-value was essentially lower than the required one (50-400 mg/l DOC).

Based on the observed elimination after 3 h it is assumed that elimination preferentially occured by adsorption and stripping

Reliability : (2) valid with restrictions
Flag : Critical study for SIDS endpoint
31.08.2000 (14)

3.6 BOD5, COD OR BOD5/COD RATIO

3.7 BIOACCUMULATION

Species : Cyprinus carpio (Fish, fresh water)
Exposure period : 56 day(s) at °C
Concentration : .045 mg/l
BCF : 20 - 112
Elimination :
Method : other: see remarks
Year :
GLP :
Test substance :

Remark : Method: "Bioaccumulation test of chemical substance in fish and shellfish" stipulated in the Order Prescribing the Items of the Test Relating to the New Chemical Substance (1974, Order of the Prime Minister, the Minister of Health and Welfare, the MITI No. 1). This guideline corresponds to "305C, Bioaccumulation: Degree of Bioconcentration in Fish" stipulated in the OECD Guidelines for Testing of Chemicals (May 12, 1981).
Reliability : (1) valid without restriction
Flag : Critical study for SIDS endpoint
23.09.1999 (15)

Species : Cyprinus carpio (Fish, fresh water)
Exposure period : 56 day(s) at °C
Concentration : .45 mg/l
BCF : 41.6 - 87.2
Elimination :
Method : other: see remarks
Year :
GLP :
Test substance :

Remark : Method: "Bioaccumulation test of chemical substance in fish and shellfish" stipulated in the Order Prescribing the Items of the Test Relating to the New Chemical Substance (1974, Order of the Prime Minister, the Minister of Health and Welfare, the MITI No. 1). This guideline corresponds to "305C, Bioaccumulation: Degree of Bioconcentration in Fish" stipulated in the OECD Guidelines for Testing of Chemicals (May 12, 1981).
Reliability : (1) valid without restriction
Flag : Critical study for SIDS endpoint
23.09.1999 (15)

Species : Pimephales promelas (Fish, fresh water)
Exposure period : at °C
Concentration :

BCF	:	890
Elimination	:	
Method	:	other: see remark
Year	:	
GLP	:	
Test substance	:	
Remark	:	Test conducted for US-EPA in 1984. No detailed documentation is given. The BCF is stated as a mean steady state BCF but without the reference point, i.e. reference to fish fat, fish tissue or whole fish.
Reliability	:	(3) invalid not reliable, documentation insufficient for assessment
Flag	:	Critical study for SIDS endpoint

29.09.2000 (16)

3.8 ADDITIONAL REMARKS

4.1 ACUTE/PROLONGED TOXICITY TO FISH

Type	:	flow through
Species	:	Oncorhynchus mykiss (Fish, fresh water)
Exposure period	:	96 hour(s)
Unit	:	mg/l
LC50	:	2.3
Limit test	:	
Analytical monitoring	:	yes
Method	:	other: see remarks
Year	:	
GLP	:	no data
Test substance	:	other TS: 100 %
Remark	:	95 % confidence interval LC 50: 1.8 - 3.1 mg/l; test species: Oncorhynchus mykiss formerly named Salmo gairdneri Test conducted according to "Methods for acute toxicity tests with fish, macroinvertebrates, and amphibians" (US-EPA, 1975) a nd the protocol entitled "EG&G, Bionomics methods for conducting flow-through toxicity tests with freshwater fish" (1981)
Reliability	:	(1) valid without restriction
Flag	:	Critical study for SIDS endpoint

06.02.2002 (16)

Type	:	static
Species	:	Alburnus alburnus (Fish, estuary)
Exposure period	:	96 hour(s)
Unit	:	mg/l
LC50	:	6.7 - 9.1
Method	:	other: see remark
Year	:	
GLP	:	
Test substance	:	
Remark	:	No testmethod specified. Six concentrations with ten fishes each in 70 l glass aquaria with 60 l of natural brackish water (0.7% salinity) at 10°C were tested per substance. The authors further state: no aeration, no feeding, pH 7.8 (no pH adjustment), no analytical monitoring. Substances with a low solubility in water were first dissolved in acetone (acetone conc. < 500 µl/l). For the chlorotoluenes only intervals are given, indicating that several tests were performed. This was due to evaporation resulting in a poor correlation between dose and response. The subsequent probit analysis did not result in acceptable 96 hour-LC50 values, but based on repeated tests, the possible range was estimated (Original statement of the authors).
Reliability	:	(2) valid with restrictions
Flag	:	Critical study for SIDS endpoint

11.10.2000 (17) (18)

Type	:	
Species	:	Oryzias latipes (Fish, fresh water)
Exposure period	:	48 hour(s)
Unit	:	mg/l
LC50	:	9.6

Method	:	other: Japanese Industrial Standard (JIS K 0102-1986-71) "Testing methods for industrial waste water"
Year	:	
GLP	:	
Test substance	:	
Reliability	:	(2) valid with restrictions
Flag	:	Critical study for SIDS endpoint

05.07.2000 (15)

4.2 ACUTE TOXICITY TO AQUATIC INVERTEBRATES

Type	:	
Species	:	Daphnia magna (Crustacea)
Exposure period	:	24 hour(s)
Unit	:	mg/l
EC0	:	9
EC50	:	20
Method	:	other: acute Daphnia test (according to DIN 38 412, part 11)
Year	:	1988
GLP	:	
Test substance	:	
Remark	:	Test results imparted within the publication of the test on reproduction with Daphnia magna (see chapter 4.5.2). No detailed documentation.
Reliability	:	(2) valid with restrictions
Flag	:	Critical study for SIDS endpoint

08.09.2000 (19)

Type	:	
Species	:	Nitocra spinipes (Crustacea)
Exposure period	:	96 hour(s)
Unit	:	mg/l
EC50	:	40 - 50
Method	:	other: see remark
Year	:	
GLP	:	
Test substance	:	
Remark	:	No testmethod specified. Six concentrations with 2x10 N. spinipes each in 15 ml standard test tubes with 10 ml of natural brackish water (0.7% salinity) at 20-22°C were tested per substance. Adult animals from 3-6 week old cultures were used. The authors further state: no aeration, no feeding, pH 7.8 (no pH adjustment), no analytical monitoring. Substances with a low solubility in water were first dissolved in acetone (acetone conc. < 500 µl/l). For the chlorotoluenes only intervals are given, indicating that several test were performed. This was due to evaporation resulting in a poor correlation between dose and response. The subsequent probit analysis did not result in acceptable 96 hour-LC50 values, but based on repeated tests, the possible range was estimated (Original statement of the authors).
Reliability	:	(2) valid with restrictions

Flag : Critical study for SIDS endpoint
11.10.2000 (17) (18)

4.3 TOXICITY TO AQUATIC PLANTS E.G. ALGAE

Species : Scenedesmus subspicatus (Algae)
Endpoint : other: biomass, cell units
Exposure period : 72 hour(s)
Unit : mg/l
EC50 : > 100
Method : other: Scenedesmus -Zellvermehrungs -Hemmtest, DIN 38412 Teil 9, Bestimmung der Hemmwirkung von Wasserinhaltsstoffen auf Gruenalgen
Year : 1990
GLP :
Test substance :

Remark : EbC10 = 60 mg/l
EbC50 = > 100 mg/l
EuC10 = > 100 mg/l
EuC50 = > 100 mg/l
nominal concentrations, test vessels with gas space and loose metal caps. Eb = Ebiomass, Eu = Ecell-units
Reliability : (2) valid with restrictions
Flag : Critical study for SIDS endpoint
11.10.2000 (20)

4.4 TOXICITY TO MICROORGANISMS E.G. BACTERIA

Type :
Species : Pseudomonas putida (Bacteria)
Exposure period : 16 hour(s)
Unit : mg/l
EC3 : 15
Method : other: Zellvermehrungshemmtest nach Bringmann und Kühn
Year : 1977
GLP :
Test substance :

Remark : Test vessels with gas space and loose metal caps; EC3 = TT (toxic thres hhold)
Reliability : (2) valid with restrictions
Flag : Critical study for SIDS endpoint
29.09.2000 (21)

4.5.1 CHRONIC TOXICITY TO FISH

Species : Pimephales promelas (Fish, fresh water)
Endpoint : other: embryo-larval toxicity
Exposure period : 30 day(s)
Unit : mg/l
NOEC : 1.4 - 2.9
Analytical monitoring : yes

Method	:	other: see remark
Year	:	
GLP	:	no data
Test substance	:	other TS: purity 100 %
Remark	:	Test was conducted in a flow through system according to "Methods for conducting early-life stage toxicity tests with fathead minnow (Pimephales promelas)", prepared by EG&G Bionomics Test conditions are in accordance with the later OECD-Guideline 210 (Earl-life Stage Toxicity Test with Fish) 1992.
Reliability	:	(1) valid without restriction Comparable to guideline study
Flag	:	Critical study for SIDS endpoint

06.02.2002 (16)

4.5.2 CHRONIC TOXICITY TO AQUATIC INVERTEBRATES

Species	:	Daphnia magna (Crustacea)
Endpoint	:	reproduction rate
Exposure period	:	21 day(s)
Unit	:	mg/l
NOEC	:	.14 - .27
LCEC	:	.27 - .55
Analytical monitoring	:	yes
Method	:	other: see remarks
Year	:	1988
GLP	:	
Test substance	:	
Remark	:	Test was performed in accordance with "Proposed Preliminary Testing Method: Prolonged Toxicity Test on Daphnia magna (Determination of NOEC for reproduction rate, mortality and time of the first appearance of offspring; 21 d), as of 1 January 1984, published as " recommendation of the Federal Environmental Agency for the Performance of Testing according to § 5, para. 1, No. 3 of the Regulations on Documents to be Submitted and Evidence of Testing under the Chemicals Act". Due to analytical problems with the low dosis ranges at that time (determination limit 10 mg/l), a recovery rate of 50 % after 48 h was determined at a test concentration of 80 mg/l. Thus the authors give the higher nominal values (NOEC = 0.27 and LOEC = 0.55 mg/l) and the lower minimal values (NOEC = 0.14 and LOEC = 0.27 mg/l) based on the recovery rate.
Test condition	:	semi static, water change after 48 h, closed test system (ground glass stopper vessels without gas space)
Reliability	:	(1) valid without restriction
Flag	:	Critical study for SIDS endpoint

06.02.2002 (19)

Species	:	Daphnia magna (Crustacea)
Endpoint	:	other: survival
Exposure period	:	21 day(s)
Unit	:	mg/l
NOEC	:	.08

Analytical monitoring	:	yes
Method	:	other: acc. to SBI's test protocol "Study plan for conducting a flow through chronic toxicity test with o-chlorotoluene and Daphnia magna (1984)
Year	:	1984
GLP	:	yes
Test substance	:	other TS: 91.9 %
Remark	:	21 d NOEC = 0.21 mg/l (reproduction)
Test condition	:	flow-through, test vessels covered with plastic wrap
Reliability	:	(1) valid without restriction
Flag	:	Critical study for SIDS endpoint

06.02.2002 (22)

4.6.1 TOXICITY TO SEDIMENT DWELLING ORGANISMS

4.6.2 TOXICITY TO TERRESTRIAL PLANTS

Species	:	Avena sativa (Monocotyledon)
Endpoint	:	other: biomass
Exposure period	:	14 day(s)
Unit	:	mg/kg soil dw
EC50	:	89
Method	:	other: Guideline of German Biologische Bundesanstalt "Phytotoxizitätstest an einer monocotylen Pflanzenart (Avena sativa) und an einer dicotylen Pflanzenart (Brassica rapa)
Year	:	1986
GLP	:	no
Test substance	:	
Remark	:	no analytical monitoring
Reliability	:	(2) valid with res trictions
Flag	:	Critical study for SIDS endpoint

11.10.2000 (23)

Species	:	Brassica rapa (Dicotyledon)
Endpoint	:	other: biomass
Exposure period	:	14 day(s)
Unit	:	mg/kg soil dw
EC50	:	> 1000
Method	:	other: Guideline of German Biologische Bundesanstalt "Phytotoxizitätstest an einer monocotylen Pflanzenart (Avenia sativa) und an einer dicotylen Pflanzenart (Brassica rapa)
Year	:	1986
GLP	:	no
Test substance	:	
Remark	:	no analytical monitoring
Reliability	:	(2) valid with restrictions
Flag	:	Critical study for SIDS endpoint

11.10.2000 (23)

4.6.3 TOXICITY TO SOIL DWELLING ORGANISMS

4.6.4 TOX. TO OTHER NON MAMM. TERR. SPECIES

Species	:	other: gallus domesticus
Endpoint	:	mortality
Exposure period	:	14 day(s)
Unit	:	mg/kg bw
Method	:	Sex: male and female number of animals: 5 per dose method: single application (gavage)
Remark	:	at 2710 mg/kg bw all birds showed hypoactivity and anorexia for 48 hours; at 5410 mg/kg bw all birds showed anorexia for 6 days and hypoactivity and ataxia. Two other species (anas platyrhynchos and colinus virginianus) were tested in parallel and showed no mortality at 5410 mg/kg bw.
Result	:	2710 mg/kg bw no lethality (female: 0/5 ; male: 0/5) 5410 mg/kg bw lethality (female: 2/4 ; male: 3/5)
Flag	:	Critical study for SIDS endpoint

11.10.2000 (24)

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	:	= 3227 mg/kg bw
Species	:	rat
Strain	:	
Sex	:	male
Number of animals	:	15
Vehicle	:	other: lutrol
Doses	:	
Method	:	other: single application by gavage, 1000, 2500, 2750, 3000, 3500, 4000, 5000 mg/kg bw, 0.5 ml/100 g bw, observation period: 14 d
Year	:	1976
GLP	:	no
Test substance	:	other TS: purity: technical pure
Remark	:	signs of intoxication: poor condition until the 10th day post application and for at least 3 days accompanied by sedation and difficulties in breathing and at higher doses by quasi-narcotic effects. at necropsy 14 days post application: reduced size of the abdominal organs, especially liver size, mucus membrane of the stomach with focus of inflammation, stomach content appeared to be bloody LD: 3060-3430 mg/kg bw
Reliability	:	(2) valid with restrictions
Flag	:	Critical study for SIDS endpoint

03.07.2000 (25)

Type	:	LD50
Value	:	= 3860 mg/kg bw
Species	:	rat
Strain	:	
Sex	:	female
Number of animals	:	15
Vehicle	:	other: lutrol
Doses	:	
Method	:	other: single application by gavage, 500, 1000, 2500, 3000, 4000, 5000 mg/kg bw, 0.5 ml/100g bw, observation period: 14 d
Year	:	1976
GLP	:	no
Test substance	:	other TS: purity: technical pure
Remark	:	signs of intoxication: poor condition until the 10th day post application and for at least 3 days accompanied by sedation and difficulties in breathing and at higher doses by quasi-narcotic effects. at necropsy 14 days post application: reduced size of the abdominal organs, especially liver size, mucus membrane of the stomach with focus of inflammation, stomach content appeared to be bloody LD: 3542-4198 mg/kg bw
Reliability	:	(2) valid with restrictions
Flag	:	Critical study for SIDS endpoint

03.07.2000 (25)

Type	:	LD50
Value	:	2700 - 5420 mg/kg bw
Species	:	rat
Strain	:	
Sex	:	male
Number of animals	:	3
Vehicle	:	other: see remark
Doses	:	
Method	:	other: single application by gavage, dosage: 2700, 5420, 10800 mg/kg bw, diluted in an inert dispersing medium so that animals were given 1 mlof the emulsion per 100 g bw, observation period: 7d
Year	:	1970
GLP	:	no
Test substance	:	other TS: purity no data
Remark	:	mortality: 0/3 at 2700 mg/kg bw and 2/3 at 5420 mg/kg bw, 3/3 at 10800 mg/kg bw; deaths occurred within 48 hrs of dosing. Signs of intoxication within 1 hr of dosing: slight loss of muscle control survivors recovered, made normal weight gain and were healthy throughout the test Necropsy: dead animals showed congested lungs and distension of the bladder; survivors showed no macroscopic changes Microscopically all the males showed an increase in splenic haemopoiesis, and a reduction in spermatogenesis (no further detail reported); 1/3 males: minimal degenerative changes of the renal proximal tubules, mild inflammatory changes in the stomach
Flag	:	Critical study for SIDS endpoint

05.09.2000 (26)

5.1.2 ACUTE INHALATION TOXICITY

Type	:	LC50
Value	:	= 7119 ppm
Species	:	rat
Strain	:	
Sex	:	male
Number of animals	:	10
Vehicle	:	
Doses	:	
Exposure time	:	4 hour(s)
Method	:	other: exposed at various nominal concentrations: 3471, 6402, 8406, 8819 ppm, observation period: 14 d, calculated LC50
Year	:	1981
GLP	:	no
Test substance	:	other TS: purity: > 98 %
Remark	:	value: 7119 (6131-8266) ppm = ca. 37.517 mg/l clinical signs: during exposure: hypoactivity, dyspnea, abdominal respiration, exudation from eyes and nose, tremors and prostration, duration: 2-4 days at necropsy: uneven coloration on the surface of the lungs and liver and foci of red and black discoloration on the

surface of the lungs.

Reliability : (2) valid with restrictions
Flag : Critical study for SIDS endpoint
03.07.2000 (27)

5.1.3 ACUTE DERMAL TOXICITY

Type : LD50
Value : > 1083 mg/kg bw
Species : rat
Strain :
Sex : male/female
Number of animals : 5
Vehicle : other: none
Doses :
Method : other: 5 rats/sex, hairs removed from the trunk, chemical applied to this prepared area of the skin, single application of 1 ml/kg for 24 hours, during exposure covered with pluster backed with aluminium foil
Year : 1969
GLP : no
Test substance : other TS: technically pure

Remark :
immediately after the application, the animals showed excitation obviously induced by pain and lasting for up to 2 h; within 24 h difficulty of breathing occurred; the general condition of the animals was impaired up to 8 d after administration of the test substance; no deaths occurred; after 24 h, the treated areas of skin showed no da

Flag : Critical study for SIDS endpoint
28.09.2000 (25)

Type : LD0
Value : = 2165 mg/kg bw
Species : rabbit
Strain :
Sex : male/female
Number of animals : 3
Vehicle : other: none
Doses :
Method : other: single application of 2165 mg/kg bw undiluted to the clipped and/or abraded skin for 24 hours, occlusive dressing, observation period: 14 d
Year : 1974
GLP : no
Test substance : other TS: purity: no data

Remark : there were no signs of systemic toxicity; all animals developed slight oedema and erythema at the application sites; these areas healed normally during the observation period of 14 d
Test substance : compound applied without dilution
Flag : Critical study for SIDS endpoint
16.12.1999 (28)

5.1.4 ACUTE TOXICITY, OTHER ROUTES

5.2.1 SKIN IRRITATION

Species	:	rabbit
Concentration	:	undiluted
Exposure	:	Semiocclusive
Exposure time	:	4 hour(s)
Number of animals	:	3
Vehicle	:	
PDII	:	
Result	:	slightly irritating
Classification	:	
Method	:	OECD Guide-line 404 "Acute Dermal Irritation/Corrosion"
Year	:	1988
GLP	:	yes
Test substance	:	other TS: purity: 99.8 %
Reliability	:	(1) valid without restriction
Flag	:	Critical study for SIDS endpoint

10.01.2002 (29)

5.2.2 EYE IRRITATION

Species	:	rabbit
Concentration	:	undiluted
Dose	:	
Exposure time	:	24 hour(s)
Comment	:	rinsed after (see exposure time)
Number of animals	:	3
Vehicle	:	
Result	:	slightly irritating
Classification	:	
Method	:	OECD Guide-line 405 "Acute Eye Irritation/Corrosion"
Year	:	1988
GLP	:	yes
Test substance	:	other TS: purity: 99.8 %
Remark	:	slightly irritating in 1/3 rabbits
Reliability	:	(1) valid without restriction
Flag	:	Critical study for SIDS endpoint

10.01.2002 (29)

5.3 SENSITIZATION

Type	:	Guinea pig maximization test
Species	:	guinea pig
Concentration	:	1st: Induction 5 % intracutaneous 2nd: Induction 100 % occlusive epicutaneous 3rd: Challenge 100 % semiocclusive
Number of animals	:	20
Vehicle	:	other
Result	:	not sensitizing

Classification	:	
Method	:	other: OECD Guide-line 406, 2 x 10 animals as control
Year	:	1991
GLP	:	yes
Test substance	:	other TS: purity: 99.78 %
Remark	:	Doses for induction and challenge treatments were selected on the basis of the results of dose-range finding studies. Due to lack of skin irritation sodium laurylsulfate (10%) was applied before topical induction.
Reliability	:	(1) valid without restriction
Flag	:	Critical study for SIDS endpoint

10.01.2002 (30)

5.4 REPEATED DOSE TOXICITY

Type	:	
Species	:	rat
Sex	:	male/female
Strain	:	other: Crl: COBS CD (SD) BR
Route of admin.	:	inhalation
Exposure period	:	14 d
Frequency of treatm.	:	daily, 6 h/d
Post exposure period	:	no
Doses	:	0, 4, 8, 12, 16 mg/l (4.0, 7.7, 11.4 or 15.3 mg/l analytic concentrations)
Control group	:	yes, concurrent no treatment
LOAEL	:	ca. 4 mg/l
Method	:	other: 10 rats/sex and group, whole body exposure,
Year	:	1982
GLP	:	yes
Test substance	:	other TS: purity 96.5 %
Remark	:	dose-finding study for further embryotoxicity studies
Result	:	all dose groups: dose-related suppression of bodyweight gain in males, increase in water consumption, increase in liver and kidney weights of males 4.0 mg/l: slight signs of irritation and CNS depression 4.0 and 15.3 mg/l: haemoglobin levels increased in males; urinalysis: increase in the volume of urine (exception: females at 4.0 mg/l); pH of urine lowered 7.7, 11.4 or 15.3 mg/l: dose-related salivation, lachrymation, CNS depression, ataxia, decrease in food consumption for male rats; alopecia, brown staining of fur (incidence dose-related); increase in liver and kidney weights of females; decrease in the spleen weights of males 11.4 mg/l: mortality: 1/10 females 11.4 and 15.3 mg/l: decrease in spleen weights of females 15.3 mg/l: mortality: 1/10 males and 1/10 females; haematology: PCV increased in males; blood chemistry: sodium and chloride levels decreased in females; microscopic pathology: apparent centrilobular hepatocyte enlargement in the livers of 6/9 females
Flag	:	Critical study for SIDS endpoint

02.11.1999 (31)

Type	:	
Species	:	rat
Sex	:	male/female

Strain	:	no data
Route of admin.	:	gavage
Exposure period	:	14 d
Frequency of treatm.	:	daily
Post exposure period	:	7 d
Doses	:	270 mg/kg bw/d
Control group	:	yes
Method	:	other: see remarks, TS was diluted with an inert dispersing medium
Year	:	1970
GLP	:	no
Test substance	:	other TS: purity no data
Remark	:	2/7 males and 2/7 females were killed for examination 24 h after the last dose; livers were submitted for electron microscope examination; the remainder were killed 6 d later
Result	:	healthy appearance; body weights and liver weights comparable with control animals; no haematological abnormalities; autopsy findings 24 h after completion of dosing: pale reticulated kidneys in 1/2 males and in 1/2 females; no microscopic changes of the kidneys; inflammation and oedema of the stomach; electron microscopic changes of the liver: dilatation of smooth and rough endoplasmic reticulum, evidence of slight mitochondrial damage and hypertrophy of Golgi apparatus with increased lysosomal activity; autopsy findings 7 d after the last dose: reticulation of the kidneys, no microscopic renal changes, minimal signs of inflammation in the stomachs
Flag	:	Critical study for SIDS endpoint

02.11.1999 (26)

Type	:	
Species	:	rat
Sex	:	male/female
Strain	:	other: Harlan
Route of admin.	:	gavage
Exposure period	:	3 months (103 - 104 days)
Frequency of treatm.	:	daily
Post exposure period	:	no
Doses	:	0, 20, 80 or 320 mg/kg bw/d in a 5 % acacia solution
Control group	:	yes, concurrent vehicle
Method	:	other: 20 rats/sex and group, interim kill on day 14: 5 rats/sex and group, necropsy from each rat, determination of hematological data and clinical biochemistry, Statistically analyzed
Year	:	1974
GLP	:	no
Test substance	:	other TS: purity: 96.4 %
Remark	:	NOEL: 20 mg/kg bw
Result	:	all dose groups: no treatment-related changes in behaviour, survival, haematology, clinical chemistry or histopathology 80 mg/kg bw/d only: blood urea nitrogen elevated 320 mg/kg bw/d only: white blood cell count elevated; prothrombintime reduced in males 80 and 320 mg/kg bw/d: depressed growth in the males; relative weights of adrenals increased in males 320 mg/kg bw/d: relative heart and testes weights increased in the males

(the changes of relative organ weights found were the result of growth depression, because the mean absolute weights of these organs were similar to the controls and there were no changes found in these tissues examined histologically)

Reliability : (2) valid with restrictions
Flag : Critical study for SIDS endpoint
05.09.2000 (32) (33)

Type :
Species : rabbit
Sex : female
Strain : New Zealand white
Route of admin. : inhalation
Exposure period : 23 d
Frequency of treatm. : daily, 6 h/d
Post exposure period : no
Doses : 0,4, 8, 12, 16 mg/l (4.0, 7.8, 11.5 or 15.6 mg/l analytic concentration)
Control group : yes, concurrent no treatment
LOAEL : ca. 8 mg/l
Method : other: 6 female rabbits/group, whole body exposure
Year : 1982
GLP : yes
Test substance : other TS: purity: 96.5 %

Remark : dose-finding study for further embryotoxicity studies
Result : mortality: 1/6 (control group); 1/6 (12 mg/l -group)
all dose groups: increased respiration, dose-related suppression of bodyweight gain; findings of macroscopic or microscopic pathology considered unlikely to be related to o-chlorotoluene exposure
4.0, 7.8 and 11.5 mg/l: dose-related decrease in food consumption without statistical significance
7.8 mg/l: slight salivation
11.5 mg/l: sacrifice of 1/6 rabbits because of the debilitated condition of the animal: macroscopic post mortem findings being consistent with the presence of severe respiratory disease
11.5 and 15.6 mg/l: salivation and lachrymation
15.6 mg/l: significant loss in bodyweight; food consumption significantly decreased
Flag : Critical study for SIDS endpoint
05.09.2000 (31)

Type :
Species : dog
Sex : male/female
Strain : Beagle
Route of admin. : other: oral (capsule)
Exposure period : 3 months
Frequency of treatm. : daily
Post exposure period : no
Doses : 0, 5, 20 or 80 mg/kg bw/d in a 5 % aqueous accacia solution
Control group : yes, concurrent vehicle
Method : other: 4 dogs/sex and group, treatment time: males 96 d; females: 95 d
Year : 1974
GLP : no
Test substance : other TS: purity: 96.4%

Remark	:	NOEL: 20 mg/kg bw
Result	:	all dose groups: no effects on behaviour, survival, eyes, haematology, clinical chemistry, bone marrow; no findings in the histopathological examinations attributable to treatment 80 mg/kg bw/d: 1/4 females vomited 3 times between test day 10 and 17 and during the 3rd treatment week, red blood was observed in this animal feces (no further information)
Reliability	:	(2) valid with restrictions
Flag	:	Critical study for SIDS endpoint

05.09.2000 (34) (35)

5.5 GENETIC TOXICITY 'IN VITRO'

Type	:	Ames test
System of testing	:	Salmonella typhimurium TA 98, TA 100, TA 1535, TA 1537, TA 1538
Test concentration	:	7 doses of 0.02 ul to 1.17 ul per plate in DMSO (1.17 ul: toxic level); DMSO was used as solvent
Cycotoxic concentr.	:	
Metabolic activation	:	with and without
Result	:	negative
Method	:	other: Ames et al. 1975, Mutation Res. 31, 347-364
Year	:	1982
GLP	:	yes
Test substance	:	other TS: purity: 96.5 %
Remark	:	Depending on Salmonella typhimurium strain, cytotoxicity occurred from 0.29 ul/plate
Reliability	:	(2) valid with restrictions
Flag	:	Critical study for SIDS endpoint

10.01.2002 (36) (37)

Type	:	other: Chromosome aberration assay
System of testing	:	Chinese Hamster Ovary (CHO) cells
Test concentration	:	0.83-250 nl/ml (250 nl/ml: toxic level)
Cycotoxic concentr.	:	
Metabolic activation	:	with and without
Result	:	negative
Method	:	other: see ME
Year	:	1982
GLP	:	yes
Test substance	:	other TS: purity not mentioned, clear, colorless liquid
Method	:	incubation time: without metabolic activation for 8.5 to 10 hours, cultures were washed, addition of culure medium containing colcemid at a final concentration of 0.1 ug/ml; with methabolic activation for 2 hours in the presence of test substance and S9 mixture, cells were washed and incubation was continued in normal grwowth medium further 8 to 10 h with colcemic present during the last 2 or 2.5 h
Reliability	:	(2) valid with restrictions
Flag	:	Critical study for SIDS endpoint

10.01.2002 (38)

Type	:	Mouse lymphoma assay
System of testing	:	mouse lymphoma cell line, L5178Y TK+/-
Test concentration	:	7.5-40 nl/ml assay medium in the nonactivation assay and 10-60 nl/ml assay medium in the presence of metabolic activation

Cycotoxic concentr.	:	
Metabolic activation	:	with and without
Result	:	negative
Method	:	other: Clive D. and Spector JFS, 1975, Mutation Res. 31, 17-29, solvent: DMSO
Year	:	1982
GLP	:	yes
Test substance	:	other TS: purity not mentioned, clear,colorless liquid
Reliability	:	(2) valid with restrictions
Flag	:	Critical study for SIDS endpoint

10.01.2002 (39)

5.6 GENETIC TOXICITY 'IN VIVO'

Type	:	Cytogenetic assay
Species	:	rat
Sex	:	male/female
Strain	:	Sprague-Dawley
Route of admin.	:	gavage
Exposure period	:	once/day, 5 days
Doses	:	0, 30, 100, 300 mg/kg bw
Result	:	negative
Method	:	other: according to EMS, Toxicol. Appl. Pharmacol. 22, 269-275 (1972): 4 rats/sex/dose/treatmrnt time, killed 6 hrs after the last dosing
Year	:	1982
GLP	:	yes
Test substance	:	other TS: purity: 96.5 %
Reliability	:	(2) valid with restrictions
Flag	:	Critical study for SIDS endpoint

22.08.2000 (40)

Type	:	Cytogenetic assay
Species	:	rat
Sex	:	male/female
Strain	:	Sprague-Dawley
Route of admin.	:	gavage
Exposure period	:	once
Doses	:	0, 30, 100 or 300 mg/kg bw
Result	:	negative
Method	:	other: according to EMS, Toxicol. Appl. Pharmacol. 22, 269-275 (1972): 4 rats/sex/dose/treatmrnt time, killed 6, 24 and 48 hrs after dosing
Year	:	1982
GLP	:	yes
Test substance	:	other TS: purity: 96,5 %
Reliability	:	(2) valid with restrictions
Flag	:	Critical study for SIDS endpoint

22.08.2000 (41)

5.7 CARCINOGENICITY

5.8.1 TOXICITY TO FERTILITY

5.8.2 DEVELOPMENTAL TOXICITY/TERATOGENICITY

Species	:	rat
Sex	:	female
Strain	:	other: CrL : COBS CD (SD) BR
Route of admin.	:	inhalation
Exposure period	:	days 6-19 of gestation
Frequency of treatm.	:	6 h/d
Duration of test	:	on day 20 of gestation the dams were killed
Doses	:	0, 1.1, 3.1 or 9.0 mg/l
Control group	:	yes, concurrent no treatment
NOAEL maternal tox.	:	ca. 1.1 mg/l
LOAEL Teratogenicity	:	ca. 1.1 mg/l
Method	:	other: 25 females/dose, whole-body exposure, animals were kept individually during exposure
Year	:	1982
GLP	:	yes
Test substance	:	other TS: purity: 96.5 %
Remark	:	analytical concentrations
Result	:	1.1 mg/l: no maternal effects being obviously attributable to treatment fetal effects: 4 malformed fetus compatred to 3 in the control group. One showing brachygnathia, one showing retro-oesophageal aortic arch, one showing cardiac ventricular septal defect and one showing brachydactyly and bachymelia of all four limbs. The last malformation was similiar with the observed malformation of six fetuses at 9 mg/l 3.1 mg/l: maternal effects: slight ataxia observable during the exposure periods fetal effects: no notable or significant deviations from control values among litter parameters and among indices of malformations, anomalies and skeletal variants of the offspring 3.1 and 9 mg/l: maternal effects: dosage-related reduction in food consumption and in bodyweight gain and dosage-related increase in water consumption 9 mg/l: maternal effects: ataxia, lachrymation and/or salivation among occasional animals during exposure, and brown fur staining; fetal effects: mean values for litter and mean fetal weight significantly reduced; increase in the incidence of fetal malformations mainly due to the occurrence of six fetuses (distributed among four litters) showing brachydactyly of a single fore- or hindpaw; for five of the 6 fetuses the brachydactyly was associated with a terminal haemorrhagic area on the affected paw; 3 other malformations (1 microphthalmia,1 anophthalmia amd 1 cardiac ventricular septal defect); correlating with the lower mean fetal weight, reduced skeletal ossification observable, providing an increased incidence of fetuses with sternebral variants and contributing to a significant increase in fetuses with skeletal anomaly; incidence of visceral anomalies unaffected
Test substance	:	composition of the test substance: 96.5 % o-chlorotoluene, 3.4 % p-chlorotoluene and 0.1 % toluene
Reliability	:	(2) valid with restrictions

Flag	:	Critical study for SIDS endpoint
31.01.2002		(42)
Species	:	rabbit
Sex	:	female
Strain	:	New Zealand white
Route of admin.	:	inhalation
Exposure period	:	days 6-28 of gestation
Frequency of treatm.	:	6 h/d
Duration of test	:	on day 29 of gestation the dams were killed
Doses	:	0, 1.5, 4.0 or 10.0 mg/l
Control group	:	yes, concurrent no treatment
NOAEL maternal tox.	:	ca. 1.5 mg/l
NOAEL teratogen.	:	ca. 4 mg/l
Method	:	other: 16 females/dose, whole-body exposure, rabbits were held individually during exposure
Year	:	1983
GLP	:	yes
Test substance	:	other TS: purity: 96.5 %
Remark	:	analytical concentrations
Result	:	There were 6 deaths associated with pulmonary disorder. Although four of these occurred at 10 mg/l, there was no conclusive association with treatment. all dose groups: no significant effect on litter size, pre- and post implantation loss, or litter and mean fetal weight; the mean percentage incidence of fetuses with skeletal anomaly was higher than the control incidence; the difference were neither statistically significant (P<0.05) nor dosage-related. In addition the incidences were within the range of historical control data. 1.5 mg/l: no maternal effects obviously attributable to treatment fetal effcts: 4 malformed fetuses, 3 occurred in a single litter and all showed vertebral defects. A fouth fetus in a second litter showed cebocephaly and hydrocephaly. 4 mg/l: maternal effects: partial ptosis observable in occasional animals fetal effects: 1 malformed fetus showed a major heart vessel defect. 4 and 10 mg/l: maternal effects: rapid respiration detectable shortly following exposure (at the 4 mg/l level, to a lesser extent); dosage-related reduction in food consumption and in bodyweight gain during the initial part of the treatment period 10 mg/l: maternal effects: lachrymation, salivation and ptosis observable during initial exposures fetal effects: 1 fetus showed unilateral microphthalmia, major heart defect and forelimb brachydactyly.
Test substance	:	composition of the test substance: 96.5 % o-chlorotoluene, 3.4 % p-chlorotoluene and 0.1 % toluene
Reliability	:	(2) valid with restrictions
Flag	:	Critical study for SIDS endpoint
31.01.2002		(43)

5.8.3 TOXICITY TO REPRODUCTION, OTHER STUDIES

5.9 SPECIFIC INVESTIGATIONS

5.10 EXPOSURE EXPERIENCE

Remark : experience with occupational exposure to a mixture of o- and p-chlorotoluene (composition of the mixture unspecified): at a concentration of 400 ppm (= 2.106 mg/l), chlorotoluene causes severe toxic effects in persons exposed by inhalation for 60 min.; at a concentration of 200 ppm (= 1.053 mg/l), chlorotoluene leads to symptoms of illness in persons, if the exposure continues for more than a short time; concentrations in general atmosphere of plant which are greater than 75 ppm (= 0.395 mg/l) indicate unsatisfactory conditions

Flag : Critical study for SIDS endpoint

(44)

5.11 ADDITIONAL REMARKS

6.1 ANALYTICAL METHODS

6.2 DETECTION AND IDENTIFICATION

7.1 FUNCTION

7.2 EFFECTS ON ORGANISMS TO BE CONTROLLED

7.3 ORGANISMS TO BE PROTECTED

7.4 USER

7.5 RESISTANCE

8.1 METHODS HANDLING AND STORING

8.2 FIRE GUIDANCE

8.3 EMERGENCY MEASURES

8.4 POSSIB. OF RENDERING SUBST. HARMLESS

8.5 WASTE MANAGEMENT

8.6 SIDE-EFFECTS DETECTION

8.7 SUBSTANCE REGISTERED AS DANGEROUS FOR GROUND WATER

8.8 REACTIVITY TOWARDS CONTAINER MATERIAL

(1) GDCh-Advisory Committee on Existing Chemicals, VCH, Weinheim

(2) Ullmann's Encyclopedia of Industrial Chemistry, 5th edition, Vol. A6, Weinheim: VCH (1986), p.340

(3) Safety Data Sheet Bayer AG (25.05.1999)

(4) Handbook of Environmental Data on Organic Chemicals, Ed. : Karel Verschueren. 3rd ed. (1996), S. 519

(5) Leo, A. et al. Chemical Reviews 71(6), 1971

(6) Bayer AG data, Test on water solubility (1987)

(7) Calculation Bayer AG (1999), SCR-AOP / AOPWIN 1994

(8) UBA-Immissionsatlas, Berlin

(9) Calculation Bayer AG, EPIWIN 2.30 (1999)

(10) Bayer AG, unpublished test (1992)

(11) Bayer AG, unpublished calculation (1987)

(12) Banerjee, P. Piwoni, M.D. Ebeid, K. (1985) Sorption of organic contaminants to a low carbon subsurface core. Chemosphere 14, 1057-1067

(13) Bayer AG data, Biodegradation Test (Respiration Test) 1991

(14) Bayer AG data, Biodegradation Test (Zahn Wellens Test) 1991

(15) Biodegradation and Bioaccumulation Data of Existing Chemicals Based on the CSCL Japan, Compiled under the Supervision of Chemical Products Safety Division, Basic Industries Bureau MITI, Ed. by CITI, October 1992. Published by Japan Chemical Industry Ecology-Toxicology & Information Center

(16) Federal Register, Office of Federal Register 47, 231, 54160 - 54161 (1982), Ed.: National Archives and Records Administration, Washington DC 20408

(17) Bengtsson, B.-E. and Tarkpea, M., Marine Pollution Bulletin Vol. 14 (6), 213-214 (1983)

(18) Linden, E. et al., Chemosphere 11/12, 843-851 (1979)

(19) Kühn, R., Pattard M.: Damaging effects of environmental chemicals in the Daphnia reproduction test as a basis for evaluation of the environmental hazard in aquatic system, report of Umweltbundesamt, Berlin (UFOPLAN -Nr. 10603052), 1988

(20) Kuehn, R. und Pattard, M., Water Research 24 (1), 31-38 (1990)

(21) Bringmann, G. , Kühn, R.: Grenzwerte der Schadwirkung wassergefaehrdender Stoffe gegen Bakterien (Pseudomonas putida) und Grünalgen (Scenedsmus quadricauda) im Zellvermehrungshemmtest. Z. Wasser und Abwasser-Forsch. 10 (1977) 87-89

(22) Springborn Bionomics, Inc. (1986): The chronic toxicity of o-chlorotoluene to Daphnia magna under flow-through conditions. Research report submitted to Occidental Chemical Corp., Niagara Falls, New York. Report #BW-86-9-2121; Study #10826.0885.6100. Springborn Bionomics, Inc., Wareham, Massachusetts, August 1986

(23) Bayer AG, Test on Phytotoxicity of o-chlorotoluene, unpublished (1986)

(24) Arthur, B.H. et al., "The effects on laboratory animals from single exposures to o-chlortoluene" unpublished report, Toxicology Division, Lilly Research Laboratories (1974)

(25) Bayer AG data, Report No. 5799, January 5, 1976

(26) Barry, E.S.: Toxicological report o-chlorotoluene. ICI-Ltd., unpublished report, Report Number: HO/IH/T/768 (division: Nobel), July 10, 1970

(27) Hazelton (1972), Acute Vapor Inhalation Toxicity (LC50) of Orthochlorotoluene and Orthodichlorobenzene in Rats (To Hooker Industrial Chemicals Division): cited in Hooker Chemicals and Plastics Corporation: 2-Chlorotoluene proposal for voluntary testing program, unpublished report, December 22, 1981

(28) Arthur, B.H. et al., The effects on laboratory animals from single exposures to o-chlorotoluene, unpublished report, Toxicology Devision, Lilly Research Laboratories, 13 pages (June 1974), cited also in Microfiche No.: OTS 05073

(29) Bayer AG data, Report No. 16899, July 14, 1988

(30) Bayer AG data, Report No. 20859, November 29, 1991

(31) Huntingdon Research Centre: HRC Report No. HKR 5/82802, 2-Chlorotoluene, a preliminary inhalation study in the rat and rabbit, January 13, 1983 (at the request of Hooker Chemicals and Plastcs Cooperation): cited in US-EPA: 2-Chlorotoluene; decision not to test. Fed. Reg. 50, 40445-40449 (1985); in MF-No.: OTS 0507456; in MF-No.: OTS0557419

(32) Gibson, W.R. et al.: The toxicity of daily oral doses of o-chlorotoluene in the rat, unpublished report, Lilly Research Laboratories, Toxicology Division, June, 1974; also cited in MF-No.; OTS 0507456

(33) Hill, R.M.: The safety evaluation of o-chlorotoluene, Elanco Products Company, unpublished report, August 12, 1981: cited in US-EPA: 2-Chlorotoluene; decision not to test, Fed. Reg. 50, 40445-40449 (1985): also cited in Mf-No.: OTS0507354

(34) Gibson, W.R. et al.: The toxicity of daily oral doses of o-chlorotoluene in the dog, unpublished report, Lilly Research Laboratories, To xicology Division, June, 1974, also cited in MF.: OTS 0507456

(35) Hill, R.M.: The safety evaluation of o-chlorotoluene, Elanco Products Company, unpublished report, August 12, 1981: cited in US-EPA: 2-Chlorotoluene; decision not to test, Fed. Reg. 50, 40445-40449 (1985)

(36) Litton Bionetics Inc.: Mutagenicity evaluation of ortho-chlorotoluene in the Ames Salmonella/microsome plate test, Final Report, LBI Project No. 20988 , March, 1982, (at the request of Hooker Chemical and Plastics Corporation); MF-No.: OTS 0507442

(37) Litton Bionetics Inc.: Mutagenicity evaluation of ortho-chlorotoluene. A composition of 2-chlorotoluene (96.5 percent), 4-chlorotoluene (3.4 percent) and toluene (0.1 percent) in the Ames Salmonella/microsome plate test: amendment to the final report, LBI-Proj. No. 20988, April 1982 (at the request of Hooker Chemical and Plastics Corporation), MF-No.: 507442, and cited in US-EPA: 2-Chlorotoluene; decision not to test. Fed. Reg. 50, 40445-40449 (1985)

(38) Litton Bionetics Inc.: Mutagenicity evaluation of ortho-chlorotoluene in an vitro cytogenetic assay measuring chromosome aberration frequencies in Chinese hamster ov-ary (CHO) cells, Final Report, LBI Project no. 20990, June, 1982 (at the repquest of Hooker Chemical Company), MF.-No.: OTS0507446

(39) Litton Bionetics Inc.: Mutagenicity evaluation of ortho-chlorotoluene in the mouse lymphoma forward mutation as-say, Final Report, LBI Project No.:20989, July, 1982 (at the request of Hooker Chemicals and Plastics Corporation), Mf.-No.: OTS0507444

(40) Litton Bionetics Inc.: Mutagenicity evaluation of ortho-chlorotoluene in the rat bone marrow cytogenetic assay, Final Report, unpublished report, July, 1982

(41) Litton Bionetics Inc.: Mutagenicity evaluation of ortho-chlorotoluene in the rat bone marrow cytogenetic assay, Final Report, July 1982

(42) Huntingdon Research Centre: Effect of 2-chlorotoluene va-pour on pregnancy of the rat, Final Report, HKR 8/821122, August, 1983 (at the request of Occidental Chemical Corporation, Hooker Industrial and Specialty Chemicals), Mf No.: 0507458, 0557419, 0507453, 0537014, 0557418, 0507455

(43) Huntingdon Research Centre: Effect of 2-chlorotoluene vapour on pregnancy of the New Zealand white rabbit, HKR 8/821122, Final Report, August 1983 (at tthe request of Occidental Chemical Corporation, Hooker Industrial and Specialty Chemicals), MF. No.: 0507457, 0557419, 0557416

(44) Goldblatt, M.W.: Br. J. Ind. Med. 12, 1-20 (1955)

10.1 END POINT SUMMARY

10.2 HAZARD SUMMARY

10.3 RISK ASSESSMENT