

[FOREWORD](#)

[INTRODUCTION](#)

TRIBUTYL PHOSPHATE
CAS N°: 126-73-8

**SIDS Initial Assessment Report
for
12th SIAM**

(Paris, France June 2001)

Chemical Name : Tributyl Phosphate

CAS No: 126-73-8

Sponsor Country: U.S.A

National SIDS Contact Point in Sponsor Country:

US EPA
Dr. Oscar Hernandez (7403M)
ICC Building
1200 Pennsylvania Avenue, N.W.
Washington, DC 20460 U.S.A.
e-mail: Hernandez.oscar@epa.gov
phone: 202-564-7641

HISTORY: First time considered for a SIAM. No new testing was performed. All available data was provided from company files and public databases.

COMMENTS: An IPCS document is available for this chemical. IPCS Environmental Health Criteria Document No. 112, WHO, 1991.

Deadline for circulation:

Date of Circulation: April 2001 (updated March 2002)

SIDS INITIAL ASSESSMENT PROFILE

CAS No.	126-73-8
Chemical Name	Tributyl phosphate
Structural Formula	(C ₄ H ₉ O) ₃ PO
RECOMMENDATIONS	
The chemical is a candidate for further work under conditions specified below.	
SUMMARY CONCLUSIONS OF THE SIAR	
Human Health	
<p>The toxicology database for tributyl phosphate (TBP) is large and well documented. There are adequate data with which to evaluate the potential hazard to human health of this compound. Acute oral toxicity values in rodents range from 1390 to 3350 mg/kg-bw in rats and from 400 to 1240 mg/kg-bw in mice. A rat six-hour LC50 of > 4.2 mg/L (highest dose tested) was reported. Dermal studies exist in rabbits (LD50s of >3100 mg/kg-bw and > 10,000 mg/kg-bw) and in guinea pigs (LD50 of 9700 – 19,400 mg/kg-bw). Repeat dose studies have been performed in animals via the inhalation (4 month studies in rats and rabbits) and oral (gavage studies in rats [one week to 18 weeks] and rabbits [two weeks] and dietary feeding studies in rats [nine weeks to two years] and mice [four weeks to two years]) routes. Effects observed in the inhalation studies were depressed cholinesterase levels (reversible after exposure stopped) at the highest tested dose (13.6 mg/m³) in both rats and rabbits. Overall, the results of the rodent dietary/gavage studies consistently showed cellular and/or weight changes in the liver, kidney, and bladder. In the rat, two-year dietary study, the NOAEL is 200 ppm (9 mg/kg-bw/day males and 12 mg/kg/day females) for cytotoxicity/hyperplasia in the urinary bladder. In an 18 month dietary study using CD-1 mice the NOAEL was 150 ppm (28.9 mg/kg/day for females and 24.1 mg/kg/day for males), the lowest dose tested. TBP did not affect reproductive performance in a two-generation feeding study in rats (NOAEL of > 225 mg/kg-bw/day). Developmental toxicity was observed in the two-generation study, but only at levels at which maternal toxicity was observed (NOAEL < 15 mg/kg-bw/day; reduced pup weights along with reduced maternal body weight gain and decreased food consumption). In three separate teratology experiments (two with rats and one with rabbits), teratogenic (delayed ossification and rudimentary ribs) and developmental (reduced fetal weights) effects were observed only at maternally toxic doses and only in rats (NOAEL in rabbit study was the highest dose tested – 400 mg/kg-bw/day). The NOAEL for teratogenic effects was 750 mg/kg-bw/day, but the NOAEL for maternal toxicity was 62.5 mg/kg-bw/day. TBP is an animal carcinogen when administered in the diet at levels greater than 200 ppm in rats (9 mg/kg-bw/day) or 150 ppm in mice (24 mg/kg-bw/day). Overall the results of genetic toxicity studies indicate that TBP is not genotoxic. These include <i>in vitro</i> and <i>in vivo</i> data. A mechanistic study in rats found that the effects of TBP on the bladder were reversible upon withdrawal of treatment and thus likely due to the direct urothelial cytotoxicity of the chemical itself (or its metabolites), and not a result of urinary changes.</p> <p>The neurotoxicity of TBP has been studied in several species including the rat, hen, and rabbit. In these studies, TBP produced either no signs of neurotoxicity or only slight or transient effects on measured endpoints. TBP is irritating to the skin and eye of humans and laboratory animals but does not cause sensitization in humans. The primary exposure to TBP is through dermal contact in the occupational setting. Based on this exposure route and the NOAEL levels reported, the most likely effects of TBP exposure are irritation of the skin and eyes.</p>	

Environment

In both soil and water, TBP is expected to adsorb to sediments or particulate matter and biodegrade. In the atmosphere, TBP will exist as a vapour and will be subject to rapid photodegradation. Bioconcentration is not expected to occur. Numerous acute and chronic toxicity data are available for fish, invertebrates, and algae. The acute toxicity values for fish (96-hr LC50) from over a dozen studies range from 4.2 to 18 mg/L. Toxicity values for six species of algae ranged from a 72-hr EC50 (biomass) of 1.1 mg/L (*Scenedesmus subspicatus*) to a 48 hr EC50 of 5-10 mg/L (*Chlorella emersonii*). Algal NOECs have been reported in two different studies (0.37 mg/L as an EC10 for biomass in *Scenedesmus subspicatus* and 2.2 mg/L in a 96-hr study with *Selanastrum capricornatum*). Daphnid chronic NOECs range from 0.87 mg/L (21-day study) to 3.1 mg/L (14-day study). The lowest fish NOEC occurred at a concentration of 0.82 mg/L (95-day early life-stage study). Using an assessment factor of 10, since long-term NOECs are available for three species representing three trophic levels (fish, *Daphnia*, and algae), and the lowest valid NOEC (0.37 mg/L for algae, the resulting aquatic predicted no-effect concentration (PNEC) is 0.037 mg/L.

Exposure

The production volume of TBP is estimated at 3,000 – 5,000 tonnes worldwide. The major uses of TBP in industry are as a component of aircraft hydraulic fluid and as a solvent for rare earth extraction and purification. Minor uses of TBP include use as a defoamer additive in cement casings for oil wells, an anti-air entrainment additive for coatings and floor finishes, as well as a carrier for fluorescent dyes. The major uses of TBP comprise over 80 percent of the volume produced. No current consumer product uses of TBP have been identified. The primary occupational exposure to TBP results from its use as an ingredient in aircraft hydraulic fluids. The potential for exposure to TBP varies with the type of maintenance activity, but is almost always via a dermal pathway.

NATURE OF FURTHER WORK RECOMMENDED

The chemical is considered a candidate for further work, in the context of a risk assessment, if it is used as a herbicide or has other dispersive uses.

FULL SIDS SUMMARY

CAS NO 126-73-8:		TEST SPECIES	PROTOCOL/ EPA GUIDELINE	RESULTS
PHYSICAL-CHEMICAL				
2.1	Melting Point			-70°C
2.2	Boiling Point			130°C at 5hPa
2.3	Density			0.97 g/m ³
2.4	Vapor Pressure			3.47 x 10 ⁶ hPa at 25°C
2.5	Partition Coefficient (Log Pow)			2.5 – 4 (experimental) 3.5 (calculated)
2.6A.	Water Solubility			400 mg/L at 20°C
B	pH			not reported
	pKa			not reported
2.12	Oxidation: Reduction Potential			not reported
ENVIRONMENTAL FATE AND PATHWAY				
3.1.1	Photodegradation			85% after 1 hour
3.1.2	Stability in Water			Stable
3.2	Monitoring Data			In Air 3.1 – 41.4 ng/m ³ (Japan) In Water 6 – 4,500 ng/L (Japan) In Water 100 – 3,900 ng/L (Europe) In Sediment 0.9 – 350 ug/kg (Japan) Biota 1.1 – 250 ug/kg
3.3	Transport and Distribution		Mackay Level III, equal distribution	In Air 0% In Water 1% In Sediment 99% In Soil 0%
3.5	Biodegradation			Ready Biodegradability 301D and 301E: 89 – 90.8% after 28 days
ECOTOXICOLOGY				
4.1	Acute/Prolonged Toxicity to Fish	various	797.1400	LC ₅₀ (96 hr) = 4.2 – 18 mg/L
4.2	Acute Toxicity to Aquatic Invertebrates	<i>Daphnia magna</i>	797.1300	EC ₅₀ (24 hr) = 4.2 – 35 mg/L EC ₅₀ (48 hr) = 2.6 – 9 mg/L
		<i>Hyalella azteca</i>	795.120	EC ₅₀ (96 hr) = 2.4 mg/l
		<i>Grammarus</i>	795.120	EC ₅₀ (96 hr) = 1.7 mg/l
		<i>Pseudolimnaeus</i>		
4.3	Toxicity to Aquatic Plants e.g., Algae	various	797.1050	EC ₅₀ (72 hr) = 1.1 – 2.8 mg/L EC ₅₀ (96 hr) = 4.4 mg/L EC ₁₀ (72 hr) = 0.37 – 0.92 mg/L NOEC (96 hr) = 2.2 mg/L
4.5.1	Chronic Toxicity to Fish	<i>Oncorhynchus mykss</i>	797.1600	NOEC (95 d) = 0.82 mg/L
4.5.2	Chronic Toxicity to Aquatic Invertebrates	<i>Daphnia magna</i>	797.1330	NOEC (21d) = 0.87 mg/L
4.6.1	Toxicity to Soil Dwelling Organisms	<i>Tetranychus urticae</i>		No mortality at 2 g/kg
4.6.2	Toxicity to Terrestrial Plants			Damage to leaf surface, defoliant, leaf drying
4.6.3	Toxicity to Other Non- Mammalian Terrestrial Species (Including Birds)			No information available
TOXICOLOGY				
5.1.1	Acute Oral Toxicity	rat	798.2650	LD ₅₀ = 1,390 – 11,265 mg/kg
		mouse	798.2650	LD ₅₀ = 400 – 1,240 mg/kg
		hen		LD ₅₀ = 1,500 – 1,800 mg/kg
5.1.2	Acute Inhalation Toxicity	rat	798.2450	LC ₅₀ = >4.242 – >42 mg/L; LC ₀ = 1.5 mg/L
		mouse		LC ₅₀ = 1.3 mg/L
		cat		LC ₅₀ = 24.51 mg/L
5.1.3	Acute Dermal Toxicity	rabbit	798.2250	LD ₅₀ = >3,100 - >10,000 mg/L
		guinea pig	798.4100	LD ₅₀ = 9,700 – 19,400 mg/L
5.2	Corrosiveness/Irritation			

CAS NO 126-73-8:		TEST SPECIES	PROTOCOL/ EPA GUIDELINE	RESULTS
	Skin	rabbit, guinea pig		Irritating to highly irritating (intact and abraded skin)
	Eye	rabbits		Slightly irritating to irritating
5.3	Sensitization	guinea pig	798.4100	Non-sensitizing
5.4	Repeated Dose Toxicity	rat, mouse, rabbit	798.2650	NOAEL = 150 ppm in diet
5.5	Genetic Toxicity In Vitro			
A.	Bacterial Test (Gene mutation)		798.5265	4-, 1+ w & w/out metabolic activation - (negative) – two studies
B.	Non-Bacterial In Vitro Test (Chromosomal aberrations)			- (negative) – one study
5.6	Genetic Toxicity In Vivo		798.5375	- (negative) – two studies
5.7	Carcinogenicity	Sprague-Dawley rat	798.5385	NOAEL = 200 ppm in diet (chronic toxicity) Transitional cell carcinomas in high dose groups
		CD-1 Mouse	798.3300	NOAEL = 150 ppm in diet (chronic toxicity) Hepatocellular adenoma in high dose males
5.8	Toxicity to Reproduction	Sprague-Dawley rat	798.3320	NOAEL = < 200 ppm (Parental toxicity) NOAEL = <200 ppm (post-natal toxicity)
5.9	Developmental Toxicity/ Teratogenicity	Sprague-Dawley rat	798.4700	NOAEL > 3000 ppm (Parental reprod. toxicity)
		Wistar rat		NOAEL <62.5 mg/kg bw/d (Maternal toxicity)
		New Zealand rabbit	798.4900	NOAEL = >750 mg/kg bw/d (Teratogenicity) NOAEL = 375 mg/kg/d (Fetal toxicity)
5.11	Experience with Human Exposure			Skin Permeability = 0.18 ug/cm ³ /min Reported symptoms: nausea, headache, skin irritation, and skin rash

SIDS INITIAL ASSESSMENT REPORT

1. IDENTITY

Chemical name: tributyl phosphate
Synonyms: phosphoric acid, tributyl ester
CAS-number: 126-73-8
Empirical formula: C₁₂H₂₇O₄P
Molecular weight: 266.32
Structural formula: (C₄H₉O)₃PO
Degree of purity: 100 % w/w
Major impurities: none

1.1 Physical-Chemical Properties

Melting point: -70 °C (1)
Boiling point: 130 °C at 5 hPa (1)
Density: 0.97 g/cm³ at 20 °C (1)
Vapor Pressure: 3.47 x 10⁻⁶ hPa at 25 °C* (2.6 x 10⁻⁶ mmHg) (2)

*Two values are provided in the SIDS Dossier. The above value was chosen as the most accurate because it was derived in a GLP compliant 1990 study.

Octanol/water partition coefficient: Log K_{ow} = 2.5 (experimentally determined) (3)
Log K_{ow} = 4 (experimentally determined)* (4)
Log K_{ow} = 3.5 (calculated using CLOGP) (5)

*The Log K_{ow} of 4 is considered the most reliable value because it was determined experimentally by an experienced laboratory and published in a peer-reviewed journal. While the Log K_{ow} of 2.5 was experimentally determined, the conditions under which it was determined are not known.

Water solubility: 0.4 g/L at 20 °C (1)
Flash point: >150 °C (1)

2. GENERAL INFORMATION ON USE AND EXPOSURE

Volume Produced: Estimated 3,000 – 5,000 tonnes worldwide (from Producers).

Use Pattern: The major uses of tributyl phosphate (TBP) in industry are as a flame retardant component of aircraft hydraulic fluid and as a solvent for rare earth extraction and purification. Minor uses of TBP include use as a defoamer additive in cement casings for oil wells, as an anti-air entrainment additive for coatings and floor finishes, as a solvent in nuclear fuel processing, and as a carrier for fluorescent dyes. The major uses of TBP comprise over 80 percent of the volume produced. There are no consumer products that are known to contain TBP. Non-specific plant herbicides that contained TBP were reformulated in the mid-1980s and are no longer available for use.

2.1 Environmental Exposure and Fate

2.1.2 Photodegradation

In the atmosphere, TBP should exist primarily as a vapor based upon the vapor pressure of 3.47×10^{-6} hPa (2.6×10^{-6} mmHg) at 25°C. In one study, the photodegradation of TBP was observed with 85 percent decrease in concentration after 1 hour. (13)

2.1.3 Stability in Water

In water, TBP hydrolyzes by a base-catalyzed reaction. However, hydrolytic degradation was not observed after 30 days in [sterile] water with pH ranging from 3 to 11 (11). In another study, TBP in the presence of bacteria (*Pseudomonas diminuta*) showed greater than 50 percent degradation after 2 hours and 100 percent degradation after 43 hours. (12)

2.1.4 Biodegradation (biotic and abiotic)

Degradation of TBP has been evaluated under a variety of conditions. In a 28-day biodegradation study, using domestic activated sludge from a sewage treatment plant, the rate of biodegradation was determined to be 90.8% (4). In addition, supporting data from another 28-day biodegradation study, the percent degradation of TBP was considered to be 89% (7). Due to data limitations it is unclear if this study result along with the remaining study entries in the dossier required activation. As a result, the reliability of this data is unknown but supports the conclusion that TBP is considered to be biodegradable.

2.1.5 Transport and Distribution

2.1.5.1 Transport: Koc values experimentally determined for silty loam, clay loam, and sandy loam were 1460, 1188, and 378, respectively, indicating low mobility of TBP in silty and clay loam soils and medium mobility in sandy loam soils. (16)

The water solubility of TBP at room temperature is 0.4 g/L. Based on its estimated Henry's Law constant (1.5×10^{-7} atm-m³/mol), it is unlikely that volatilization from surface water will occur to a significant extent.

2.1.5.2 Distribution: Calculated using Mackay, Level III with input values of: MW 266.32; WS 0.4 g/L at 20°C; VP 0.000347 Pa at 25°C; Log Kow = 4 and MP-70C.

Compartment	Air%	Water%	Soil%	Sediment%
Air only (1000 kg/hr)	0.67	<0.3	99	0
Water only (1000 kg/hr)	0	63	23	14
Soil only (1000 kg/hr)	0	0	100	0
Equal distribution				
(1000 kg/hr) Air, water and soil	0	1	99	0

The reported TBP concentrations in Japanese air and surface water are 3.1 to 41.4 ng/m³ and 6 to 4,500 ng/L. European surface water TBP concentrations range from 100 to 3,900 ng/L. TBP in Japanese sediment range from 0.9 to 350 ug/kg.

Other reported environmental concentrations in biological matrices include: (6)

Species	Concentration
fish	1.1 – 26 ug/kg
crustacea	10 – 20 ug/kg
birds	20 – 250 ug/kg

2.1.6 Bioaccumulation

Bioconcentration factors (BCFs) have been determined experimentally for several fish species:

Species	BCF	
<i>Carassius auratus</i> (Goldfish)	6 – 11	(14)
<i>Cyprinus carpio</i> (carp)	5.5 – 10	(8)
	6.9 – 20	(8)
<i>Oryzias latipes</i> (Rice fish)	11 – 49	(15)
	30 – 35	(14)
	16 – 27	(6)

2.1.7 Degradation Products And Their Environmental Fate And Pathways

There is no information available on this subject.

2.2 Human Exposure

Included in the SIAR is information obtained from the “1987 US. Survey of Tributyl Phosphate Uses, Potential Exposure, and Safety Procedures,” prepared for the Tributyl Phosphate Task Force.

2.2.1 Occupational Exposure

Workers that manufacture, formulate, process, or distribute TBP may be exposed during these activities. These workers may be exposed by activities such as transfer of TBP from partial tank trucks to process storage tanks or smaller end-use containers (e.g., 55-gallon drums), sampling, and maintenance of processing facilities. This potential worker exposure would be mainly dermal.

The primary occupational exposure to TBP results from its use as an ingredient in aircraft hydraulic fluids. These products contain TBP in concentrations ranging from 25 to 75 percent, depending upon the specific brand or formulation. Aircraft hydraulic fluid users may be exposed to TBP through one of three basic aircraft maintenance procedures: 1) routine checking of fluid levels in an aircraft reservoir; 2) performing any of several types of aircraft maintenance that involves draining and refilling hydraulic systems or

removing hydraulic system parts from an aircraft; and, 3) testing the operation of a hydraulic system part in a test stand in a maintenance shop.

Aircraft hydraulic fluid is generally marketed for direct use in small volume cans (quart, gallon, and 5-gallon), but some maintenance facilities purchase in 55-gallon drums and transfer to smaller, more mobile containers for shop use.

The potential for exposure to TBP varies with the type of maintenance activity, but is almost always via a dermal pathway. Any exposure to mists of hydraulic fluid reported has been as a result of accidental leaks during hydraulic system operation or maintenance, or from venting of pressure prior to draining a system. Any exposure of aircraft passengers and/or crew to TBP, as a constituent of aircraft hydraulic fluid, is the result of a mechanical component failure during operations. When such failure occurs, TBP is typically decomposed.

2.2.1.1 OSHA Standards:

Permissible Exposure Limit:	5 mg/m ³
-----------------------------	---------------------

2.2.1.2 Threshold Limit Values:

8 hr time-weighted average (TWA):	0.2 ppm
10 hr time-weighted average:	0.2 ppm (NIOSH)
Immediately dangerous to life or health (IDLH):	30 ppm (NIOSH)
Australia	0.2 ppm
UK (10 minute STEL):	5 mg/m ³

The TBP BEI is 70% of an individual's red blood cell cholinesterase activity.

2.2.2 Consumer Exposure

No current consumer product uses of TBP have been identified.

2.2.3 Indirect Exposure In the Environment

There is minimal information to indicate indirect exposure. The presence of TBP in sewage sludge suggests this could be an indirect route of exposure.

2.2.4 Conclusions

The primary and most probable route of exposure to TBP is through dermal contact in the occupational setting. The dermal toxicity of TBP has been shown to be very low. A secondary, infrequent route of exposure is to mist resulting from accidental leaks in an operating hydraulic system.

3. EFFECTS ON THE ENVIRONMENT

3.1 Aquatic Effects

The following subsections present the ecotoxicological effect concentrations and corresponding aquatic compartment.

3.1.1 Toxicity to Fish

The acute toxicity values (96-hr LC50) from over a dozen studies range from 4.2 to 18 mg/L for the following species: *Oncorhynchus mykiss* (rainbow trout), *Brachydanio rerio* (zebrafish), *Carassius auratus* (goldfish), *Leuciscus idus*, *Oryzias latipes* (medaka/Japanese rice fish), and *Pimephales promelas* (fathead minnow). Three prolonged or chronic studies up to 95 days in length have been conducted. The definitive study with rainbow trout produced a No Observed Effects Concentration (NOEC) of 0.82 mg/L and a Lowest Observed Effects Concentration (LOEC) of 1.7 mg/L. Measured endpoints included time to swim-up, survival, length and weight.

Species	Endpoint	Toxicity Value(s)	Remarks
<i>Oncorhynchus mykiss</i> ¹ (rainbow trout)	96-hr LC50	11 mg/L	Static; GLP study (17)
	96-hr LC50	4.2–11.8 mg/L	Static; 10 - 20°C (18)
	96-hr LC50	13 mg/L	Flow through (19)
	50-d NOEC*	8.3 mg/L	Embryo-larval; semi-static (20)
	95-d NOEC	0.82 mg/L	Early life stage test; GLP (21)
	95-d LOEC	1.7 mg/L	Early life stage test; GLP (21)
<i>Brachydanio rerio</i> (zebrafish)	96-hr LC50	~11.8 mg/L	Static (7)
	144-hr LC50	11.4 mg/L	Static (20)
	10-d NOEC*	13.5 mg/L	Semi-static (20)
<i>Carrasius auratus</i> (goldfish)	96-hr EC50	8.8 m g/L	Static (14)
<i>Leuciscus idus</i>	96-hr EC50	7.6 mg/L	Static (22)
<i>Oryzias latipes</i> (medaka)	96-hr EC50	9.6 mg/L	Static (14)
	96-hr LC50	4.5 mg/L	OECD 203 (23)
	48-hr LC50	18 mg/L	Static (26)
<i>Pimephales promelas</i> (fathead minnow)	96-hr LC50	6.4 mg/L	Static; GLP study (24)
	96-hr LC50	8.2 – 11 mg/L	(25)

* Threshold concentration

3.1.2 Toxicity to Invertebrates

The acute toxicity of TBP to two species of water fleas (*Daphnia magna* and *Daphnia pulex*) ranged from 4.2 to 68 mg/L when expressed as a 24-hr EC50 (median effect concentration). Concentrations affecting *D. magna* and two species of amphipods (*Gammarus pseudolimnaeus* and *Hyallela azteca*) in tests lasting from 48 to 96 hours ranged from 1.7 to 9 mg/L. In a chronic (21-day) study with *D. magna*, the NOEC and LOEC were 0.87 mg/L and 2.1 mg/L, respectively, values very close to those reported for the rainbow trout.

¹ The scientific name for the rainbow trout was formerly *Salmo gairdneri*. Several of the studies referenced refer to it by this name rather than the currently accepted scientific name.

Species	Endpoint	Toxicity Value(s)	Remarks
<i>Daphnia magna</i>	24-hr EC50	4.2 – 35 mg/L	(23, 27, 28, 29)
	48-hr EC50	2.6 – 9 mg/L	GLP study (27, 30, 31)
	48-hr NOEC	0.8 – 3.1 mg/L	(27, 30, 31)
	72-hr LC50	2.1 mg/L	ISO (1975) (27)
	14-d NOEC	3.1 mg/L	OECD 202 (23)
	21-d NOEC	0.87 mg/L	GLP study (32)
	21-d LOEC	2.1 mg/L ²	GLP study (32)
	<i>Daphnia pulex</i>	6-hr EC50	93 mg/L
24-hr EC60		68 mg/L	(29)
<i>Gammarus pseudolimnaeus</i>	96-hr EC50	1.7 mg/L	EPA 795.120 (33)
<i>Hyalella azteca</i>	96-hr EC50	2.4 mg/L	EPA 795.120 (34)

3.1.3 Toxicity to Algae

Toxicity values for six species of algae ranged from 1.1 to 5 mg/L and were of the same general order of magnitude as those producing effects on fish and invertebrates. In *Scenedesmus subspicatus*, 72 hour, EC₁₀ values ranged from 0.37 to 1.1 mg/L for biomass and 0.92 to 2.8 mg/L for growth rate.

Species	Test	Toxicity Value	Remarks
<i>Chlorella vulgaris</i>	7-d EC50	5 mg/L	OECD 201 (23)
<i>Microcystis aeruginosa</i>	8-d TT	4.1 mg/L	(35)
<i>Scenedesmus quadricauda</i>	8-d TT	3.2 mg/L	(36)
<i>Scenedesmus subspicatus</i>	72-hr EC50	1.1 mg/L	biomass (37)
	72-hr EC10	0.37 mg/L	biomass (37)
	72-hr EC50	2.8 mg/L	growth rate (37)
	72-hr EC10	0.92 mg/L	growth rate (37)
<i>Selenastrum capricornutum</i>	96-hr EC50	4.4 mg/L	(38)
	96-hr NOEC	2.2 mg/L	(38)
<i>Chlorella emersonii</i>	2-d EC50	5 – 10 mg/L	(18)

3.1.4 Toxicity to Microorganisms

Species or Test Material	Test	Toxicity Value	Remarks
Activated sludge	3-hr EC50	300 mg/L	direct weight (7)
Activated sludge of a predominantly domestic sewage	3-hr EC50	100 mg/L	(26)
<i>Pseudomonas putida</i>	16-hr TT	>100 mg/L	(39)

3.2 Terrestrial Effects

3.2.1 Toxicity to Plants

TBP was used as a solvent in herbicide formulations. Herbicides containing TBP were reformulated in the mid-1980s and are no longer available for use. It had been shown to damage the leaf surface, increase the rate of leaf drying and help herbicides penetrate bean leaves. Quantitative data is not available regarding TBP's effects on non-target plants.

² Effects were observed on length, days to first brood, and young/*Daphnia*/day

However, there does not appear to be evidence of effects at concentrations designed to produce desiccation of crop plants.

3.2.2 Toxicity to Soil Dwelling Organisms

No mortality was observed among two-spotted spider mites (*Tetranychus urticae*) fed TBP at a concentration of 2 g/kg. (40)

3.3 Other Effects

No results were reported for other non-mammalian terrestrial organisms.

3.4 Initial Assessment for the Environment

In both soil and water, TBP is expected to adsorb to sediments or particulate matter and biodegrade. In two “ready” biodegradation studies, 89 percent to 90.8 percent degradation of TPB was observed after 28 days. TBP was also observed to photodegrade rapidly in air. Although TBP Log P_{ow} values range from 2.5 to 4, study data show that its bioaccumulation potential in fish is low.

TBP does not appear to be highly toxic for aquatic organisms. Acute and chronic toxicity data are available for fish, invertebrates, and algae. Following the *Technical Guidance Documents on Risk Assessment for New and Existing Substances* (European Union), the assessment factor is 10, since long-term NOECs are available for three species representing three trophic levels (fish, *Daphnia*, and algae). The lowest valid no observed effect concentration (NOEC) occurred for algae at a concentration of 0.37 mg/L. The resulting aquatic predicted no-effect concentration (PNEC) is equal to 0.037 mg/L.

4. HUMAN HEALTH

4.1 Toxicokinetics and Metabolism

A single i.p. dose of TBP at 250 mg/kg to rats resulted in 11 phosphorus-containing metabolites in the urine within 24 hours. The principal metabolic pathway resulted in stepwise debutylation, through hydroxylated intermediates, to give dibutyl hydrogen phosphate (40-64 percent of identified dose) and butyl dihydrogen phosphate (11-21 percent of identified dose). (93)

Rats given a single oral dose of C¹⁴-labeled TBP at 14 mg/kg produced the following elimination profile: Within 1 day, 50 percent of the dose was excreted in the urine, 10 percent was excreted in exhaled air, and 6 percent was excreted in the feces. After 5 days, 82 percent of the total dose was eliminated. Similarly, rats given single oral doses of 10 or 350 mg/kg of C¹⁴-labeled TBP eliminated the major portion of the recoverable radioactivity within 48 hours in the urine and feces. The major route of elimination was via the kidneys. (94)

In mini-pig toxicokinetics studies, TBP was rapidly eliminated when dosed i.v. and poorly absorbed when administered by the dermal route. In skin studies, the hair follicle was not more penetrable than other dermal areas. There was no bioaccumulation of TBP in bladder or kidney. Metabolism was through hydroxylation followed by Phase II conjugation (glucuronide or sulfate). (95)

4.2 Acute Toxicity

Acute toxicity data for the oral, dermal, inhalation, intraperitoneal (i.p.), subcutaneous (s.c.) and intravenous (i.v.) routes of administration, or exposure, are available for several animal species.

4.2.1 Acute Oral Toxicity

Eight studies presented rat acute oral LD₅₀s ranging from 1,390 to 3,350 mg/kg and one study reported an oral LD₅₀ of 11,265 mg/kg. (41, 42, 43, 44, 45, 46, 47) Four mouse studies with oral LD₅₀s ranging from 400 to 1,240 mg/kg (42, 45, 46) and three hen studies with oral LD₅₀s ranging from 1,500 to 1,800 mg/kg (44, 48, 49) were reported. Based on the results of reported acute studies, TPB is classified as slightly to moderately toxic via acute oral exposure.

4.2.2 Acute Inhalation Toxicity

Several inhalation studies were available with most reporting that TBP is a strong respiratory irritant:

Rat inhalation LC₅₀ ranged from >4.24 mg/L to >42 mg/L with one study reporting 28 mg/L. (42, 50, 51)
One LC₀ of 1.5 mg/L was also reported. (52)

Mouse inhalation LC₅₀ = 1.3 mg/L (one study). (45)

Cat inhalation LC₅₀ = 24.51 mg/L (one study). (52)

4.2.3 Dermal Toxicity

Acute dermal LD₅₀ toxicity values for rabbit (>3,100 to >10,000 mg/kg) (44, 53) and guinea pig (9,700 to 19,400 mg/kg) (42) indicate that TBP has minimal toxicity via the dermal route.

4.2.4 Acute Toxicity Via Other Routes

Several studies were with rats and mice using the intraperitoneal (i.p.), subcutaneous (s.c.), and intravenous (i.v.) routes of administration:

Rat LD₅₀ values for the i.p. route ranged from 251.2 to 1600 mg/kg bw. (42, 45)

Mouse LD₅₀ values for the i.p. ranged from 100 to 158.5 mg/kg bw. (42, 45)

Mice administered TBP s.c. at 3000 mg/kg bw died (one study). (52)

Rats administered 100 mg/kg i.v. died from respiratory failure, but administration of 80 mg/kg bw was sublethal. (54)

TBP had a low level toxicity when administered s.c., i.p., or i.v. to rats and mice.

4.3 Corrosiveness and Irritation

4.3.1 Skin Irritation

Eight skin irritation studies were conducted in the rabbit, two in the guinea pig, and one in humans. The results follow:

In eight rabbit skin irritation studies, TBP was reported to be irritating to highly irritating using a range of application methods to intact and abraded skin. (42, 55, 56, 57, 58, 59, 60)

In two studies with guinea pigs, TBP was reported to be irritating to highly irritating to intact and abraded skin. (42, 61)

In humans, TBP was found to be irritating. (56)

When tested in three species, TBP was found to be irritating to highly irritating.

4.3.2 Eye Irritation

Three eye irritation studies with rabbits are available. In all three studies, TBP was reported to be slightly irritating to irritating. (43, 55, 59)

4.4 Sensitization

Sensitization studies are available for humans and guinea pigs.

Two sensitization studies with guinea pigs were reported. One recently conducted GLP-compliant test reported no sensitization. (62) Another test, reported in a 1971 publication, indicated sensitization but provided no supporting data. (42)

A human patch test showed no sensitization in 53 volunteers exposed to 15 applications of a <5 percent solution of TBP. (63)

In a GLP compliant test, TBP was reported to be non-sensitizing when evaluated using an open epicutaneous test according to EPA Guideline 798.4100 and in a human patch test. TBP was reported to be a sensitizing agent in 6 of 15 guinea pigs exposed by an unknown method in a test of questionable validity.

4.5 Repeated Dose Toxicity

A summary of repeated dose toxicity studies is provided in the table below.

Exposure Period	Route of Exposure	Species	Doses	SIAR Reference
4 months	Inhalation	rat	5.1 or 13.6 mg/m ³	(45)
13 weeks	Dietary feeding	rat	8 to 5,000 mg/kg diet	(64)
3 months	Dietary feeding	rat	500 to 10,000 mg/kg diet	(46)
10 weeks	Dietary feeding	rat	5,000 or 10,000 mg/kg diet	(70)
9 weeks	Dietary feeding	rat	5,000 mg/kg diet	(71)
2 weeks	Oral gavage	rat	136 or 400 mg/kg bw	(67)
18 weeks	Oral gavage	rat	200 or 300-350 mg/kg bw	(68)
2 weeks	Oral gavage	rat	270 or 400 mg/kg bw	(69)
1 week	Oral gavage	rat	140 or 200 mg/kg bw	(46)
1 months	Oral gavage	rat	130 or 460 mg/kg bw	(46)
4 weeks	Dietary feeding	mouse	100 to 20,000 mg/kg diet	(72)
3 months	Dietary feeding	mouse	500 to 8,000 mg/kg diet	(73)
3 months	Dietary feeding	mouse	500 to 10,000 mg/kg diet	(46)
4 months	Inhalation	rabbit	4.8 or 13.6 mg/m ³	(45)
14 days	Oral gavage	rabbit	100 to 1,000 mg/kg bw	(65)

4.5.1 Inhalation Studies (Rat & Rabbit)

Results are available for two repeated-dose inhalation studies.

Exposure levels were 5.1 and 13.6 mg/m³ for the rat study, and 4.8 and 13.6 mg/m³ for the rabbit study.

In rats, cholinesterase activity was decreased by 33 percent after three months at the highest dose of 13.6 mg/m³, but recovered in the post-exposure period. No effect was observed on cholinesterase in the lower exposure level. (45)

The results were the same for rabbits. (45)

4.5.2 Dietary Feeding Studies (Rat)

Data for four oral feeding studies with rats are available. The duration of these studies range from 9 to 16 weeks with varying strains of rats. Doses range from 8 to 10,000 mg/kg in the diet. (46, 64, 70, 71)

Reported effects include: depressed weight gain, decreased food consumption, prolonged blood coagulation, urinary bladder hyperplasia, no changes in hematological analyses (except for BUN), increased γ -GT levels, no decline in cholinesterase activity (brain, liver, or serum), increased liver weight, and no microscopic changes in nerve, bone marrow, or liver.

Slight, sometimes transient effects were observed at an exposure level of 200 mg/kg diet, moderate effects were observed at 700 and 1,000 mg/kg diet exposure levels, and significant effects were only observed at exposure levels ranging from 3,000 to 10,000 mg/kg diet.

4.5.3 Oral Gavage Studies (Rat)

Five studies involving repeated dose, oral gavage studies in rats are available and the results are summarized below. Treatment periods for these six studies ranged from 1 to 18 weeks. Doses administered range from 140 to 460 mg/kg/day. (46, 67, 68, 69)

Results of these oral gavage studies with rats are similar to the oral feeding studies with rats. Effects observed included: increased liver weight, some decrease in RBC cholinesterase, increased BUN levels in the blood, increased spleen weight, urothelial hyperplasia, and tubular changes in the kidney. At the high dose levels (≥ 400 mg/kg bw), additional observations included decreased spleen weight and decreased Hb levels. Studies were contradictory in reporting neurological observations (behavioral and microscopic) and microscopic testicular changes.

4.5.4 Dietary Feeding Studies (Mouse)

A repeated dose, oral feeding range-finding study in mice is summarized below. The duration of this study was 4 weeks. Exposure levels ranged from 100 to 20,000 mg/kg diet (15, 150, 750, and 3000 mg/kg body weight/day). Sufficient data on several other mice dietary studies were not available to allow summarization. (72)

Results of this mouse dietary study showed the same general observations as the rat dietary and oral gavage studies summarized above, including: increased liver weight, reduced body weight gain and food consumption, and decreased kidney weights. Animals died or were sacrificed in moribund condition at 20,000 mg/kg diet. Observations at this dose included failure to eat, hypothermia, dyspnea, lethargy, and tremor.

4.5.5 Subchronic Feeding Studies (Mouse)

Two three-month, subchronic dietary feeding studies in mice were conducted at exposure levels of 500 to 10,000 mg/kg diet (75 to 1,500 mg/kg bw/day). Reported effects included: weight loss, decrease feed consumption, increased liver weight, hematological changes, hepatocyte hypertrophy, and slight to moderate epithelial hyperplasia in the urinary bladder. In one study, all mice survived at the highest dose level (8,000 mg/kg) and a NOAEL was reported as 500 mg/kg/day. (46, 73)

4.5.6 Discussion

Results from most of the mouse and rat repeated dose studies consistently showed cellular and/or weight changes in the liver, kidney, and bladder. Other observations noted included spleen weight changes and microscopic testicular changes; however, these effects are considered spurious as they were found only in one or two short-term studies at high doses and were not confirmed in any of the longer studies, even at comparable doses. Blood chemistry, when reported, indicated decrement changes in kidney function. Two inhalation studies reported a decrease in the cholinesterase activity (33 percent) at the higher dose level (13 mg/m³); however, the activity returned to normal in the post-exposure period. Dietary exposures and oral gavage studies did not show any cholinesterase depression when reported. One study that focused on the nervous system reported morphological changes in the unmyelinated fibers; however, neurological and behavioral changes in other studies were negative.

4.5.7 Conclusions

Because it represents the lowest long-term value in the database, the NOAEL for the carcinogenicity studies with mice (150 ppm in the diet; see Section 4.2.5 below) has been selected as the NOAEL for the repeated

dose studies. This level of feeding is equivalent to 28.9 mg/kg/day for females and 24.1 mg/kg/day for males. Effects were observed at doses, or exposure levels, 10 to 100 times higher than this NOAEL.

4.6 Genetic Toxicity

Results of extensive genetic toxicity studies, both *in vitro* and *in vivo*, were almost exclusively negative, indicating TBP is not genotoxic. Of the six Ames assay results that are available (most conducted both with and without metabolic activation), five were negative. (74, 75, 76, 77, 78, 79) The one positive Ames Test was published in an obscure journal, in a foreign language. (77) A reference to the article suggests it is one page in length. A copy of the article is not available for evaluation. Three additional *in vitro* cytogenetic and mammalian cell gene mutation assays were also negative. (80, 81, 82) Results of two *in vivo* genotoxicity studies confirm the negative finding of the *in vitro* studies. (83, 84) These included a rat cytogenetic assay where there was no increase in aberrant cells in bone marrow after dosing at the maximum tolerated dose (1,200 mg/kg bw) via gavage. The weight of evidence clearly supports the conclusion that TBP does not have mutagenic activity.

4.7 Carcinogenicity

Carcinogenicity studies have been conducted with both the Sprague-Dawley rat and the CD-1 mouse. Both studies were conducted under GLP standards using EPA TSCA testing protocols.

The rat carcinogenicity study included oral feeding of TBP for 24 months at levels of 200, 700, or 3000 ppm in the diet. The NOAEL level in this study (systemic) was 200 ppm (104 wk mean intake of 8.9 mg/kg/day for males and 11.6 mg/kg/day for females). All tissues and organs underwent histopathological examination and only urinary bladder changes were observed. There was a dose-related increase in the incidence and severity of hyperplasia and the incidence of papillomas of the urinary bladder epithelium in the mid- and high-dose groups. Transitional cell carcinomas were noted in the bladders of 6/49 males and 2/50 females in the high dose groups. A squamous cell carcinoma was observed in the bladder of 1 of the 49 high dose males. (84)

The carcinogenicity study with CD-1 mice utilized feeding levels of 150, 1000, and 3500 ppm for 18 months. The NOAEL for chronic toxicity in this study was 150 ppm (28.9 mg/kg/day for females and 24.1 mg/kg/day for males). The only histological change considered to be treatment-related was a statistically significant increase in the incidence of hepatocellular adenomas in high dose male mice. No other tumor type was attributed to TBP administration on the basis of microscopic examination or statistical analysis. (85)

4.7.1 Subchronic Dietary Mechanistic Study

The mechanism by which TBP causes urinary bladder tumors was examined in male Sprague-Dawley rats. Rats were fed 0, 200, 700, or 3000 ppm (approx. 12, 38, or 160 mg/kg/day) in the diet for 10 weeks. Another group was fed 3000 ppm TBP plus 12,300 ppm NH₄Cl to lower urinary pH. A high dose recovery group (3000 ppm TBP for 10 weeks, then 10 weeks of control diet) was included to evaluate reversibility. A NOAEL of 200 ppm was established in this study. Feeding levels of 700 and 3000 ppm produced urothelial cytotoxicity with marked regenerative hyperplasia; however, no changes were observed on urinary parameters, other than a slight decrease in osmolality and creatinine at 3000 ppm. Effects on the urinary bladder were reversible upon withdrawal of treatment during the 10-week recovery period, indicating that the urinary bladder changes are due to cytotoxicity (TBP and/or metabolites) and cellular proliferation (regenerative repair), representing an epigenetic mechanism rather than a genotoxic insult. (86)

4.7.2 Conclusions

These two lifetime exposure studies provide an adequate basis for evaluating the carcinogenicity of TBP. Although there was a lack of concordance in study results for the two studies with regard to target organ and tumor type, study results suggest that TBP is an animal carcinogen when administered in the diet at high doses. A mechanism of action study showed that the urinary bladder tumors in rats were the result of a non-genotoxic mechanism (cytotoxicity and compensatory repair).

4.8 Reproductive Toxicity

A two-generation reproductive toxicity study has been conducted with Sprague-Dawley rats. Rats were fed TBP in the diet at 200, 700, or 3,000 ppm (approx. 15, 53, or 225 mg/kg bw/day). There was no evidence of reproductive organ histopathology and no effects on pre- or post-natal mortality at any dose. In adults, dose levels of 700 and 3,000 ppm produced reductions in body weights, body weight gain, and food consumption during the F₀ and F₁ prebreeding dosing periods. The 200 ppm feeding level produced transient effects on body weight and food consumption in adults and also reduced the body weights of pups. The only treatment-related postnatal effect was reduced pup weights in the high dose group, which was associated with maternal toxicity. Based on these effects, the reproductive toxicity NOAEL for TBP was >3000 ppm, while the maternal toxicity NOAEL and post-natal toxicity NOAEL were both less than 200 ppm. (87)

4.8.1 Conclusions

This study provides an adequate basis for evaluating the reproductive toxicity of TBP. The NOAEL for reproductive toxicity is >3000 ppm, a level over ten-fold higher than the general systemic level that caused pup effects and adult toxicity (<200 ppm). These findings indicate that TBP is not a reproductive toxicant in the absence of maternally toxicity.

4.9 Developmental Toxicity / Teratogenicity

Two range-finding (rat and rabbit) and three definitive (two rat, one rabbit) developmental toxicity/teratogenicity studies have been conducted with TBP. Definitive studies are briefly summarized in the table below. In all studies, TBP was administered by gavage beginning at day 6 or 7 of gestation.

Species	Exposure Period	Doses Administered (mg/kg bw/day)	Maternal Toxicity NOAEL (mg/kg bw/day)	Teratogenicity NOAEL (mg/kg bw/day)
Wistar rat	Day 7 to 17 of gestation	62.5, 125, 250 or 500	62.5	>500
New Zealand rabbit	Day 6 to 18 of gestation	50, 150, or 400	400	>400
Sprague-Dawley rat	Day 6 to 15 of gestation	188, 375, or 750	<188	>750

In these studies, there was no embryotoxicity, fetotoxicity, or teratogenicity at dose levels that were not maternally toxic. In fact, at some higher dose levels there was no developmental toxicity despite significant maternal toxicity. In the range-finding studies conducted with Sprague-Dawley rats and New Zealand White rabbits, no significant developmental effects were seen in offspring of dams at any treatment level. (88, 89) No range-finding study was conducted in Wistar rats. In a supporting study, Wistar rats (most sensitive species to TBP) were dosed at 62.5, 125, 250 and 500 with maternal toxicity occurring as low as 125 mg/kg/day and an increased incidence of rudimentary lumbar ribs at doses of 500-mg/kg bw/day. (90) However, the occurrence of rudimentary lumbar ribs is considered to be maternal toxicity effect and not a result of teratogenicity, as a result the NOAEL for this study is considered to be >500 mg/kg bw/day instead

of >250 mg/kg bw/day as indicated by the study author in the dossier. In the Sprague-Dawley rat range-finding study, 435 mg/kg was the lowest dose to cause maternal toxicity. However, in the definitive Sprague-Dawley rat study, adverse effects were observed in dams at all doses tested (188 - 750 mg/kg bw/day). The reason for this inconsistency is unknown. In this study, a treatment-related increase in the incidence of delayed skeletal ossification was found in offspring, as well as reduced fetal weight in the highest dose group (750 mg/kg/day); however, no teratogenic effects were observed at any dose. (91) In the New Zealand White rabbit range-finding study, significant maternal mortality occurred at 250 and 412 mg/kg/day, while 50 mg/kg/day was the maternal NOAEL. No fetotoxicity was evident at doses as high as 412 mg/kg/day. In the definitive rabbit study, no teratogenic, embryotoxic, or fetotoxic effects were seen at doses as high as 400 mg/kg/day. (92)

4.9.1 Conclusions

These five studies provide an adequate basis for evaluating the developmental toxicity and teratogenicity of TBP. The lowest NOAEL for developmental toxicity from these studies was 250 mg/kg/day based on an increased incidence of rudimentary lumbar ribs; however, the lowest NOAEL for maternal toxicity was considerably lower at 62.5 mg/kg/day. In all five studies, there was no embryotoxicity, fetotoxicity, or teratogenicity at dose levels that were not maternally toxic. These findings indicate that TBP does not produce developmental toxicity in offspring at levels that are not maternally toxic. These studies also indicate that TBP does not have teratogenic activity, even at maternally toxic doses.

4.10 Other Effects - Neurotoxicity

The neurotoxicity of TBP has been evaluated in several species including the rat, hen, and rabbit (44, 48, 49, 70, 96, 97, 99, 100). In these studies, TBP produced either no signs of neurotoxicity or only slight transient effects on measured endpoints. In a 13-week neurotoxicity test in rats, in which behavioral, motor, and morphologic endpoints were measured, TBP treatment did not result in neurotoxicity. This definitive rodent neurotoxicity test, in which animals received daily doses as high as 325 mg/kg/day, showed that TBP does not alter behavior, adversely affect motor activity, and does not induce neurohistopathologic changes. In delayed neurotoxicity tests in hens, in which TBP was administered either in a single high dose (1500 mg/kg) or in two high doses (1500 mg/kg each) 21 days apart, there was no relevant inhibition of neurotoxic esterase (NTE) or brain acetylcholinesterase. The hen is the most sensitive species for identifying neurotoxins that cause delayed peripheral neuropathy. In both rats and rabbits lethal doses of TBP had a maximum decrease of 35% in cholinesterase activity in serum, red blood cells and brain.

4.11 Human Experience

In human skin penetration studies there was a maximum dermal steady state penetration rate of 0.18 ug/cm³/min. Reported symptoms in exposed workers included nausea, headache, skin irritation, and skin rashes. (101, 102, 103)

One human study presented case studies with cotton swabs soaked in 10, 50, and 75 percent TBP solutions occlusive for 3, 24, and 24 hours, respectively. Irritation occurred at the 50 and 75 percent TBP solution levels. (63)

4.12 Initial Assessment for Human Health

The toxicology database for TBP is large and well documented. There are adequate data with which to evaluate the potential hazard to human health of this compound. Data indicate the following:

Repeated Dose NOAEL = 150 ppm in diet (28.9 mg/kg/day for females and 24.1 mg/kg/day for males)
Reproductive Toxicity NOAEL >3000 ppm in diet (>225 mg/kg/day)

Developmental Toxicity / Teratogenicity NOAEL = >750 mg/kg/day

Study findings indicate that TBP is not a reproductive toxicant, teratogen, or developmental toxicant at levels that are also not maternally toxic. TBP is an animal carcinogen when administered in the diet at high doses; however, at this time there is no data to demonstrate that it is a human carcinogen. Results of extensive genetic toxicity studies, both *in vitro* and *in vivo*, were almost exclusively negative and do not indicate TBP to be genotoxic. A mechanistic study in rats found that the effects of TBP on the bladder were reversible upon withdrawal of treatment and thus likely due to the direct urothelial cytotoxicity of the chemical (or its metabolites), and not a result of changes in urinary parameters. The neurotoxicity of TBP has been studied in several species including the rat, hen, and rabbit. In these studies, TBP produced either no signs of neurotoxicity or only slight or transient effects on measured endpoints. TBP is irritating to the skin and eye of humans and laboratory animals but does not cause sensitization in humans.

The primary exposure to TBP is through dermal contact in the occupational setting, when it is used as a component of aircraft hydraulic fluid. The primary symptoms reported by aircraft maintenance workers are eye, respiratory, and skin irritation. These symptoms are consistent with those observed in animal tests.

5 CONCLUSIONS AND RECOMMENDATIONS

5.1 Conclusions

The major uses of TBP in industry are as a component of aircraft hydraulic fluid and as a solvent for rare earth extraction and purification. Minor uses of TBP include use as a defoamer additive in cement casings for oil wells, an anti-air entrainment additive for coatings and floor finishes, as well as a carrier for fluorescent dyes. The major uses of TBP comprise over 80 percent of the volume produced.

During production, any release of TBP would be in the process wastewater. This wastewater is treated on-site at company facilities in their water treatment facilities, in which released TBP is recovered. This minimizes the potential for accident release into the environment.

The toxicology database for TBP is large and well documented. There are adequate data with which to evaluate the potential hazard to human health of this compound. Data indicate the following:

Repeat Dose NOAEL = 150 ppm in diet (28.9 mg/kg/day for females and 24.1 mg/kg/day for males)

Reproductive Toxicity NOAEL = >3000 ppm in diet (>225 mg/kg/day)

Developmental Toxicity / Teratogenicity NOAEL = >750 mg/kg/day

Study findings indicate that TBP is not a reproductive toxicant or a developmental toxicant at levels that are also not maternally toxic. TBP did not express teratogenic activity. TBP is an animal carcinogen when administered in the diet at high doses. Results of extensive genetic toxicity studies, both *in vitro* and *in vivo*, were almost exclusively negative and do not indicate TBP to be genotoxic. A mechanistic study in rats found that the effects of TBP on the bladder were reversible upon withdrawal of treatment, and due to the direct urothelial cytotoxicity of the chemical (or its metabolites) and not a result of changes in urinary parameters. The neurotoxicity of TBP has been studied in several species including the rat, hen, and rabbit. In these studies, TBP produced either no signs of neurotoxicity or only slight or transient effects on measured endpoints. TBP is irritating to the skin and eye of humans and laboratory animals but does not cause sensitization in humans.

The primary exposure to TBP is through dermal contact in the occupational setting. Based on this exposure route and the NOAEL levels reported, the most likely effects of TBP exposure are irritation of the skin and eyes. TBP was shown to have very low dermal toxicity.

TBP does not appear to be highly toxic to aquatic organisms. Acute and chronic toxicity data are available for fish, invertebrates, and algae. Following the *Technical Guidance Documents on Risk Assessment for New and Existing Substances*, (European Union), the assessment factor is 10, since long-term NOECs are available for three species representing three trophic levels (fish, *Daphnia*, and algae). The lowest valid no observed effect concentration (NOEC) occurred for algae at a concentration of 0.37 mg/L. The resulting aquatic PNEC is equal to 0.037 mg/L.

Studies indicate that TBP does not bioaccumulate to a significant extent in fish despite a relatively high log K_{ow} (2.5 - 4). In both soil and water, TBP is expected to adsorb to sediments and/or particulate matter and to readily biodegrade.

5.2 Recommendations

The database for TBP is large and adequate for both human health and environmental endpoints. No further testing is recommended. However, if the chemical is to be used as a herbicide or in other dispersive uses, then it should be considered as a candidate for further work, in the context of a risk assessment.

6. REFERENCES

1. Material Safety Data Sheet, Bayer AG, dated September 8, 1987.
2. ABC Laboratories. Report entitled Vapor Pressure of Tributyl Phosphate. ABC Project No. 38557. 1990. Test conducted at the request of the Synthetic Organic Chemical Manufacturers Association, Inc.
3. THOR Database Pomona 89, MedChem Software 1989. Daylight Chemical Information Systems, Claremont, CA 91771, USA
4. Saeger, V.W., Hicks, O., Kaley, R.G., Mieure, J.P., and Tucker, E. Environmental Fate of Selected Phosphate Esters. *Environ. Sci. Technol.* 13:840-844, 1979.
5. Calculation UWS-Produktsicherheit, Bayer AG, 1991.
6. BUA Report, 1999.
7. Bayer AG Study, no date available.
8. Report entitled Biodegradation and Bioaccumulation Data of Existing Chemicals Based on the CSCL Japan. Compiled under the supervision of the Ministry of International Trade and Industry, Edited by Chemical Inspection and Testing Institute, Japan. Published by Japan Chemical Industry Ecology-Toxicology & Information Center, 1992.
9. Monsanto Study No. MO-77-615. Biodegradation of Phosphate Esters. 1977.
10. Monsanto Study No. MO-77-615B. Biodegradation of Phosphate Esters. 1977.
11. ABC Laboratories. Report entitled Hydrolysis of ¹⁴C-Tributyl Phosphate as a Function of pH at 25 degrees C. ABC Report No. 38559. Study conducted at the request of the Synthetic Organic Chemical Manufacturers Association. 1990.
12. Kawai, S. et al. Annual Report of the Osaka City Institute of Public Health and Environmental Science 49:160-166, 1986.
13. Ishikawa, S. et al., *Suishitsu Odaku Kenkyo Tokyo* 8:799-807, 1985.
14. Sasaki, K., Takeda, M, and Uchiyama, M. Toxicity, Absorption and Elimination of Phosphoric Acid Triesters by Killifish and Goldfish. *Bull. Environ. Contam. Toxicol.* 27:775-782, 1981.
15. Sasaki, K., Susuki, T. and Takeda, M. Bioconcentration and Excretion of Phosphoric Acid Triesters by Killifish. *Bull. Environ. Contam. Toxicol.* 28:752-759, 1982.
16. FMC Study No. I90-1176.
17. ABC Laboratories. Report entitled Acute Toxicity of TBP to Rainbow Trout. ABC Study No. AB-78-1384337-1d, 1978. And, Monsanto Study AB-78-0386.
18. Dave, G. Blanck, H. and Gustafsson, K. Biological Effects of Solvent Extraction Chemicals on Aquatic Organisms. *J. Chem. Tech. Biotechnol.* 29:249-257, 1979.
19. ABC Laboratories. Report entitled Acute Flow-Through Toxicity of TBP to Rainbow Trout. ABC Study No. 38552. Study conducted at the request of the Synthetic Organic Chemical Manufacturers Association. 1990.

20. Dave, G., Andersson, K., Berglund, R. and Hasselrot, B. Toxicity of Eight Solvent Extraction Chemicals and of Cadmium to Water Fleas, Rainbow Trout, and Zebrafish. *Comp. Biochem. Physiol.* 69C:83-98, 1981.
21. ABC Laboratories. Report entitled Early Life-Stage Toxicity of TBP to Rainbow Trout in a Flow-Through System. ABC Study No. 38556. Study conducted at the request of the Synthetic Organic Chemical Manufacturers Association. 1991.
22. Juhnke, I. And Ludemann, D. The Results Obtained with the Golden Orfe Test. *Z. Wasser Abwasser Forsch.* 11:161-164, 1978.
23. Yoshioka, Y. and Ose, Y. *Environmental Toxicology and Water Quality* 8:87-101, 1993.
24. ABC Laboratories. Report entitled Acute Toxicity of TBP to Flathead Minnows. ABC Study No. AB-78-1384337-1C. 1978.
25. Geiger, D.L., et al., Acute Toxicities of Organic Chemicals to Fathead Minnows. Volume III. Center for Wisconsin-Superior Environmental Studies, University of Wisconsin-Superior. ISBN No. 0-9614968-2-7, 1986.
26. Yoshioka, Y. , et al., *Ecotox. Environ. Saf.* 12:206-212, 1986.
27. Bringmann, G. and Kuhn, R. Findings of the Damaging Action of Water Pollutants Against *Daphnia magna*. *Z. Wasser Abwasser Forsch.* 10:161-166, 1977.
28. Bringmann, G. and Kuhn, R. Results of Toxic Actions of Water Pollutants on *Daphnia magna* tested by an Improved Standardized Procedure. *Z. Wasser Abwasser Forsch.* 15:1-6, 1982.
29. Wakabayashi, M. et al., Tokyo-to Kankyo Kangaku Kenyusho Nenpo, 126-128. 1988.
30. ABC Laboratories. Report entitled Acute Toxicity of TBP to *Daphnia magna*. ABC Study No. AB-78-1384337-1a. 1978.
31. ABC Laboratories. Report entitled Acute Flow-Through Toxicity of TBP to *Daphnia magna*. ABC Report No. 38553. Test conducted at the request of the Synthetic Organic Chemical Manufacturers Association, Inc. 1991,
32. ABC Laboratories. Report entitled Chronic Toxicity of TBP to *Daphnia magna* Under Flow-Through Test Conditions. ABC Study No. 38556. Test conducted at the request of the Synthetic Organic Chemical Manufacturers Association, Inc. 1991.
33. ABC Laboratories. Report entitled Acute Flow -Through Toxicity Exposure of TBP to *Gammarus pseudolimnaeus*. ABC Study No. 39499. Test conducted at the request of the Synthetic Organic Chemical Manufacturers Association, Inc. 1991.
34. ABC Laboratories. Report entitled Acute Flow-Through Toxicity of TBP to the Gammarid *Hyalella azteca*. ABC Report No. 38555. Test conducted at the request of the Synthetic Organic Chemical Manufacturers Association, Inc. 1990.
35. Bringmann, G. and Kuhn, R. *Mitt. Internat. Verein. Limnol.* 21:275-284, 1978.
36. Bringmann, G. and Kuhn, R. Limiting Values for the Damaging Action of Water Pollutants against Bacteria and green Algae. *Z. Wasser Abwasser Forschung* 10:87-89, 1997.
37. Kuhn, R. and Pattard, M. *Water Research* 24:31-38, 1990.

38. ABC Laboratories. Report entitled Acute Toxicity of TBP to *Selenastrum capricornutum* Printz. ABC Report No. 38554. Test conducted at the request of the Synthetic Organic Chemical Manufacturers Association, Inc. 1990.
39. Blanck, H., Wallin, G., and Wangberg, S. Species Dependent Variation in Algal Sensitivity to Chemical Compounds. *Ecotoxicol. Environ. Saf.* 8:339-351, 1984.
40. IPC Environmental Health Criteria 112, page 40, Tributyl Phosphate. WHO, Geneva, 1991.
41. Ramm: Bayer AG Data. Untersuchung zur akuten oralen Toxizität an männlichen und weiblichen Wistar Ratten. 1986.
42. Eastman Kodak Co., Data from 1959 to 1968. NTIS Doc. No. 86860000118. 1986.
43. Smyth, H. and Carpenter, C. The Place of the Rangefinding Test In the Industrial Toxicology Laboratory. *J. Indust. Hyg. Toxicol.* 26:269-273, 1944.
44. Johannson, F., Wright, P., Gordon, D., Levinskas, G., and Graham, P. Evaluation of Delayed Neurotoxicity and Dose-response Relationships of Phosphate Esters in the Adult Hen. *Toxicol. Appl. Pharmacol.* 41:291-304. 1977.
45. Kalina, Gig. Tr. Prof. Zabol. 15:30-33, 1971.
46. Mitomo, T., Ito, T., and Terao, K. Toxicological Studies on TBP. I. Acute and Subacute Toxicities. *J. Toxicol. Sci.* 5:270-271, 1980.
47. Enslein, K. et al., QSAR Environ. Toxic. Proc. 11:91, 1987, cited in BIBRA Toxicity Profile, 1991.
48. Carrington et al., *Toxicol. Indust. Hyg.* 6:415-423, 1989.
49. Monsanto Company. Monsanto data, TSCA Section 8d Submission No. 86860000103, 1986, cited in Chem. Reg. Reporter 11-13-87.
50. FMC Corporation. FMC data, EPA OTS 86860000114, 1976. Cited in BIBRA Toxicity Profile, 1991.
51. Bayer AG data. Report No. 19466, 1990.
52. Fassett and Irish, Eds. *Patty's Industrial Hygiene and Toxicology*. Second Edition, 1993.
53. Rohm & Haas Company. Rohm & Haas data, OTS 0385-0380, 1985. Cited in Chem. Reg. Reporter, pp 1244-1322, 1987.
54. Vandekar, M. Anesthetic Effect Produced by Organophosphorus Compounds. *Nature* 179:154-155, 1957.
55. Bayer AG data. Report No. 14478, 1986.
56. I.G.W. Eiberfeld data, August 1936.
57. FMC Corporation. FMC data, submitted to the U.S. EPA in 1985. Cited in Environmental Health Criteria 112, WHO, 1991.
58. FMC Corporation. FMC data, TSCA Section 8d Submission 86860000116, 1976. Cited in Chem. Reg. Reporter, pp. 1244-1322, 1987. Also cited in BIBRA Toxicity Profile, 1991.

59. Dow Chemical Company. Dow Chemical data, EPA OTS 86860000127, 1956. Cited in BIBRA Toxicity Profile, 1991.
60. Food and Drug Research Laboratory. Report No. ICD/T-76-16, 1976. Study conducted at the request of FMC Corporation.
61. E.I. DuPont de Nemours & Company. DuPont data, EPA OTS 86860078, 1953. Cited in BIBRA Toxicity Profile, 1991.
62. FMC Corporation. FMC Study No. I89-1102, 1990. Test conducted at the request of the Synthetic Organic Chemical Manufacturers Association, Inc.
63. Monsanto Chemical Company. Monsanto data, submitted to the U.S. EPA in 1980. Cited in BIBRA Toxicity Profile, 1991.
64. Cascieri, T., Ballester, E., McConnell, R., and Fletcher, M. Subchronic Toxicity Study with TBP in Rats. *Toxicologist* 5:97, 1985.
65. FMC Corporation, FMC data, EPA OTS 86860000106, 1985. Cited in BIBRA Toxicity Profile, 1991.
66. Pupyshva, G. and Peresedov, V., 1970 cited in *Berufsgenossenschaft der chemischen Industrie. Toxikologische Bewertung Ausgabe 2/89, Nr. 170, 1989.*
67. Laham, S. Long, G. and Broxup, B. Subacute Oral Toxicity of TBP in the Sprague-Dawley Rat. *J. Appl. Toxicol.* 4:150-154, 1984.
68. Laham, S. Long, G. and Broxup, B. Induction of Urinary Bladder Hyperplasia in Sprague-Dawley Rats Orally Administered TBP. *Arch. Environ. Health* 40:301-306, 1985.
69. Laham, S., Szabo, J. and Long, G. Effects of TBP on the Peripheral Nervous System of the Sprague-Dawley Rat. *Drug. Chem. Toxicol.* 6:363-377, 1983.
70. Oishi, H., Oishi, S. and Hiraga, K. Toxicity of TBP with reference to Organ Weights, Serum Components, and Cholinesterase Activity in Male Rats. *Toxicol. Lett.* 6:81-85, 1980.
71. Oishi, H., Oishi, S. and Hiraga, K. Toxicity of Several Phosphoric Acid Esters In Rats. *Toxicol. Lett.* 13:29-34, 1982.
72. Bio/dynamics Inc. Report entitled A Four-week Rangefinding Study of TBP in the Mouse via Dietary Administration. Project No. 89-3530. 1990. Test conducted at the request of the Synthetic Organic Chemical Manufacturers Association, Inc.
73. Bio/dynamics Inc. Project No. 89-3531. Subchronic Dietary Toxicity Study with TBP in the Mouse. 1991. Test conducted at the request of the Synthetic Organic Chemical Manufacturers Association, Inc.
74. Bayer AG data. Report No. 13805. 1985.
75. Hanna, P. and Dyer, K. Mutagenicity of organophosphorus Compounds in Bacteria and Drosophila. *Mutat. Research* 28:405-420, 1975.
76. FMC Corporation. FMC notice to EPA OTS 86860000112, 1978. Cited in BIBRA Toxicity Profile, 1991. Also cited in *Chem. Reg. Reporter* pp. 1244-1322, 1987.
77. Gafieva, Z. and Chudin, V. Evaluation of the Mutagenic Action of TBP on *Salmonella typhimurium*. *Gig. Sanit.* 9:81, 1986.

78. Blevins, R. *Envir. Mutagen.* 9:17, 1987. Cited in BIBRA Toxicity Profile, 1991.
79. Watanabe, K., Sakamoto, K., and Sasaki, T. Comparisons on Chemically Induced Mutagenicity Among Four Bacterial Strains. *Mutation Res.* 361:143-155, 1996.
80. Microbiological Associates Inc. Report entitled Chromosome Aberrations in Chinese Hamster Ovary Cells. Report No. T9145.337, 1990. Test conducted at the request of the Synthetic Organic Chemical Manufacturers Association, Inc.
81. Mueller et al., *Health Physics* 53:667-671, 1987.
82. Microbiological Associates Inc. Report entitled CHO/HGPRT Mutation Assay. Report No. T9145.332, 1990. Test conducted at the request of the Synthetic Organic Chemical Manufacturers Association, Inc.
83. Microbiological Associates Inc. Report No. T9145.105011, 1991. Test conducted at the request of the Synthetic Organic Chemical Manufacturers Association, Inc.
84. Pharmaco LSR Inc. Pharmaco report entitled An Oncogenicity Study of TBP in the Rat via Dietary Administration. Report No. 89-3533, 1994. Test conducted at the request of the Synthetic Organic Chemical Manufacturers Association, Inc.
85. Pharmaco LSR Inc. Pharmaco report entitled An Oncogenicity Study of TBP in the Mouse via Dietary Administration. Report No. 89-3532, 1994. Test conducted at the request of the Synthetic Organic Chemical Manufacturers Association, Inc.
86. Arnold, L., Cohen, S., Christensen, R., Cano, M. and Wahle, B. TBP Effects on Urine and Bladder Epithelium in Male Sprague-Dawley Rats. *Toxicologist* 36:173, 1997. . Test conducted at the request of the Synthetic Organic Chemical Manufacturers Association, Inc.
87. Research Triangle Institute. Report entitled Two Generation Study of Dietary TBP in CD Rats. Project No. 60C-4652. 1992. Test conducted at the request of the Synthetic Organic Chemical Manufacturers Association, Inc.
88. Bio/dynamics Inc. Project No. 89-3534, 1991. Test conducted at the request of the Synthetic Organic Chemical Manufacturers Association, Inc.
89. Bio/dynamics Inc. Bio/dynamics Report entitled A Rangefinding Study to Evaluate the Toxicity of TBP in the Pregnant Rabbit. Project No. 89-3536, 1991. Test conducted at the request of the Synthetic Organic Chemical Manufacturers Association, Inc.
90. Noda, T., Yamano, T., Shimizu, M. and Morita, S. Effects of TBP on Pregnancy in Rats. *Food Chem. Toxicol.* 32:1031-1036, 1994.
91. Bio/dynamics Inc. Bio/dynamics Report: A Developmental Toxicity Study in Rats with TBP. Project No. 89-3535, 1991. Test conducted at the request of the Synthetic Organic Chemical Manufacturers Association, Inc.
92. Bio/dynamics Inc. Bio/dynamics Report: A Developmental Toxicity Study in Rabbits with TBP. Project No. 89-3537, 1991. Test conducted at the request of the Synthetic Organic Chemical Manufacturers Association, Inc.
93. Suzuki, T., Sasaki, K., and Uchiyama, M. Some S-containing Metabolites of TBP in the Rat. *J. Agri. Food Chem.* 32:1278-1283, 1984.
94. Suzuki, T., Sasaki, K., Takeda, M. and Uchiyama, M. Metabolism of TBP in Male Rats. *J. Agri. Food Chem.* 32:603-610, 1984.

95. Midwest Research Institute. Project entitled: Metabolism of TBP in Yucatan Minipigs following Intravenous and Dermal Exposure. 1994. Test conducted at the request of the Synthetic Organic Chemical Manufacturers Association, Inc.
96. Carrington, C., Lapadula, D., Othman, M., Farr, C., Nair, R., Johannsen, F. and Abou-Donia, M. Assessment of Delayed Neurotoxicity of TBP, tributoxyethylphosphate, and dibutylphenylphosphate. *Toxicology and Industrial Health* 6:415-432, 1990.
97. Healy, C., Beyrouy, P., and Broxup, B. Acute and Subchronic Neurotoxicity Studies with TBP in Adult Sprague-Dawley Rats. *AIHA J.* 56:349-355, 1995.
98. Monsanto Chemical Company. Monsanto Study No. DU-84-433, 1984.
99. Industrial Biotest Laboratories. Study entitled: Neurotoxicity Study with TBP in Chickens. Study No. J2157. (no date provided).
100. Mandel et al. *Am. J. Ind. Med.* 15:207-212, 1989.
101. Marzulli, F., Callahan, J., and Brown, D. Chemical Structure and Skin Penetrating Capacity of a Short Series of Organic Phosphates and Phosphoric Acid, *J. Invest. Dermatol.* 44:339-341, 1965.
102. Mastromateo, E. Personal Communication to ACGIH TLV Committee. Cited in the ACGIH Documentation of TLV Values, 1980.
103. Anon., *Pesticide and Toxic Chemicals News* Vol. 14, 1986. Cited in BIBRA Toxicity Profile, 1991.

I U C L I D D a t a S e t

Existing Chemical ID: 126-73-8
CAS No. 126-73-8
EINECS Name tributyl phosphate
EINECS No. 204-800-2
TSCA Name Phosphoric acid tributyl ester
Molecular Formula C12H27O4P

Producer Related Part

Company: FMC Corporation
Creation date: 22-JUL-1997

Substance Related Part

Company: FMC Corporation
Creation date: 22-JUL-1997

Printing date: 16-APR-2001
Revision date:
Date of last Update: 06-APR-1999

Number of Pages: 79

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

1. GENERAL INFORMATION

1.0.1 OECD and Company Information

1.0.2 Location of Production Site

1.0.3 Identity of Recipients

1.1 General Substance Information

Substance type: organic
Physical status: liquid
Purity: = 100 % w/w
05-NOV-1997

1.1.0 Details on Template

1.1.1 Spectra

1.2 Synonyms

Phosphoric acid, tributyl ester
05-NOV-1997

TBP
05-NOV-1997

1.3 Impurities

CAS-No:
EINECS-No:
EINECS-Name:
Remark: no impurities above normal regulatory levels (1%, 0.1%)
12-JAN-1999

1.4 Additives

CAS-No:
EINECS-No:
EINECS-Name:
Remark: no data currently available
27-JAN-1999

1.5 Quantity

Quantity produced :100 - 500 tonnes in 1998
27-JAN-1999

1.6.1 Labelling

Labelling: as in Directive 67/548/EEC
Symbols: Xn
Specific limits: no

1. GENERAL INFORMATION

R-Phrases: (22) Harmful if swallowed
S-Phrases: (2) Keep out of reach of children
(25) Avoid contact with eyes

05-NOV-1997

1.6.2 Classification

Classification: as in Directive 67/548/EEC
Class of danger: harmful
R-Phrases: (22) Harmful if swallowed
05-NOV-1997

1.7 Use Pattern

Type: type
Category: Non dispersive use
26-JAN-1999

Type: use
Category: Solvents
12-FEB-1998

Type: use
Category: other: aircraft hydraulic fluid
26-JAN-1999

Type: use
Category: other: plasticizer for cellulose acetate, nitrocellulose and
chlorinated rubber
12-FEB-1998

1.7.1 Technology Production/Use

1.8 Occupational Exposure Limit Values

Type of limit: TLV (US)
Limit value: 2.2 mg/m³
05-NOV-1997

1.9 Source of Exposure

Remark: no information available
05-FEB-1999

1.10.1 Recommendations/Precautionary Measures

1.10.2 Emergency Measures

1.11 Packaging

1.12 Possib. of Rendering Subst. Harmless

1. GENERAL INFORMATION

1.13 Statements Concerning Waste

1.14.1 Water Pollution

Classified by:

Labelled by:

Class of danger:

Remark: not applicable

26-JAN-1999

1.14.2 Major Accident Hazards

Legislation: other

Substance listed:

Remark: not applicable

26-JAN-1999

1.14.3 Air Pollution

Classified by: other

Labelled by:

Number:

Class of danger:

Remark: not applicable

26-JAN-1999

1.15 Additional Remarks

Remark: no data

26-JAN-1999

1.16 Last Literature Search

1.17 Reviews

1.18 Listings e.g. Chemical Inventories

2. PHYSICO-CHEMICAL DATA

2.1 Melting Point

Value: < -70 degree C
22-JUL-1997 (1)

2.2 Boiling Point

Value: 130 degree C at 5 hPa
22-JUL-1997 (1)

2.3 Density

Type: density
Value: .97 g/cm3 at 20 degree C
22-JUL-1997 (1)

2.3.1 Granulometry

2.4 Vapour Pressure

Value: .008 hPa at 20 degree C
22-JUL-1997 (1)

Value: = .00000347 hPa at 25 degree C
Remark: Guideline D-63-9 to comply with U.S. EPA TSCA Section 4 for
tributyl phosphate
06-OCT-1997 (2)

Value: 1 hPa at 97 degree C
22-JUL-1997 (3)

Value: 10 hPa at 144 degree C
22-JUL-1997 (3)

2.5 Partition Coefficient

log Pow: 2.5
Method:
Year:
GLP: no data
Remark: experimentally determined
26-JAN-1999 (4)

log Pow: 3.5
Method: other (calculated): Leo, A.: CLOGP-3.54 MedChem Software 1989.
Daylight, Chemical Information Systems, Claremont, CA 91711,
USA
Year:
GLP: no data
26-JAN-1999 (5)

log Pow: 4
Method:

2. PHYSICO-CHEMICAL DATASUBSTANCE ID: 126-73-8

Year:
GLP: no data
Remark: experimentally determined
26-JAN-1999 (6)

2.6.1 Water Solubility

Value: .4 g/l at 20 degree C
22-JUL-1997 (1)

2.6.2 Surface Tension

2.7 Flash Point

Value: > 150 degree C
Type:
Method: other: DIN 51376
Year:
GLP: no data
26-JAN-1999 (1)

2.8 Auto Flammability

2.9 Flammability

2.10 Explosive Properties

2.11 Oxidizing Properties

2.12 Additional Remarks

3. ENVIRONMENTAL FATE AND PATHWAYS

SUBSTANCE ID: 126-73-8

3.1.1 Photodegradation

Type: other: degradation by UV-radiation
INDIRECT PHOTOLYSIS

Degradation: 85 % after 1 hour(s)

Method:

Year: GLP: no data

Test substance: no data

26-JAN-1999

(7)

3.1.2 Stability in Water

Type: abiotic

Method:

Year: GLP:

Test substance:

Result: After 30 days, there was no evidence of hydrolytic degradation of ¹⁴C-tributyl phosphate in any of the buffered solutions.

Test condition: The hydrolysis of ¹⁴C-tributyl phosphate was studied in aqueous buffered solutions of pH 5, 7, and 9 at a nominal concentration of 10.0 ppm. The test was conducted in the dark at 25 degrees C for 30 days.

29-SEP-1997

(8)

Type:

Method:

Year: GLP: no data

Test substance: no data

Remark: stable in the range pH 3 - 11

26-JAN-1999

3.1.3 Stability in Soil

Type: laboratory Radiolabel: yes

Concentration:

Soil temp.: 25 degree C

Cation exch.
capac.

Microbial
biomass:

Method:

Year: GLP: no data

Test substance: no data

Remark: The adsorption/desorption properties of ¹⁴C-tributyl phosphate (9B-125, PL89-289, radiopurity 98%) were studied in three different soil types (silt loam, clay loam, sandy loam) at 25 degrees C. The adsorption of TBP reached an equilibrium after 48 hours in all soils using a 0.01M Ca(NO₃)₂ solution: soil ratio of 5:1. Definitive mean measured test concentrations ranged from 0.516 to 0.101 (0.516, 0.387, 0.300, 0.205 and 0.101) ug/mL. The mean ¹⁴C-material balances for all definitive test concentrations with silt loam, clay loam and sandy loam were 95.8%, 101% and 97.7%, respectively. The Freundlich constants (K_d) for silt loam, clay loam and sandy loam were 5.84, 7.72, and 3.02, respectively. The adsorption constants as a function

3. ENVIRONMENTAL FATE AND PATHWAYS

SUBSTANCE ID: 126-73-8

of carbon (Koc) were 1460, 1188 and 378 for silt loam, clay loam and sandy loam, respectively. The Koc values indicate that TBP has low mobility in silty loam and clay loam soil types with a medium mobility in sandy loam types.

26-JAN-1999

(9)

3.2 Monitoring Data (Environment)

Type of
measurement:

Medium: air

Method:

Concentration

Remark: Japan (industrial area): 3.1 - 41.4 ng/m³
(non-industrial): < 10 ng/m³

22-JUL-1997

(10)

Type of
measurement:

Medium: surface water

Method:

Concentration

Remark:	place	concentration (ng/l)	number of proof	number of measurements analyzed	Year
	Rhein	max. 3800			1990
	Ruhr	600			1990
	Emscher	3900			1990
	Lippe	800			1990
	Wupper	600			1989
	Sieg	100			1984
	Zuericher See	54 - 82	2	2	1973
	Norwegen (River Nitaiva)	100 - 900	3	7	1979
	Japan (Dogo Plein, Ozu Basin area)	ND - 187	4	10	1974
	Japan	20 - 710	16	100	1975
	Japan	6 - 580	39	117	1977
	Japan (Osaka)	20 - 4500	12	13	1976
	Japan (Tokyo)	60 - 2100	12	12	1978
	Japan (Kitakyushu City)	5 - 36	8	16	1980
	Japan (Niigata City)	140	1	1	1982

25-SEP-1997

(10)

Type of
measurement:

Medium: sediment

Method:

Concentration

3. ENVIRONMENTAL FATE AND PATHWAYS

SUBSTANCE ID: 126-73-8

Remark:	place	concentration ug/kg	number of measurement proof analyzed		year
	Japan	1.0 - 350	34	100	1975
	Japan	1.9 - 240	48	117	1977
	Japan (Tokyo) river	0.9 - 7.7	13	15	1978
	sea	1.7 - 2.6	3	3	1978
	Japan (Kitakyushu City)	NN**	0	6	1980
22-JUL-1997					(10)

Type of
measurement:

Medium: biota

Method:

Concentration

Remark: Fish : 1.1 - 26 ug/kg
Crustacea : 10 - 20 ug/kg
Birds : 20 - 250 ug/kg

22-JUL-1997 (10)

3.3.1 Transport between Environmental Compartments

Type: adsorption

Media: soil - air

Air (Level I):

Water (Level I):

Soil (Level I):

Biota (L.II/III):

Soil (L.II/III):

Method:

Year:

Remark: coefficient Koc 1460
Koc 1188
Koc 378

22-JUL-1997 (10)

3.3.2 Distribution

Media:

Method: Calculation according Mackay, Level I

Year:

Remark: air 11 %
water 58 %
soil 16 %
sediment 15 %

22-JUL-1997 (10)

3.4 Mode of Degradation in Actual Use

3.5 Biodegradation

Type: aerobic

Inoculum: predominantly domestic sewage

3. ENVIRONMENTAL FATE AND PATHWAYS

SUBSTANCE ID: 126-73-8

Concentration: 100 mg/l
 Degradation: 77 % after 28 day

Method: Directive 84/449/EEC, C.7 "Biotic degradation - modified MITI test"
 Year: 1985 GLP: no
 Test substance: no data
 Remark: related to O2-demand
 26-JAN-1999 (3)

Type: aerobic
 Inoculum: predominantly domestic sewage
 Concentration: 3.68 mg/l
 Degradation: 92 % after 28 day
 Method: OECD Guide-line 301 D "Ready Biodegradability: Closed Bottle Test"
 Year: 1985 GLP: no
 Test substance: no data
 Remark: related to BOD
 26-JAN-1999 (3)

Type: aerobic
 Inoculum: predominantly domestic sewage
 Concentration: 20 mg/l related to DOC (Dissolved Organic Carbon)
 Degradation: 89 % after 28 day
 Method: OECD Guide-line 301 E "Ready biodegradability: Modified OECD Screening Test"
 Year: 1985 GLP: no
 Test substance: no data
 Remark: Primary degradation by activated sludge
 96 % 13 w (3 mg/l/24 h)
 56 % +/- 21 % 21 w (13 mg/l/24 h)
 No difference between biological and chemical degradation.
 26-JAN-1999 (6)

Type: aerobic
 Inoculum: activated sludge, domestic, adapted
 Concentration: .2 mg/l related to Test substance
 Degradation: = 91 % after 28 day
 Method: other: Method similar to OECD 301B
 Year: GLP: no
 Test substance: no data
 Remark: Biodegradation variable; ranged from 3% of theoretical to 91% of theoretical amount of carbon dioxide evolved in 28 days
 26-JAN-1999 (11)

Type: aerobic
 Inoculum: activated sludge
 Concentration: 30 mg/l related to Test substance
 Degradation: = 0 - 40 % after 14 day
 Method: other: see remarks
 Year: GLP: no data
 Test substance: no data
 Remark: Method: "Biodegradation test of chemical substance by organisms etc." stipulated in the Order Prescribing the Items of the Test Relating to the Sewage Chemical Substance

3. ENVIRONMENTAL FATE AND PATHWAYS

SUBSTANCE ID: 126-73-8

(1974, Order of the Prime Minister, the Minister of Health and Welfare, the MITI No. 1). This guideline corresponds to "302C, Inherent Biodegradability: Modified MITI Test II" stipulated in the OECD Guidelines for Testing of Chemicals (May 12, 1981).

sludge conc: 100 mg/l related to BOD

26-JAN-1999 (12)

Type: aerobic
 Inoculum: activated sludge, domestic, adapted
 Concentration: 3 mg/l related to Test substance
 Degradation: > 96 % after 24 hour(s)
 Method: other: Method similar to OECD 302-A
 Year: GLP: no

Test substance: no data
 Remark: Biodegradation at 13 mg/L was 56% as loss of parent material
 23-SEP-1997 (13)

Type: aerobic
 Inoculum: activated sludge, domestic, adapted
 Concentration: related to Test substance
 Degradation: = 50 % after 5 day
 Result: other
 Method: other: River Die-away; Test material spiked into river water and time to 50% degradation determined
 Year: GLP: no

Test substance: no data
 25-SEP-1997 (14)

Type: aerobic
 Inoculum: activated sludge
 Degradation: ca. 30 % after 2 day
 Method:
 Year: GLP: no data

Test substance: no data
 Remark: no details
 26-JAN-1999 (7)

Type: aerobic
 Inoculum: activated sludge
 Degradation: ca. 100 % after 2 day
 Method:
 Year: GLP: no data

Test substance: no data
 Remark: acclimatization
 no details
 26-JAN-1999 (7)

3.6 BOD5, COD or BOD5/COD Ratio

3.7 Bioaccumulation

Species: Carassius auratus (Fish, fresh water)
 Exposure period:
 Concentration:

3. ENVIRONMENTAL FATE AND PATHWAYS

SUBSTANCE ID: 126-73-8

BCF: 6 - 11
 Elimination:
 Method: OECD Guide-line 305 D "Bioaccumulation: Static Fish Test"
 Year: GLP: no data
 Test substance: no data
 Remark: Carassius auratus: 0.8-2.8 g
 Concentration: 1.7-3.5 mg/l
 26-JAN-1999 (15)

Species: Cyprinus carpio (Fish, fresh water)
 Exposure period:
 Concentration: 60 µg/l
 BCF: 5.5 - 10
 Elimination:
 Method: other: see remarks
 Year: GLP: no data
 Test substance: no data
 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).
 26-JAN-1999 (16)

Species: Cyprinus carpio (Fish, fresh water)
 Exposure period:
 Concentration: 6 µg/l
 BCF: 6.9 - 20
 Elimination:
 Method: other: see remarks
 Year: GLP: no data
 Test substance: no data
 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).
 26-JAN-1999 (16)

Species: Oryzias latipes (Fish, fresh water)
 Exposure period:
 Concentration:
 BCF: 11 - 49
 Elimination:
 Method: OECD Guide-line 305 D "Bioaccumulation: Static Fish Test"
 Year: GLP: no data
 Test substance: no data
 Remark: Concentration: 0.06-4.0 mg/l
 26-JAN-1999 (17)

Species: Oryzias latipes (Fish, fresh water)
 Exposure period:

3. ENVIRONMENTAL FATE AND PATHWAYS

SUBSTANCE ID: 126-73-8

Concentration:
BCF: 30 - 35
Elimination:
Method: OECD Guide-line 305 D "Bioaccumulation: Static Fish Test"
Year: GLP: no data
Test substance: no data
Remark: Oryzias latipes: 0.1-0.2 g
Concentration: 2-4 mg/l
26-JAN-1999 (15)

Species: Oryzias latipes (Fish, fresh water)
Exposure period:
Concentration:
BCF: 16 - 27
Elimination:
Method: OECD Guide-line 305 E "Bioaccumulation: Flow-through Fish Test"
Year: GLP: no data
Test substance: no data
Remark: Concentration: 0.1-0.84 mg/l
26-JAN-1999 (10)

3.8 Additional Remarks

Remark: Degradation by bacteria (*Pseudomonas diminuta*) isolated from river water and adapted for two months
> 50 % after 2 h
100 % after 43 h
(Concentration: 2 mg/l, temperature: 40 degree C)
22-JUL-1997 (18)

4. ECOTOXICITY

AQUATIC ORGANISMS

4.1 Acute/Prolonged Toxicity to Fish

Type: flow through
Species: Oncorhynchus mykiss (Fish, fresh water)
Exposure period: 96 hour(s)
Unit: mg/l Analytical monitoring:
LC0: 4.3
LC50: 13
LC100: 19
Method: other: Methods for Acute Toxicity Tests with Fish, Macroinvertebrates and Amphibians. EPA, Ecological Research Series EPA-660/3-75-009, April 1975, U.S. EPA-TSCA, 40 CFR, Part 797 (1985)
Year: GLP: no data
Test substance: no data
Test condition: Temperature: 12 degree C
26-JAN-1999 (19)

Type: semistatic
Species: Brachydanio rerio (Fish, fresh water)
Exposure period: 10 day
Unit: mg/l Analytical monitoring: no
* : 13.5
Method:
Year: GLP: no data
Test substance: no data
Remark: * threshold concentration
Embryo-larval toxicity test
Nominal concentration; without feeding;
25 degree C
26-JAN-1999 (20)

Type: semistatic
Species: Salmo gairdneri (Fish, estuary, fresh water)
Exposure period: 50 day
Unit: mg/l Analytical monitoring: no
* : 8.3
Method:
Year: GLP: no data
Test substance: no data
Remark: * threshold concentration
Embryo-larval toxicity test
Nominal concentration; without feeding;
8 degree C
26-JAN-1999 (20)

Type: static
Species: Brachydanio rerio (Fish, fresh water)
Exposure period: 144 hour(s)
Unit: mg/l Analytical monitoring:
LC50: 11.4
Method: other: ISO 1975
Year: GLP: no data
Test substance: no data
Test condition: pH 7.3 - 8.5

4. ECOTOXICITY

	Temperature: 25 degree C	
26-JAN-1999		(20)
Type:	static	
Species:	Brachydanio rerio (Fish, fresh water)	
Exposure period:	96 hour(s)	
Unit:	mg/l	Analytical monitoring: no
LC0:	10	
LC100:	14	
Method:	other: Letale Wirkung beim Zebrabaerbling, UBA-Verfahrensvorschlag, Mai 1984, Letale Wirkung beim Zebrabaerbling Brachydanio rerio LC0, LC50, LC100, 48-96h	
Year:	1985	GLP: no
Test substance:	no data	
Remark:	geom. mean: 11.8 Nominal concentration	
26-JAN-1999		(3)
Type:	static	
Species:	Carassius auratus (Fish, fresh water)	
Exposure period:	96 hour(s)	
Unit:	mg/l	Analytical monitoring: yes
LC50:	8.8	
Method:		
Year:		GLP: no data
Test substance:	no data	
Test condition:	Temperature: 25 degree C	
26-JAN-1999		(15)
Type:	static	
Species:	Leuciscus idus (Fish, fresh water)	
Exposure period:	96 hour(s)	
Unit:	mg/l	Analytical monitoring: no
LC0:	5.8	
LC50:	7.6	
LC100:	8.7	
Method:	other: DEV, L 15 (1976)	
Year:		GLP: no
Test substance:	no data	
26-JAN-1999		(21)
Type:	static	
Species:	Oncorhynchus mykiss (Fish, fresh water)	
Exposure period:	96 hour(s)	
Unit:	mg/l	Analytical monitoring: no
NOEC:	= 4.9	
LC50:	= 11	
Method:	other: method similar to OECD 203	
Year:		GLP: yes
Test substance:	no data	
Remark:	24 hour LC50 = 13 mg/l; 48 hour LC50 = 11 mg/l.	
23-SEP-1997		(22)
Type:	static	
Species:	Oncorhynchus mykiss (Fish, fresh water)	
Exposure period:	96 hour(s)	
Unit:	mg/l	Analytical monitoring: yes
LC50:	11.5 - 13.5	

4. ECOTOXICITY

Method:			
Year:		GLP: no data	
Test substance:	no data		
Remark:	Nominal concentration measured concentration: 5 - 9 mg/l, no details about control; only 4 fish for each concentration.		
Test condition:	15 degree C		
26-JAN-1999			(23)
Type:	static		
Species:	Oryzias latipes (Fish, fresh water)		
Exposure period:	96 hour(s)		
Unit:	mg/l	Analytical monitoring: yes	
LC50:	9.6		
Method:			
Year:		GLP: no data	
Test substance:	no data		
Test condition:	Temperature: 25 degree C		
26-JAN-1999			(15)
Type:	static		
Species:	Pimephales promelas (Fish, fresh water)		
Exposure period:	96 hour(s)		
Unit:	mg/l	Analytical monitoring: no	
NOEC:	= 3.2		
LC50:	= 6.4		
Method:	other: method similar to OECD 203		
Year:		GLP: yes	
Test substance:	no data		
Remark:	24 hour LC50=10 mg/l; 48 hour LC50=9.6 mg/l		
26-JAN-1999			(24)
Type:	static		
Species:	Salmo gairdneri (Fish, estuary, fresh water)		
Exposure period:	96 hour(s)		
Unit:	mg/l	Analytical monitoring:	
LC50:	4.2		
Method:			
Year:		GLP: no data	
Test substance:	no data		
Remark:	Nominal concentration		
Test condition:	20 degree C		
26-JAN-1999			(25)
Type:	static		
Species:	Salmo gairdneri (Fish, estuary, fresh water)		
Exposure period:	96 hour(s)		
Unit:	mg/l	Analytical monitoring:	
LC50:	8.2		
Method:			
Year:		GLP: no data	
Test substance:	no data		
Remark:	Nominal concentration		
Test condition:	15 degree C		
26-JAN-1999			(25)
Type:	static		

4. ECOTOXICITY

Type:
 Species: Salmo gairdneri (Fish, estuary, fresh water)
 Exposure period: 96 hour(s)
 Unit: mg/l Analytical monitoring:
 LC50: 11.8
 Method:
 Year: GLP: no data
 Test substance: no data
 Remark: Nominal concentration
 Test condition: 10 degree C
 26-JAN-1999 (25)

Type:
 Species: Oryzias latipes (Fish, fresh water)
 Exposure period: 48 hour(s)
 Unit: mg/l Analytical monitoring:
 LC50: 4.5
 Method: OECD Guide-line 203 "Fish, Acute Toxicity Test"
 Year: GLP: no data
 Test substance: no data
 26-JAN-1999 (26)

Type:
 Species: Oryzias latipes (Fish, fresh water)
 Exposure period: 96 hour(s)
 Unit: mg/l Analytical monitoring:
 LC50: 4.5
 Method: OECD Guide-line 203 "Fish, Acute Toxicity Test"
 Year: GLP: no data
 Test substance: no data
 26-JAN-1999 (26)

Type:
 Species: Oryzias latipes (Fish, fresh water)
 Exposure period: 48 hour(s)
 Unit: mg/l Analytical monitoring:
 LC50: 14.2
 Method: other: Japanese Industrial Standard (JIS K 0102-1986-71)
 "Testing methods for industrial waste water"
 Year: GLP: no data
 Test substance: no data
 26-JAN-1999 (16)

Type:
 Species: Oryzias latipes (Fish, fresh water)
 Exposure period: 48 hour(s)
 Unit: mg/l Analytical monitoring:
 LC50: 18
 Method:
 Year: GLP: no data
 Test substance: no data
 26-JAN-1999 (27)

Type:
 Species: Pimephales promelas (Fish, fresh water)
 Exposure period: 96 hour(s)
 Unit: mg/l Analytical monitoring: yes
 LC50: 8.18
 EC50 : 7.79

4. ECOTOXICITY

Method:
 Year: GLP: no data
 Test substance: as prescribed by 1.1 - 1.4
 Remark: gas-liquid chromatography
 Test condition: Temperature: 25.9 degree C
 26-JAN-1999 (28)
 Type:
 Species: Pimephales promelas (Fish, fresh water)
 Exposure period: 96 hour(s)
 Unit: mg/l Analytical monitoring: yes
 LC50: 11
 EC50 : 6.56
 Method:
 Year: GLP: no data
 Test substance: as prescribed by 1.1 - 1.4
 Remark: gas-liquid chromatography
 Test condition: Temperature: 26.7 degree C
 26-JAN-1999 (28)

4.2 Acute Toxicity to Aquatic Invertebrates

Type:
 Species: Daphnia magna (Crustacea)
 Exposure period: 24 hour(s)
 Unit: mg/l Analytical monitoring:
 EC50: 4.2
 Method: OECD Guide-line 202, part 1 "Daphnia sp., Acute
 Immobilisation Test"
 Year: GLP: no data
 Test substance: no data
 26-JAN-1999 (26)

Type:
 Species: Daphnia magna (Crustacea)
 Exposure period: 24 hour(s)
 Unit: mg/l Analytical monitoring: no
 EC0: 2.5
 EC50: 5.8
 EC100: 20
 Method: other: Daphnien-Schwimmunfaehigkeits-Test,
 UBA-Verfahrensvorschlag Mai 1984, Bestimmung der
 Schwimmunfaehigkeit beim Wasserfloh Daphnia magna, EC0, EC50,
 EC100 24h, statisches System
 Year: 1985 GLP: no
 Test substance: no data
 26-JAN-1999 (3)

Type:
 Species: Daphnia magna (Crustacea)
 Exposure period: 24 hour(s)
 Unit: mg/l Analytical monitoring:
 EC50: 12.8
 Method: other: ISO (1975)
 Year: GLP: no data
 Test substance: no data
 26-JAN-1999 (29)

4. ECOTOXICITY

Type:
 Species: Daphnia magna (Crustacea)
 Exposure period: 48 hour(s)
 Unit: mg/l Analytical monitoring:
 EC50: 3.65
 Method: other: ISO (1975)
 Year: GLP: no data
 Test substance: no data
 26-JAN-1999 (29)

Type:
 Species: Daphnia magna (Crustacea)
 Exposure period: 72 hour(s)
 Unit: mg/l Analytical monitoring:
 EC50: 2.1
 Method: other: ISO (1975)
 Year: GLP: no data
 Test substance: no data
 26-JAN-1999 (29)

Type:
 Species: Daphnia magna (Crustacea)
 Exposure period: 14 day
 Unit: mg/l Analytical monitoring:
 NOEC: 3.1
 Method: other: OECD Guide-line 202, Daphnia sp., acute immobilization and reproduction test
 Year: GLP: no data
 Test substance: no data
 26-JAN-1999 (26)

Type:
 Species: Daphnia magna (Crustacea)
 Exposure period: 48 hour(s)
 Unit: mg/l Analytical monitoring: no
 NOEC: = 1.8
 EC50: = 9
 Method: other: method similar to OECD 202
 Year: GLP: yes
 Test substance: no data
 Remark: 24 hour EC50 = 23 mg/l.
 26-JAN-1999 (30)

Type:
 Species: Daphnia magna (Crustacea)
 Exposure period: 24 hour(s)
 Unit: mg/l Analytical monitoring:
 EC0: 5
 EC50: 30
 EC100: 41
 Method: other: static
 Year: GLP: no
 Test substance: no data
 26-JAN-1999 (31)

Type:
 Species: Daphnia magna (Crustacea)

4. ECOTOXICITY

Exposure period: 24 hour(s)
 Unit: mg/l Analytical monitoring:
 EC0: 7
 EC50: 33
 EC100: 58
 Method: other: static
 Year: GLP: no
 Test substance: no data
 Remark: Nominal concentration
 Test condition: Temperature: 20 - 22 degree C
 26-JAN-1999 (32)

Type:
 Species: Daphnia magna (Crustacea)
 Exposure period: 6 hour(s)
 Unit: mg/l Analytical monitoring:
 EC50: 52
 Method:
 Year: GLP: no data
 Test substance: no data
 26-JAN-1999 (33)

Type:
 Species: Daphnia magna (Crustacea)
 Exposure period: 24 hour(s)
 Unit: mg/l Analytical monitoring:
 EC0: 9.3
 EC50: 35
 Method:
 Year: GLP: no data
 Test substance: no data
 Remark: Nominal concentration
 26-JAN-1999 (34)

Type:
 Species: Daphnia magna (Crustacea)
 Exposure period: 24 hour(s)
 Unit: mg/l Analytical monitoring:
 EC50: 35
 Method:
 Year: GLP: no data
 Test substance: no data
 26-JAN-1999 (33)

Type:
 Species: Daphnia magna (Crustacea)
 Exposure period: 48 hour(s)
 Unit: mg/l Analytical monitoring: yes
 NOEC: = .75
 EC50: = 2.6
 Method:
 Year: 1990 GLP: yes
 Test substance: no data
 26-JAN-1999 (35)

Type:
 Species: Daphnia pulex (Crustacea)
 Exposure period: 6 hour(s)

4. ECOTOXICITY

Unit: mg/l Analytical monitoring:
 EC50: 93
 Method:
 Year: GLP: no data
 Test substance: no data
 26-JAN-1999 (33)

Type:
 Species: Daphnia pulex (Crustacea)
 Exposure period: 24 hour(s)
 Unit: mg/l Analytical monitoring:
 EC50: 68
 Method:
 Year: GLP: no data
 Test substance: no data
 26-JAN-1999 (33)

Type:
 Species: other: Gammarus pseudolimnaeus
 Exposure period: 96 hour(s)
 Unit: mg/l Analytical monitoring:
 NOEC: .52
 LC50 : 1.7
 Method: other: see remarks
 Year: GLP: no data
 Test substance: no data
 Remark: Methods for Acute Toxicity Tests with Fish,
 Macroinvertebrates and Amphibians, 795.120 of the Federal
 Register Guideline "Gammarid Acute Toxicity Test" and
 Standard Methods for Examination of Water and Wastewater
 (flow-through bioassay)
 Length: 2 - 3 mm
 Mortality and Immobilisation
 Nominal concentration
 26-JAN-1999 (36)

Type:
 Species: other: Hyalella azteca
 Exposure period: 96 hour(s)
 Unit: mg/l Analytical monitoring:
 NOEC: < 1.9
 LC50 : 2.4
 Method: other: see remarks
 Year: GLP: no data
 Test substance: no data
 Remark: Length: 1 - 2 mm
 Nominal concentration
 Methods for Acute Toxicity Tests with Fish,
 Macroinvertebrates and Amphibians, 795.120 of the Federal
 Register Guideline "Gammarid Acute Toxicity Test" and
 Standard Methods for Examination of Water and Wastewater
 (flow-through bioassay).
 26-JAN-1999 (37)

4.3 Toxicity to Aquatic Plants e.g. Algae

Species: Chlorella vulgaris (Algae)

4. ECOTOXICITY

- Endpoint:
 Exposure period: 7 day
 Unit: mg/l Analytical monitoring:
 EC50: 5
 Method: OECD Guide-line 201 "Algae, Growth Inhibition Test"
 Year: GLP: no data
 Test substance: no data
 26-JAN-1999 (26)
- Species: Microcystis aeruginosa (Algae, blue, cyanobacteria)
 Endpoint:
 Exposure period: 8 day
 Unit: mg/l Analytical monitoring: no
 TT : 4.1
 Method: other: cell multiplication inhibition test
 Year: GLP: no
 Test substance: no data
 Test condition: Temperature: 27 degree C
 26-JAN-1999 (38)
- Species: Scenedesmus quadricauda (Algae)
 Endpoint:
 Exposure period: 8 day
 Unit: mg/l Analytical monitoring: no
 TT : 3.2
 Method: other: cell multiplication inhibition test
 Year: GLP: no
 Test substance: no data
 Test condition: Temperature: 25 degree C
 26-JAN-1999 (39)
- Species: Scenedesmus subspicatus (Algae)
 Endpoint:
 Exposure period: 72 hour(s)
 Unit: mg/l Analytical monitoring:
 Method: other: Scenedesmus-Zellvermehrungs-Hemmtest, DIN 38412 Teil 9, Bestimmung der Hemmwirkung von Wasserinhaltsstoffen auf Gruenalgen
 Year: GLP: no data
 Test substance: no data
 Remark: EC10 (biomass): 0.37; EC50 (biomass): 1.1
 EC10 (growth rate): 0.92; EC50 (growth rate): 2.8
 26-JAN-1999 (40)
- Species: Selenastrum capricornutum (Algae)
 Endpoint:
 Exposure period: 96 hour(s)
 Unit: mg/l Analytical monitoring:
 NOEC: 2.2
 EC50: 4.4
 Method: other: static (ABC Protocol 8004-PMN)
 Year: GLP: no data
 Test substance: no data
 Test condition: Temperature: 24 degree C
 26-JAN-1999 (41)
- Species: other algae: Chlorella emersonii
 Endpoint:

4. ECOTOXICITY

Exposure period: 2 day
 Unit: mg/l Analytical monitoring:
 EC50: 5 - 10
 Method:
 Year: GLP: no data
 Test substance: no data
 Test condition: Temperature: 25 degree C
 26-JAN-1999 (25)

Species: other aquatic plant: Phytoplankton (13 species)
 Endpoint: growth rate
 Exposure period: 14 day
 Unit: mg/l Analytical monitoring:
 EC100 : 50
 Method: other: Microtiter-Plates, visual evaluation
 Year: GLP: no data
 Test substance: no data
 Remark: LOEC 5 mg/l
 26-JAN-1999 (42)

4.4 Toxicity to Microorganisms e.g. Bacteria

Type: aquatic
 Species: activated sludge
 Exposure period: 3 hour(s)
 Unit: mg/l Analytical monitoring: no
 EC50: 300
 Method: ISO 8192 "Test for inhibition of oxygen consumption by activated sludge"
 Year: 1985 GLP: no
 Test substance: no data
 Remark: direct weight
 26-JAN-1999 (3)

Type: aquatic
 Species: activated sludge of a predominantly domestic sewage
 Exposure period: 3 hour(s)
 Unit: mg/l Analytical monitoring:
 EC50: 100
 Method: OECD Guide-line 209 "Activated Sludge, Respiration Inhibition Test"
 Year: GLP: no data
 Test substance: no data
 26-JAN-1999 (27)

Type: aquatic
 Species: Pseudomonas putida (Bacteria)
 Exposure period: 16 hour(s)
 Unit: mg/l Analytical monitoring: no
 TT : > 100
 Method:
 Year: GLP: no
 Test substance: no data
 Test condition: Temperature: 25 degree C
 26-JAN-1999 (43)

4. ECOTOXICITY

SUBSTANCE ID: 126-73-8

4.5 Chronic Toxicity to Aquatic Organisms

4.5.1 Chronic Toxicity to Fish

Species: Oncorhynchus mykiss (Fish, fresh water)
 Endpoint: other: time to swim-up stage; survival, length and weight
 Exposure period: 95 day
 Unit: mg/l Analytical monitoring: yes
 NOEC: = .82
 LOEC: = 1.7
 MATC : = 1.2
 Method: other: U.S. EPA. 1987. Fish Early Life Stage Toxicity Test
 (Amended. Federal Register, Vol. 52, No. 97/Wed., May 20,
 1987; Part 797.1600 Amended: 19064-19066
 Year: 1991 GLP: yes
 Test substance: no data
 Remark: Results based on measured concentrations.
 26-JAN-1999 (44)

4.5.2 Chronic Toxicity to Aquatic Invertebrates

Species: Daphnia magna (Crustacea)
 Endpoint: other: EC50: based on immobilization; 21-Day LOEC: based on
 length, days to first brood and Y/D/D
 Exposure period: 21 day
 Unit: mg/l Analytical monitoring: yes
 NOEC: = .87
 LOEC: = 2.1
 EC50: > 2.1
 MATC : = 1.35
 Method:
 Year: 1991 GLP: yes
 Test substance: no data
 26-JAN-1999 (45)

Species: Daphnia magna (Crustacea)
 Endpoint:
 Exposure period: 21 day
 Unit: mg/l Analytical monitoring:
 NOEC: 1.3
 Method: other: "Verlaengerter Toxizitaetstest bei Daphnia magna
 (Bestimmung der NOEC fuer Reproduktionsrate, Mortalitaet und
 den Zeitpunkt des ersten Auftretens von Nachkommen; 21 d)
 Stand: 01.01.1984"
 Year: GLP: no data
 Test substance: no data
 Remark: Nominal concentration
 measured value: 1.0 mg/l
 26-JAN-1999 (34)

TERRESTRIAL ORGANISMS

4.6.1 Toxicity to Soil Dwelling Organisms

Type:

Species:

Endpoint:

Exposure period:

Unit:

Method:

Year:

GLP:

Test substance:

Remark: No mortality was observed among two-spotted spider mites
(Tetranychus urticae) fed TBP at a concentration of 2 g/kg.

06-OCT-1997

(46)

4.6.2 Toxicity to Terrestrial Plants

Species:

Endpoint:

Expos. period:

Unit:

Method:

Year:

GLP: no data

Test substance: no data

Remark: TBP is used as a constituent of cotton defoliants,
producing leaf scorching, and is associated with an
increase in the rate of leaf drying.

27-JAN-1999

(46)

Species:

Endpoint:

Expos. period:

Unit:

Method:

Year:

GLP: no data

Test substance: no data

Remark: TBP increases the drying rate of lucerne, resulting
in excessive leaf loss.

27-JAN-1999

(46)

Species:

Endpoint:

Expos. period:

Unit:

Method:

Year:

GLP: no data

Test substance: no data

Remark: TBP applied by spraying as an emulsion (at a rate
equivalent to 0.25 % of freshly harvested leaf/weight)
doubled the drying rate of ryegrass leaves. Leaf respir-
ation stopped and did not resume in the subsequent 4 days.

27-JAN-1999

(46)

Species:

Endpoint:

Expos. period:

Unit:
Method:
Year: GLP: no data
Test substance: no data
Remark: TBP has been shown to damage the leaf surface and help herbicides penetrate bean leaves.
27-JAN-1999 (46)

Species:
Endpoint:
Expos. period:
Unit:
Method:
Year: GLP: no data
Test substance: no data
Remark: There is no information on the effects of TBP on non-target plants, even at concentrations designed to produce desiccation of crop plants.
27-JAN-1999 (46)

4.6.3 Toxicity to other Non-Mamm. Terrestrial Species

4.7 Biological Effects Monitoring

4.8 Biotransformation and Kinetics

4.9 Additional Remarks

Remark: TT 14 mg/l (Entosiphon sulcatum, 3 d)
TT 21 mg/l (Uronema Parduczi, 20 h)
TT 42 mg/l (Chilomonas parameaecium, 2 d)
Source: Bayer AG Leverkusen 1
22-JUL-1997 (47)

Remark: EC50 20 mg/l (Tetrahymena pyriformis, 24 h)
22-JUL-1997 (27)

5. TOXICITY

5.1 Acute Toxicity

5.1.1 Acute Oral Toxicity

Type: LD50
Species: rat
Strain:
Sex:
Number of
Animals:
Vehicle:
Value: = 1552 mg/kg bw
Method:
Year: GLP: no data
Test substance: no data
Remark: = 1.6 ml/kg
27-JAN-1999 (48)

Type: LD50
Species: rat
Strain:
Sex:
Number of
Animals:
Vehicle:
Value: 1600 - 3200 mg/kg bw
Method:
Year: GLP: no data
Test substance: no data
20-JAN-1999 (49)

Type: LD50
Species: rat
Strain:
Sex:
Number of
Animals:
Vehicle:
Value: = 3000 mg/kg bw
Method:
Year: GLP: no data
Test substance: no data
20-JAN-1999 (49) (50)

Type: LD50
Species: rat
Strain:
Sex:
Number of
Animals:
Vehicle:
Value: = 1400 mg/kg bw
Method:
Year: GLP: no data
Test substance: no data
27-JAN-1999 (51)

5. TOXICITY

Type: LD50
Species: rat
Strain:
Sex:
Number of
Animals:
Vehicle:
Value: = 3350 mg/kg bw
Method:
Year: GLP: no data
Test substance: no data
20-JAN-1999 (52)

Type: LD50
Species: rat
Strain:
Sex:
Number of
Animals:
Vehicle:
Value: = 1390 mg/kg bw
Method:
Year: GLP: no data
Test substance: no data
Remark: male rats
20-JAN-1999 (53)

Type: LD50
Species: rat
Strain:
Sex:
Number of
Animals:
Vehicle:
Value: = 1530 mg/kg bw
Method:
Year: GLP: no data
Test substance: no data
Remark: female rats
20-JAN-1999 (54)

Type: LD50
Species: rat
Strain:
Sex:
Number of
Animals:
Vehicle:
Value: = 11265 mg/kg bw
Method:
Year: GLP: no data
Test substance: no data
27-JAN-1999 (55)

Type: LD50
Species: rat
Strain:

5. TOXICITY

Sex:
Number of
Animals:
Vehicle:
Value: < 20000 mg/kg bw
Method:
Year: GLP: no
Test substance: no data
20-JAN-1999 (56)

Type: LD50
Species: mouse
Strain:
Sex:
Number of
Animals:
Vehicle:
Value: 400 - 800 mg/kg bw
Method:
Year: GLP: no data
Test substance: no data
20-JAN-1999 (49)

Type: LD50
Species: mouse
Strain:
Sex:
Number of
Animals:
Vehicle:
Value: = 1189 mg/kg bw
Method:
Year: GLP: no data
Test substance: no data
20-JAN-1999 (52)

Type: LD50
Species: mouse
Strain:
Sex:
Number of
Animals:
Vehicle:
Value: = 1240 mg/kg bw
Method:
Year: GLP: no data
Test substance: no data
Remark: male mice
20-JAN-1999 (54)

Type: LD50
Species: mouse
Strain:
Sex:
Number of
Animals:
Vehicle:

5. TOXICITY

Value: = 900 mg/kg bw
Method:
Year: GLP: no data
Test substance: no data
Remark: female mice
20-JAN-1999 (54)

Type: LD50
Species: hen
Strain:
Sex:
Number of
Animals:
Vehicle:
Value: = 1500 mg/kg bw
Method:
Year: GLP: no data
Test substance: no data
27-JAN-1999 (57)

Type: LD50
Species: hen
Strain:
Sex:
Number of
Animals:
Vehicle:
Value: = 1800 mg/kg bw
Method:
Year: GLP: no data
Test substance: no data
27-JAN-1999 (51)

Type: LD50
Species: hen
Strain:
Sex:
Number of
Animals:
Vehicle:
Value: = 1500 mg/kg bw
Method:
Year: GLP: no data
Test substance: no data
27-JAN-1999 (58)

5.1.2 Acute Inhalation Toxicity

Type: LC0
Species: rat
Strain:
Sex:
Number of
Animals:
Vehicle:
Exposure time: 6 hour(s)
Value: = 1.5 mg/l

5. TOXICITY

Method:

Year: GLP: no data
Test substance: no data
Remark: = 123 ppm
mortality: 0/3
strong skin and respiratory irritant
27-JAN-1999 (59)

Type: LC50
Species: rat
Strain:
Sex:
Number of
Animals:
Vehicle:
Exposure time: 6 hour(s)
Value: > 42 mg/l
Method:
Year: GLP: no data
Test substance: no data
Remark: with 3800 ppm (calculated): mortality 1/3, irritation
= 42 mg/l 6h
with 350 ppm (calculated, = 4 mg/l): irritation, no
mortalities (no further data).
20-JAN-1999 (49)

Type: LC50
Species: rat
Strain:
Sex:
Number of
Animals:
Vehicle:
Exposure time: 1 hour(s)
Value: = 28 mg/l
Method:
Year: GLP: no data
Test substance: no data
20-JAN-1999 (60)

Type: LC50
Species: rat
Strain:
Sex:
Number of
Animals:
Vehicle:
Exposure time: 4 hour(s)
Value: > 4.242 mg/l
Method:
Year: GLP: no data
Test substance: no data
Remark: maximum producible concentration = 4.242 mg/l,
aerosol, analytical value.
2/5 male animals died, 0/5 female animals died
test according OECD guideline 403

5. TOXICITY

27-JAN-1999 (61)

Type: LC50
 Species: rat
 Strain:
 Sex:
 Number of
 Animals:
 Vehicle:
 Exposure time: 1 hour(s)
 Value: < 200 mg/l
 Method:
 Year: GLP: no data
 Test substance: no data

20-JAN-1999 (62) (56)

Type: LC50
 Species: mouse
 Strain:
 Sex:
 Number of
 Animals:
 Vehicle:
 Exposure time:
 Value: = 1.3 mg/l
 Method:
 Year: GLP: no data
 Test substance: no data
 Remark: only calculated value, no experimental study

20-JAN-1999 (52)

Type: other: LC
 Species: cat
 Strain:
 Sex:
 Number of
 Animals:
 Vehicle:
 Exposure time: 5 hour(s)
 Value: = 24.51 mg/l
 Method:
 Year: GLP: no data
 Test substance: no data

27-JAN-1999 (63)

5.1.3 Acute Dermal Toxicity

Type: LD50
 Species: rabbit
 Strain:
 Sex:
 Number of
 Animals:
 Vehicle:
 Value: > 3100 mg/kg bw
 Method:
 Year: GLP: no data
 Test substance: no data

5. TOXICITY

27-JAN-1999 (51)

Type: LD50
Species: rabbit
Strain:
Sex:
Number of
Animals:
Vehicle:
Value: > 10000 mg/kg bw
Method:
Year: GLP: no
Test substance: no data

20-JAN-1999 (56) (64)

Type: LD50
Species: guinea pig
Strain:
Sex:
Number of
Animals:
Vehicle:
Value: 9700 - 19400 mg/kg bw
Method:
Year: GLP: no data
Test substance: no data

Remark: application of 10 - 20 ml/kg bw
20-JAN-1999 (49)

5.1.4 Acute Toxicity, other Routes

Type: LD50
Species: rat
Strain:
Sex:
Number of
Animals:
Vehicle:
Route of admin.: i.p.
Value: 800 - 1600 mg/kg bw
Method:
Year: GLP: no data
Test substance: no data

20-JAN-1999 (49)

Type: LD50
Species: rat
Strain:
Sex:
Number of
Animals:
Vehicle:
Route of admin.: i.p.
Value: = 251.2 mg/kg bw
Method:
Year: GLP: no data
Test substance: no data

5. TOXICITY

20-JAN-1999 (52)

Type: LD50
Species: mouse
Strain:
Sex:
Number of
Animals:
Vehicle:
Route of admin.: i.p.
Value: 100 - 200 mg/kg bw
Method:
Year: GLP: no data
Test substance: no data

20-JAN-1999 (49)

Type: LD50
Species: mouse
Strain:
Sex:
Number of
Animals:
Vehicle:
Route of admin.: i.p.
Value: = 158.5 mg/kg bw
Method:
Year: GLP: no data
Test substance: no data

20-JAN-1999 (52)

Type: other: LD
Species: rat
Strain:
Sex:
Number of
Animals:
Vehicle:
Route of admin.: i.p.
Value: = 1000 mg/kg bw
Method:
Year: GLP: no data
Test substance: no data
Remark: 1000 or 5000 mg/kg bw were fatal within 1/2 to 4 hours.
With 500 mg/kg bw coma for 24 hours, than recovery.
with 50 or 100 mg neither behavioral nor pathological
changes.

27-JAN-1999 (23)

Type: other: LD
Species: mouse
Strain:
Sex:
Number of
Animals:
Vehicle:
Route of admin.: s.c.
Value: = 3000 mg/kg bw

5. TOXICITY

Method:
Year: GLP: no data

Test substance: no data
27-JAN-1999 (63)

Type: other: LD
Species: rat
Strain:
Sex:
Number of
Animals:
Vehicle:
Route of admin.: i.v.
Value: 80 - 100 mg/kg bw
Method:
Year: GLP: no data

Test substance: no data
Remark: 80 mg/kg sublethal, 100 mg/kg lethal, no cholinergic
symptoms
27-JAN-1999 (65)

5.2 Corrosiveness and Irritation

5.2.1 Skin Irritation

Species: rabbit
Concentration:

Exposure:
Exposure Time:
Number of
Animals:
PDII:
Result: slightly irritating
EC classificat.:
Method: OECD Guide-line 404 "Acute Dermal Irritation/Corrosion"
Year: GLP: no data

Test substance: no data
27-JAN-1999 (66)

Species: rabbit
Concentration:

Exposure:
Exposure Time:
Number of
Animals:
PDII:
Result: irritating
EC classificat.:
Method: other: see remarks
Year: GLP: no data

Test substance: no data

5. TOXICITY

Remark: - concentrated tributyl phosphate:
ear, occlusive 24 hours, soaked cotton swab or
single painted ear: irritation
- 50 % in Lanoline:
ear, occlusive, 24 hours: irritation
- 10 % in Lanoline:
no irritation

27-JAN-1999 (67)

Species: rabbit
Concentration:

Exposure:
Exposure Time:
Number of
Animals:
PDII:
Result: highly irritating
EC classificat.:
Method: other: no data
Year: GLP: no
Test substance: no data
20-JAN-1999 (68) (50)

Species: rabbit
Concentration:

Exposure:
Exposure Time:
Number of
Animals:
PDII:
Result: slightly irritating
EC classificat.:
Method: other: no data
Year: GLP: no
Test substance: no data
20-JAN-1999 (62)

Species: rabbit
Concentration:

Exposure:
Exposure Time:
Number of
Animals:
PDII:
Result: highly irritating
EC classificat.:
Method: other: see remarks
Year: GLP: no
Test substance: no data
Remark: single dermal application of 500 mg/animal on intact or
abraded skin of six rabbits.
20-JAN-1999 (69)

Species: rabbit

5. TOXICITY

Concentration:

Exposure:

Exposure Time:

Number of

Animals:

PDII:

Result: irritating

EC classificat.:

Method: other: see remarks

Year: GLP: no data

Test substance: no data

Remark: the neat liquid or 10 % aqueous solutions applied on three to ten occasions to the intact or abraded skin: slight hyperaemia, tissue damage (no further data).

27-JAN-1999

(70)

Species: rabbit

Concentration:

Exposure:

Exposure Time:

Number of

Animals:

PDII:

Result: highly irritating

EC classificat.:

Method: other: exposure period 24 hours, no further data

Year: GLP: no

Test substance: no data

20-JAN-1999

(71)

Species: guinea pig

Concentration:

Exposure:

Exposure Time:

Number of

Animals:

PDII:

Result: irritating

EC classificat.:

Method: other: see remarks

Year: GLP: no data

Test substance: no data

Remark: skin, 24 hours contact under an impervious covering.

20-JAN-1999

(49)

Species: guinea pig

Concentration:

Exposure:

Exposure Time:

Number of

Animals:

PDII:

Result: highly irritating

5. TOXICITY

EC classificat.:

Method: other: see remarks

Year: GLP: no data

Test substance: no data

Remark: covered contact with the neat liquid for 24 hours (no further data).

A 10 % solution in dimethyl phthalate was slightly irritating when applied to intact skin and moderately irritating when applied to abraded skin, whereas 2 % concentration caused no irritation (no further data).

27-JAN-1999

(72)

Species: human

Concentration:

Exposure:

Exposure Time:

Number of

Animals:

PDII:

Result: irritating

EC classificat.:

Method: other: see remarks

Year: GLP: no data

Test substance: no data

Remark: - concentrated tributyl phosphate:
arm, soaked cotton swab: irritation.
- 75 % in Lanoline:
arm, occlusive, 3 hours: irritation.
- 50 % in Lanoline:
arm, soaked cotton swab, 24 hours: mild irritation
- 10 % in Lanoline:
arm, soaked cotton swab, occlusive, 24 hours: no irritation

27-JAN-1999

(67)

Species: rat

Concentration:

Exposure:

Exposure Time:

Number of

Animals:

PDII:

Result: highly irritating

EC classificat.:

Method: other: see remarks

Year: GLP: no data

Test substance: no data

Remark: covered contact with the neat liquid for 5 days

27-JAN-1999

(73)

5.2.2 Eye Irritation

Species: rabbit

Concentration:

Dose:

5. TOXICITY

Exposure Time:

Comment:

Number of

Animals:

Result: slightly irritating

EC classificat.:

Method: OECD Guide-line 405 "Acute Eye Irritation/Corrosion"

Year: GLP: no data

Test substance: no data

27-JAN-1999

(66)

Species: rabbit

Concentration:

Dose:

Exposure Time:

Comment:

Number of

Animals:

Result: irritating

EC classificat.:

Method: other: no data

Year: GLP: no

Test substance: no data

Remark: eye injury after 24 hour instillation

not irritant if washed out 4 seconds after instillation

20-JAN-1999

(62) (71) (50)

Species: rabbit

Concentration:

Dose:

Exposure Time:

Comment:

Number of

Animals:

Result: slightly irritating

EC classificat.:

Method: other: see remarks

Year: GLP: no

Test substance: no data

Remark: instillation of 100 mg/animal, observation period min. 7 days

20-JAN-1999

(69)

Species: other: no data

Concentration:

Dose:

Exposure Time:

Comment:

Number of

Animals:

Result: irritating

EC classificat.:

Method: other: no data

Year: GLP: no data

Test substance: no data

Remark: transient irritation

5. TOXICITY

SUBSTANCE ID: 126-73-8

20-JAN-1999

(49)

5.3 Sensitization

Type: Open epicutaneous test
 Species: guinea pig
 Number of Animals:
 Vehicle:
 Result: not sensitizing
 Classification:
 Method: other: test according EPA final test rule 1989, Test standard 40CFR 798.4100
 Year: GLP: yes
 Test substance: as prescribed by 1.1 - 1.4
 Remark: once weekly dermal application until a total of 3 applications, 14 day rest period, dermal challenge on a virgin site.

20-JAN-1999

(74)

Type: Patch-Test
 Species: human
 Number of Animals:
 Vehicle:
 Result:
 Classification:
 Method:
 Year: GLP: no data
 Test substance: no data
 Remark: 53 volunteers, 15 applications of a formulation, said to contain less than 25 % tributyl phosphate, were made on alternate days. No volunteer gave local reactions 24 hours after the final patch, therefore no evidence of sensitization.

27-JAN-1999

(75)

Type: other: standard test
 Species: guinea pig
 Number of Animals:
 Vehicle:
 Result: sensitizing
 Classification:
 Method: other: standard sensitization test
 Year: GLP: no data
 Test substance: no data
 Remark: positive with 6 out of 15 animals (no further data).

20-JAN-1999

(49)

5.4 Repeated Dose Toxicity

Species: rat Sex: no data
 Strain: no data
 Route of admin.: inhalation

5. TOXICITY

Exposure period: 4 months
Frequency of treatment: 5 days/week, 5 hours/day
Post. obs. period: 1 months
Doses: 5.1 or 13.6 mg/m³
Control Group: no data specified
Method:
Year: GLP: no data
Test substance: no data
Remark: group size and purity not mentioned
Result: in the high concentration decrease of cholinesterase activity to 33 % after 3 months, effects on physiological and biochemical parameters esp. of the liver. The cholinesterase activity returned to normal in the postexposure period. In the low concentration no effect on cholinesterase activity (no further data).

20-JAN-1999

(52)

Species: rat Sex: male/female
Strain: Sprague-Dawley
Route of admin.: oral feed
Exposure period: 13 weeks
Frequency of treatment: daily (feeding study)
Post. obs. period: no
Doses: 8, 40, 200, 1000 or 5000 mg/kg diet (0.6, 3, 15, 75 or 375 mg/kg)
Control Group: yes
Method:
Year: GLP: yes
Test substance: as prescribed by 1.1 - 1.4
Remark: 15 animals/sex/group
purity not known
Result: depressed red blood counts and increased prothrombin and thromboplastin times in males (5000 ppm), increased gamma-GT levels and increased absolute and relative liver weights in both sexes at 5000 ppm. Histopathology: transitional cell hyperplasia in the urinary bladders of both sexes at the 5000 ppm level and males at the 1000 ppm level. No microscopic changes in nerve tissues, bone marrow or liver, or remarkable changes in cholinesterase levels were seen.

20-JAN-1999

(76)

Species: rat Sex: male
Strain: Wistar
Route of admin.: oral feed
Exposure period: 3 months
Frequency of treatment: daily (feeding study)
Post. obs. period: no
Doses: 500, 2000 or 10000 mg/kg diet (37.5, 150 or 750 mg/kg bw)
Control Group: yes
Method:

5. TOXICITY

Year: GLP: no data
Test substance: no data
Remark: purity and group size not mentioned

Result: dose-dependent depression of body weight gain, increments of liver, kidney and testis weight, and decrease in uterus weight, no changes in hematological analysis except an increment on BUN value with high level of TBP (no further data).

20-JAN-1999 (54)

Species: rat Sex: male
Strain: Wistar
Route of admin.: oral feed
Exposure period: 10 weeks
Frequency of treatment: daily (feeding study)
Post. obs. period: no
Doses: 5000 or 10000 mg/kg diet (375 or 750 mg/kg bw)
Control Group: yes
Method:
Year: GLP: no data
Test substance: other TS: purity > 97 %
Remark: 10-11 animals/group
Result: dose dependent decrease of body weight gain, decreased food consumption, decreased absolute weight of brain and kidneys, increase of total protein and cholesterol in the high dose group, increase of urea nitrogen and prolongation of blood coagulation in both treatment groups, decrease of activity of transaminases in both treatment groups, brain cholinesterase activity in the treatment groups was higher than in the control group, no change of cholinesterase activity in liver and serum.

20-JAN-1999 (77)

Species: rat Sex: male
Strain: Wistar
Route of admin.: oral feed
Exposure period: 9 weeks
Frequency of treatment: daily (feeding study)
Post. obs. period: no
Doses: 5000 mg/kg diet (375 mg/kg bw)
Control Group: yes
Method:
Year: GLP: no data
Test substance: no data
Remark: 8 rats in the treatment group, 18 rats in the control group, purity not known
Result: decreased body weight gain, increased absolute and relative liver weight, unchanged hematologic values, increase of blood urea nitrogen, unchanged serum enzyme activity (transaminases, phosphatase, cholinesterase).

20-JAN-1999 (78)

5. TOXICITY

Species: rat Sex: male/female
Strain: Sprague-Dawley
Route of admin.: gavage
Exposure period: 2 weeks
Frequency of treatment: daily
Post. obs. period: no
Doses: 0.14 or 0.42 ml/kg bw (136 or 400 mg/kg bw)
Control Group: yes
Method:
Year: GLP: no data
Test substance: other TS: purity 98.4 %
Remark: 10 animals/sex/group
Result: no overt signs of toxicity, decrease of Hb in high dose females, some changes of clinical chemistry parameters, increase of liver weight and liver to body ratio in high-dose groups, decrease of spleen weight in the high-dose female group, no gross morphological changes, one out of four male rats (high-dose group) showed microscopic degenerative changes in seminiferous tubules.

20-JAN-1999

(79)

Species: rat Sex: male/female
Strain: Sprague-Dawley
Route of admin.: gavage
Exposure period: 18 weeks
Frequency of treatment: 5 days/week
Post. obs. period: no
Doses: 0.2 or 0.3-0.35 ml/kg bw (200 or 300-350 mg/kg bw)
Control Group: yes
Method:
Year: GLP: no data
Test substance: other TS: purity 98.4 %
Remark: 12 animals/sex/group
Result: No overt signs of toxicity, decrease of body weight in high-dose males, no changes in hematological and biochemical parameters besides decrease of red blood cell acetylcholin-esterase, in high-dose females increase of liver weight and spleen weight, diffuse urothelial hyperplasia of urinary bladder in both sexes, no testicular changes.

20-JAN-1999

(80)

Species: rat Sex: male/female
Strain: Sprague-Dawley
Route of admin.: gavage
Exposure period: 2 weeks
Frequency of treatment: daily
Post. obs. period: no
Doses: 0.28 or 0.42 ml/kg bw (270 or 400 mg/kg bw)
Control Group: yes
Method:

5. TOXICITY

SUBSTANCE ID: 126-73-8

Year: GLP: no data
Test substance: other TS: purity 98.4 %
Remark: 10 animals/sex/group

Result: no overt signs of toxicity, reduction in conduction velocity of caudal nerve in high dose males, electron microscopic examination showed morphological changes such as retraction of Schwann cell processes surrounding unmyelinated fibres in high dose groups.

20-JAN-1999 (81)

Species: rat Sex: male
Strain: Wistar
Route of admin.: gavage
Exposure period: 7 days
Frequency of treatment: daily
Post. obs. period: no
Doses: 140 or 200 mg/kg bw
Control Group: no data specified
Method:
Year: GLP: no data
Test substance: no data
Remark: purity and group size not mentioned
Result: marked increments of relative weights of liver and kidneys with increase of BUN value and tubular degeneration (no further data).

20-JAN-1999 (54)

Species: rat Sex: male
Strain: Wistar
Route of admin.: gavage
Exposure period: one month
Frequency of treatment: daily
Post. obs. period: no
Doses: 130 or 460 mg/kg bw
Control Group: no data specified
Method:
Year: GLP: no data
Test substance: no data
Remark: purity and group size not mentioned
Result: marked depression of body weight gain and lethal cases by 20 and 40 % respectively, tubular damage (no further data).

20-JAN-1999 (54)

Species: rat Sex: no data
Strain: no data
Route of admin.: dermal
Exposure period: chronic poisoning
Frequency of treatment: no data
Post. obs. period: no data
Doses: no data

5. TOXICITY

Control Group: no data specified
Method:
Year: GLP: no data
Test substance: no data

Remark: NOEL: no data
purity and group size not mentioned
Result: effects on central nervous system, liver and kidneys (no further data).

20-JAN-1999 (52)

Species: mouse Sex: male/female
Strain: CD-1
Route of admin.: oral feed
Exposure period: 4 weeks
Frequency of treatment: daily (feeding study)
Post. obs. period:
Doses: 100, 1000, 5000 and 20000 mg/kg diet (15, 150, 750, 3000 mg/kg bw)
Control Group: yes
Method:
Year: GLP: yes
Test substance: as prescribed by 1.1 - 1.4
Remark: 5/sex/group
Result: all animals receiving 20000 ppm in diet died or were sacrificed in a moribund condition (failure to eat, hypothermia, dyspnea, lethargy, tremor). After 10 days the lowest dietary concentration was changed from 100 ppm to 10000 ppm. No mortality or clinical signs in the 1000, 5000, and 10000 ppm groups. Body weight changes in the 5000 and 10000 ppm groups, increases in liver weight and/or liver weight ratios in male mice at all dose levels and in female mice in the 5000 and 10000 ppm groups, decrease in absolute kidney weight in male mice (10000 ppm).

20-JAN-1999 (82)

Species: mouse Sex: male
Strain: other: ddy
Route of admin.: oral feed
Exposure period: 3 months
Frequency of treatment: daily (feeding study)
Post. obs. period: no
Doses: 500, 2000 and 10000 mg/kg diet (75, 300 and 1500 mg/kg bw)
Control Group: yes
Method:
Year: GLP: no data
Test substance: no data
Remark: purity and group size not mentioned
Result: dose-dependent depression of body weight gain, increments of liver, kidney and testis weight, and decrease in uterus weight, no changes in hematological analysis except an increment on BUN value with high level of TBP (no further data).

5. TOXICITY

SUBSTANCE ID: 126-73-8

20-JAN-1999

(54)

Species: mouse Sex: male/female
Strain: CD-1
Route of admin.: oral feed
Exposure period: 3 month
Frequency of treatment: daily (feeding study)
Post. obs. period: no
Doses: 500, 2000 and 8000 mg/kg diet (75, 300 and 1200 mg/kg bw/day)
Control Group: yes
Method:
Year: GLP: yes
Test substance: as prescribed by 1.1 - 1.4
Remark: 15/sex/group
Result: All animals survived, in the highest concentration body weight loss and reduced body weight gain with reduced food consumption and reduced fecal volume, elevation of absolute and relative liver weights with hepatocyte hypertrophy, slight to moderate epithelial hyperplasia of the urinary bladder, some slight hematological alterations and some effects on clinical chemistry parameters of liver function. In the middle concentration slight decrease of weight gains, elevated terminal ALT and AST in females and moderately elevated liver weights in both sexes, slight hepatocyte hypertrophy and minimal or slight epithelial hyperplasia of the urinary bladder.
NOEL: 500 mg/kg bw/day (120 mg/kg bw/day females and 90 mg/kg bw/day males)

20-JAN-1999

(83)

Species: rabbit Sex: no data
Strain: no data
Route of admin.: inhalation
Exposure period: 4 months
Frequency of treatment: 5 days/week, 5 hours/day
Post. obs. period: 1 month
Doses: 4.8 or 13.6 mg/m³
Control Group: no data specified
Method:
Year: GLP: no data
Test substance: no data
Remark: group size and purity not mentioned
Result: in the high concentration decrease of cholinesterase activity to 33 % after 3 months, effects on physiological and biochemical parameters esp. of the liver. The cholinesterase activity returned to normal in the postexposure period. In the low concentration no effect on cholinesterase activity (no further data).

20-JAN-1999

(52)

Species: rabbit Sex: no data
Strain: no data
Route of admin.: gavage

5. TOXICITY

Exposure period: 14 days
 Frequency of treatment: 7 applications
 Post. obs. period: no data
 Doses: 100, 500 or 1000 mg/kg bw
 Control Group: no data specified
 Method:
 Year: GLP: no
 Test substance: no data
 Remark: purity and size of groups not mentioned
 Result: with 1000 mg/kg transient excretion of protein with urine, no other effects

20-JAN-1999 (67)

Species: other: see remarks Sex: no data
 Strain: no data
 Route of admin.: gavage
 Exposure period: no data
 Frequency of treatment: daily
 Post. obs. period: no data
 Doses: 0.2 to 5 mg/kg/day
 Control Group: no data specified
 Method:
 Year: GLP: no data
 Test substance: no data
 Remark: NOEL: no data
 rabbit and rat
 purity and group size not mentioned
 Result: liver necrosis, increased liver weight, in one of two studies increased kidney weight and tubulus dystrophia (no further data).

20-JAN-1999 (84) (85)

Species: other: see remarks Sex: no data
 Strain: no data
 Route of admin.: dermal
 Exposure period: no data
 Frequency of treatment: no data
 Post. obs. period: no data
 Doses: no data
 Control Group: no data specified
 Method:
 Year: GLP: no data
 Test substance: no data
 Remark: rat, guinea pig and rabbit
 Result: purulent-necrotic fissures (no further data).

20-JAN-1999 (52)

5.5 Genetic Toxicity 'in Vitro'

Type: Ames test

5. TOXICITY

- System of testing: Salmonella typhimurium TA102 and TA2638 and Escherichia coli WP2/pKM101 and WP2 uvr/pKM101
- Concentration:
Cytotoxic Conc.:
Metabolic activation: with and without
- Result: negative
- Method: other: Maron, D.M. and Ames, B.M. (1983)
- Year: GLP: no data
- Test substance: no data
- 20-JAN-1999 (86)
- Type: Ames test
- System of testing: S. typhimurium TA1535, TA100, TA1537, TA98
- Concentration:
Cytotoxic Conc.:
Metabolic activation: with and without
- Result: negative
- Method:
- Year: GLP: no data
- Test substance: no data
- 27-JAN-1999 (87)
- Type: Ames test
- System of testing: S. typhimurium LT-2 (hisC117, hisG46, TA1530, hisD3052, TA1531, TA1532)
- Concentration:
Cytotoxic Conc.:
Metabolic activation: without
- Result: negative
- Method:
- Year: GLP: no data
- Test substance: no data
- 20-JAN-1999 (88)
- Type: Ames test
- System of testing: S. typhimurium TA1535, TA1538, TA1537, TA98, TA100
- Concentration:
Cytotoxic Conc.:
Metabolic activation: with and without
- Result: negative
- Method:
- Year: GLP: no data
- Test substance: as prescribed by 1.1 - 1.4
- 20-JAN-1999 (89)
- Type: Ames test
- System of testing: S. typhimurium TA1535, TA1538
- Concentration:

5. TOXICITY

Cytotoxic Conc.:
 Metabolic
 activation: with and without
 Result: positive
 Method:
 Year: GLP: no data
 Test substance: no data
 27-JAN-1999 (90)

Type: Ames test
 System of
 testing: no data
 Concentration:
 Cytotoxic Conc.:
 Metabolic
 activation: with and without
 Result: negative
 Method:
 Year: GLP: no data
 Test substance: no data
 27-JAN-1999 (91)

Type: Bacterial reverse mutation assay
 System of
 testing: E. coli WP2 isogenic strains
 Concentration:
 Cytotoxic Conc.:
 Metabolic
 activation: without
 Result: negative
 Method:
 Year: GLP: no data
 Test substance: no data
 20-JAN-1999 (88)

Type: Cytogenetic assay
 System of
 testing: chinese hamster ovary cells (CHO-K1)
 Concentration: up to 0.15 ul/ml
 Cytotoxic Conc.:
 Metabolic
 activation: with and without
 Result: negative
 Method:
 Year: GLP: yes
 Test substance: as prescribed by 1.1 - 1.4
 Remark: chromosome aberration assay
 20-JAN-1999 (92)

Type: Cytogenetic assay
 System of
 testing: mouse embryo, 48 and 144 h post conceptionem
 Concentration:
 Cytotoxic Conc.:
 Metabolic
 activation: without
 Result: negative

5. TOXICITY

Method:
 Year: GLP: no data
 Test substance: no data
 Remark: no induction of micronuclei
 27-JAN-1999 (93)

Type: Mammalian cell gene mutation assay
 System of testing: CHO-K1-BH4 cells
 Concentration: 0.11, 0.09, 0.08, 0.07, and 0.05 ul/ml without S-9 and 0.15, 0.125, 0.1, 0.08 and 0.06 ul/ml with S-9
 Cytotoxic Conc.:
 Metabolic activation: with and without
 Result: negative
 Method:
 Year: GLP: yes
 Test substance: as prescribed by 1.1 - 1.4
 20-JAN-1999 (94)

5.6 Genetic Toxicity 'in Vivo'

Type: Cytogenetic assay
 Species: rat Sex: male/female
 Strain: no data
 Route of admin.: gavage
 Exposure period: single administration
 Doses: 0, 300, 600, or 1200 mg/kg bw
 Result:
 Method:
 Year: GLP: yes
 Test substance: as prescribed by 1.1 - 1.4
 Result: the high dose was the maximum tolerated dose, mortality at the high dose level was 1/15 males and 4/15 females; clinical signs of toxicity at 600 and 1200 mg/kg. No increase of aberrant cells in bone marrow after 12, 24 or 36 hours.
 20-JAN-1999 (95)

Type: Drosophila SLRL test
 Species: Drosophila melanogaster Sex:
 Strain:
 Route of admin.: oral feed
 Exposure period:
 Doses:
 Result:
 Method:
 Year: GLP: no data
 Test substance: no data
 Remark: 11.1 % lethals; doses not mentioned.
 Result: negative
 20-JAN-1999 (88)

5.7 Carcinogenicity

Species: rat Sex: male/female
Strain: Sprague-Dawley
Route of admin.: oral feed
Exposure period: 24 months
Frequency of treatment:
Post. obs. period:
Doses: 200, 700 and 3000 ppm
Result:
Control Group: yes
Method: other: US EPA/TSCA
Year: GLP: yes
Test substance: as prescribed by 1.1 - 1.4
Remark: Results: There was a dose-related increase in the incidence and severity of hyperplasia and the incidence of papillomas of the urinary bladder epithelium in the mid and high dose groups. Transitional cell carcinomas were noted in the bladders of 6/49 males and 2/50 females in the high dose. A squamous cell carcinoma was noted in the bladder of 1/49 high dose males. The NOEL was 200 ppm TBP in the diet (104 wk mean intake of 8.9 mg/kg/day for males and 11.6 mg/kg/day for females).

06-APR-1999 (96)

Species: mouse Sex: male/female
Strain: CD-1
Route of admin.: oral feed
Exposure period: 18 months
Frequency of treatment:
Post. obs. period:
Doses: 150, 1000, 3500 ppm
Result:
Control Group: yes
Method: other: US EPA/TSCA
Year: GLP: yes
Test substance: as prescribed by 1.1 - 1.4
Remark: Results: The only histologic change considered to be treatment-related was a statistically significant increase in the incidence of hepatocellular adenoma in high dose male mice. No other tumor type was attributed to TBP administration on the basis of microscopic examinations or statistical analysis. The NOEL for chronic toxicity was 150 ppm (28.9 mg/kg/day for females and 24.1 mg/kg/day for males).

06-APR-1999 (97)

5.8 Toxicity to Reproduction

Type: Two generation study
Species: rat Sex: male/female

5. TOXICITY

Strain: Sprague-Dawley
Route of admin.: oral feed
Exposure Period:
Frequency of treatment: daily (feeding study)
Duration of test: up to two generations
Doses: 200, 700 and 3000 ppm diet (approx 15, 53 and 225 mg/kg bw/day)
Control Group: yes
Method:
Year: GLP: yes
Test substance: as prescribed by 1.1 - 1.4
Remark: 30 animals/sex/group
Result: with 700 and 3000 ppm reductions of body weights, weight gain and food consumption during F0 and F1 prebreed dosing periods, no signs of toxicity, no treatment related mortality; with 200 ppm only transient effects on body weight and food consumption. Urinary bladder epithelial hyperplasia was noted in adults in 700 and 3000 ppm groups in both generations and in F0 males and females and F1 males at 200 ppm. The NOAEL for adult toxicity was <200 ppm based on body weight effects. The NOAEL for reproductive toxicity was >3000 ppm. The NOAEL for post natal toxicity was at or below 200 ppm due to reduced pup weights.

06-APR-1999

(98)

5.9 Developmental Toxicity/Teratogenicity

Species: rat Sex: female
Strain: Sprague-Dawley
Route of admin.: gavage
Exposure period: day 6 to 15 of gestation
Frequency of treatment: daily
Duration of test: up to day 20 of gestation
Doses: 80, 435, 790, 1145, and 1500 mg/kg bw
Control Group: yes
Method:
Year: GLP: yes
Test substance: as prescribed by 1.1 - 1.4
Remark: range-finding study, 5 animals/group
Result: considerable maternal mortality at dose levels of 790, 1145 and 1500 mg/kg bw. A dose of 80 mg/kg bw was not considered to be maternally toxic, embryotoxic or fetotoxic. At 435 mg/kg bw maternal toxicity but no effect on embryo.

20-JAN-1999

(99)

Species: rat Sex: female
Strain: Wistar
Route of admin.: gavage
Exposure period: day 7 to 17 of gestation
Frequency of treatment: daily
Duration of test: day 20 of gestation
Doses: 62.5, 125, 250 or 500 mg/kg/day

5. TOXICITY

Control Group: yes
 NOAEL Maternal.: = 62.5 mg/kg bw
 NOAEL Teratogen.: > 250 mg/kg bw
 Method:
 Year: GLP: no data
 Test substance: no data
 Remark: 20 animals/group
 Result: Salivation and depression of body weight gain, adjusted body weight gain and food consumption were observed at the higher doses. There were no significant differences between the groups in the incidence of dead or resorbed fetuses, the number of living fetuses and the body weights of living fetuses of both sexes. The incidence of rudimentary lumbar rib was increased significantly at 500 mg/kg/day. There was one incident of conjoined twins exhibiting three fore-limbs and four hind-limbs at 125 mg/kg/day. This malformation is rare in the background data of teratology, and the incidence of malformed fetuses was not increased significantly. Therefore, TBP was considered not to be teratogenic in this study.

20-JAN-1999 (100)

Species: rabbit Sex: female
 Strain: other: New Zealand
 Route of admin.: gavage
 Exposure period: day 6 to 18 of gestation
 Frequency of treatment: daily
 Duration of test: up to day 30 of gestation
 Doses: 50, 150 or 400 mg/kg bw
 Control Group: yes
 NOAEL Teratogen.: > 400 mg/kg bw
 Method:
 Year: GLP: yes
 Test substance: as prescribed by 1.1 - 1.4
 Remark: 18 animals/group
 Result: at the 400 mg/kg/day dose level maternal toxic effect (mean weight loss and 5% mortality) and no statistically significant increase of resorptions, no fetotoxic or teratogenic effects. At the 50 and 150 mg/kg/day dose level no maternal toxicity, no embryotoxic, fetotoxic or teratogenic effects.

06-APR-1999 (101)

Species: rabbit Sex: female
 Strain: other: New Zealand
 Route of admin.: gavage
 Exposure period: day 6 to 18 of gestation
 Frequency of treatment: daily
 Duration of test: up to day 30 of gestation
 Doses: 50, 250, 412, 775, 1137 and 1500 mg/kg bw
 Control Group: yes
 Method:
 Year: GLP: yes
 Test substance: as prescribed by 1.1 - 1.4
 Remark: range-finding study, 5 animals/group

5. TOXICITY

Result: all animals in the 775, 1137 and 1500 mg groups died during treatment, with 250 and 412 mg/kg maternal mortality 20 %, at 50 mg/kg bw no maternal toxicity. No fetotoxicity was evident in the 50, 250 or 412 mg group.

20-JAN-1999 (102)

Species: hen Sex: no data

Strain: no data

Route of admin.: other

Exposure period: single injection in the yolk sac

Frequency of treatment:

Duration of test:

Doses: 5 mg/egg

Control Group: yes

Method:

Year: GLP: no data

Test substance: no data

Remark: post obs. period: 17 days
purity not mentioned

Result: weak effects (decrease of survival, weight and length)

27-JAN-1999 (103)

Species: rat Sex: female

Strain: Sprague-Dawley

Route of admin.: other: oral

Exposure period: day 6 to 15 of gestation

Frequency of treatment: daily

Duration of test: up to day 20 of gestation

Doses: 188, 375, or 750 mg/kg bw

Control Group: yes

NOAEL Teratogen.: > 750 mg/kg bw

Method:

Year: GLP: yes

Test substance: as prescribed by 1.1 - 1.4

Remark: 24 animals/group

Result: in all treatment groups toxicity to dams was produced as evidenced by decrease in absolute body weights and cumulative body weight gains. 29.2 % mortality in the highest dosage group. Treatment related increase in the incidence of delayed skeletal ossification (equivocal biological significance), reduced mean fetal weight in the highest dose group, no teratogenic effects.

20-JAN-1999 (104)

5.10 Other Relevant Information

Type: Cytotoxicity

Remark: Cytotoxicity in vitro: tributyl phosphate inactivate lipid-enveloped viruses, but did not alter the function of serum proteins.

11-SEP-1997 (105)

Type: Cytotoxicity

Remark: Cytotoxic effects in vitro (HeLa cells)

22-JUL-1997

(106)

Type: Metabolism
Remark: rat, single i.p. injection of 1 mmol: decrease of glutathione in liver and kidney; small amounts of oxidized butyl moieties were removed as glutathione conjugates and excreted as S-containing metabolites in urine: (3-oxobutyl)- and (3-hydroxybutyl)mercapturic acids (8.9 and 5.2 % of applied dose), other S-butylmercapturic acid derivatives were found only in traces. After i.p. injection of the probable intermediate dibutyl-hydrogenphosphate, only 0.07 and 0.02 % of the applied dose was eliminated as S-containing metabolites in the urine.

22-JUL-1997

(107)

Type: Metabolism
Remark: (14C-labelled substance was used):
- rat, oral: 14 mg/kg: within 1 day, 50 % were excreted in urine, 10 % in exhaled air and 6 % in feces; total elimination after 5 days 82 %
- rat, i.p.: 14 mg/kg: within 1 day, 70 % were excreted with urine, 7 % with exhaled air and 4 % in feces; total elimination after 5 days 90 %.
- rat, i.p.: 250 mg/kg: 11 phosphorous-containing metabolites in 24-h urine were identified in the neutral and acid fractions with a total recovery of 25 and 12 %. Major metabolites: dibutylhydrogen phosphate(40-64 % of identified dose), butyl dihydrogen phosphate(11-21 % of identified dose), butyl bis (3-hydroxybutyl) phosphate (3-4 % of identified dose) and small amounts of derivatives hydroxylated at the butyl moieties.
1 unidentified neutral metabolite was shown in the gas chromatogram. The butanol-extractable metabolites (25 % of the dose), which were not quantitated, were butyl-3-hydroxybutylphosphat, 3-hydroxybutylphosphat and monobutylphosphat.
47.6 % of dibutyl hydrogenphosphate recovered intact in urine after i.p. infection, therefore the authors concluded that dibutyl hydrogen phosphate produced as an intermediate in the metabolism of tributylphosphate would be mostly excreted. The data after administration of probable metabolic intermediate suggest, that hydroxylation at C-3 is an early metabolic process, which is followed by further metabolic reactions (oxidation to produce carboxylic acids and ketones). The oxo compound (dibutyl 3-oxobutyl phosphate) dibutyl hydrogen phosphate.

04-NOV-1997

(108)

Type: Metabolism
Remark: cholinesterase inhibition: rat, i.p., 16-266 mg/kg bw (0.062-1 mmole/kg): 21 % inhibition of cholinesterase, increased activity of beta-glucuronidase in plasma.

22-JUL-1997

(109)

Type: Metabolism

5. TOXICITY

- Remark: skin of living pigs: hair follicle is not more penetrable than other dermal area; in fact, regions of the skin devoid of follicles were penetrated slightly more rapidly than areas containing follicles.
22-JUL-1997 (110)
- Type: Metabolism
Remark: following single or repeated oral dosing in rats, tributyl phosphate was detected in the gastrointestinal tract, blood and liver (no further data).
22-JUL-1997 (111)
- Type: Metabolism
Remark: tributyl phosphate is metabolized in rodents to butyl-n-cysteine (no further data).
22-JUL-1997 (112)
- Type: Metabolism
Remark: in vitro: rat liver homogenate: rapid metabolism in the presence of NADPH, but only slight breakdown in the absence of added NADPH. Dibutyl(3-hydroxybutyl)phosphate was obtained as a metabolite in the first stage. The extended incubation time yielded two metabolites: butyl di(3-hydroxy- butyl)phosphate and dibutyl hydrogen phosphate.
22-JUL-1997 (113)
- Type: Metabolism
Remark: (14C labelled tributyl phosphate was used):
rat, single i.v. injection of 5 mg/kg;
rat, single dermal application of 10 or 350 mg/kg;
rat, single oral dose of 10 and 350 mg/kg;
rat, multiple oral dose (8x) of 10 or 350 mg/kg:
no adverse signs of toxicity in any low dose group, in all high dose groups red urine and/or hypersalivation, blood in urine in all dose groups. The major proportion of the recoverable radioactivity was eliminated within 48 h in urine and feces. The major route of elimination is via the kidneys (65-85 % of dose after oral and i.v. application). The distribution pattern in the tissues was similar in all dose groups. The HPLC analysis showed 9 major and 6 minor regions of radioactivity in the urine, mass spectrometric analyses revealed monobutylphosphate, dibutylphosphate, butyl-2-hydroxybutyl phosphate and 3-carboxypropyl-dimethylphosphate. The author concluded, that the butyl groups of tributylphosphate are oxidized to alcoholic, ketonic and acetic functionalities. The oxidized chains are also hydrolysed proceeding to the di-, mono- and the unsubstituted phosphoric acids.
04-NOV-1997 (114)
- Type: Neurotoxicity
Remark: hen, oral, two doses of 1500 mg/kg bw (LD50) 21 days apart, killed 21 days after the second dose: no nerve damage or clinical signs of toxicity (purity of test material 98.37%).
--neurotoxicity: hen, single oral dose of 1500 mg/kg bw:

	no relevant inhibition of brain NTE (neurotoxic esterase) or brain acetylcholinesterase, increase of plasma cholinesterase (purity of test material 98.37%).	
22-JUL-1997		(57)
Type:	Neurotoxicity	
Remark:	hen, oral: 1840 mg/kg bw on two days: neither behavioral nor histological evidence of neurotoxicity (no further data).	
22-JUL-1997		(51)
Type:	Neurotoxicity	
Remark:	cholinesterase activity in brain and liver homogenates and serum (rat) after incubation with tributyl phosphate (purity > 97 %): no change of enzyme activity	
22-JUL-1997		(77)
Type:	Neurotoxicity	
Remark:	adult hen, oral or dermal 1500 mg/kg bw at day 0 and 21, observation up to day 42: no signs of neurotoxicity (purity not given).	
22-JUL-1997		(58)
Type:	Neurotoxicity	
Remark:	rat, rabbit: in lethal doses, oral or i.p., decrease of cholinesterase activity in serum, red blood cells, liver and brain of maximum 35 %.	
22-JUL-1997		(52)
Type:	Neurotoxicity	
Remark:	anticholinesterase activity in vitro, human red cell hemolysate or human plasma: slight decrease of cholinesterase activity (purity not mentioned).	
22-JUL-1997		(73)
Type:	Neurotoxicity	
Remark:	range-finding study on motor activity in rats: single oral application of 1000 mg/kg bw, after 0.5 h following dosing, motor activity was tested for 23 hours: one treated female was found dead after 2 days, all treated animals show clinical signs of toxicity, reduced motor activity levels. 4/sex/group purity not known	
22-JUL-1997		(115)
Type:	Neurotoxicity	
Remark:	Neurotoxicity (acute delayed) Hens, single oral dose of 1500 mg/kg with atropine protection. Second TBP dose on day 21. Cholinergic signs including salivation, miosis, and diarrhea. 4 of 20 hens died week 1 and 2, more died on week 2. No ataxia or paralysis. No histopathological lesions.	
23-JUL-1997		(116)
Type:	Neurotoxicity	
Remark:	Result: Not neurotoxic	

- Remarks: Chicken, single 1.84 g/kg oral dose. Repeated dosing at day 21. No signs of neurotoxicity based on locomotor and neuropathology examination.
- 23-SEP-1997 (117)
- Type: Neurotoxicity
 Remark: Species: Sprague-Dawley rat
 Route of admin: gavage
 Exposure period: 13 weeks
 Freq. of treatment: daily
 Post. obs. period: no
 Doses: 32, 100 325 mg/kg bw/day
 Control Group: yes
 Test substance: 99.5 %
 Remark: 12 animals/sex/group
 Result: Mortality, salivation and muzzle staining in the 325 mg group and less severe in the 100 mg group, reduced body weight gain, reduced food intake and initial weight loss in the 325 mg group, qualitative functional observational battery assessment did not reveal any significant finding, for quantitative functional observational battery measurements, there were no toxicologically significant differences. Motor activity test results were not significantly different, no abnormal gross pathology findings, neuropathological assessment revealed no effects of treatment.
- 30-SEP-1997 (118)
- Type: Toxicokinetics
 Remark: Results: Minipig - iv - rapidly eliminated; dermal - poorly absorbed (1-4% excreted); no bioaccumulation in bladder or kidney; metabolism is hydroxylation followed by Phase II (glucuronide, sulfate formation).
- Remarks: iv (5 mg/kg); dermal (10 and 350 mg/kg - 6 hr. exposure)
- 04-NOV-1997 (119)
- Type: other: Neurotoxic esterase
 Remark: Hens, single dose of 1500 mg/kg. No significant change in brain neurotoxic esterase or acetylcholine esterase activity.
- 23-SEP-1997 (120)
- Type: other: Neurotoxicity (acute delayed)
 Remark: Hens, dermal exposure 1500 mg/kg day 0-21. No signs of neurotoxicity. No atropine protection.
- 23-SEP-1997 (120)
- Type: other: Neurotoxicity, acute
 Remark: Results: Not neurotoxic
 Remarks: Rats, doses of 100, 325 and 1000 mg/kg oral. Motor activity and functional observation battery.
- 30-SEP-1997 (121)
- Type: other: Subchronic Dietary Mechanistic Study

- Remark: The dose response of TBP effects on the urinary bladder and on urinary parameters was evaluated in male Sprague-Dawley rats fed 0, 200, 700 and 3000 ppm in the diet. Ten rats per group were exposed for 10 weeks. Another group received 3000 ppm TBP plus 12,300 ppm NH₄Cl. A high dose recovery group (3000 ppm TBP for 10 wks, then 10 wks control diet) was included to evaluate reversibility.
- Results: TBP at doses of 700 and 3000 ppm appears to produce urothelial cytotoxicity with marked regenerative hyperplasia. No changes were noted on urinary parameters, other than a slight decrease in osmolality and creatinine at 3000 ppm. Effects were reversible upon withdrawal of treatment during a 10-week recovery period. The toxicity is likely due to the chemical or metabolites, not to urinary changes. A NOEL of 200 ppm was established for all parameters.
- 28-JUL-1997 (122)
- Type:
Remark: rabbit, i.p.: 100 mg/kg bw single injection: no effect
200 mg/kg bw single injection: lethal after 11 days
rabbit, s.c.: 100 or 200 mg/kg bw: no systemic effects, local inflammatory effects.
- 24-JUL-1997 (67)
- Type:
Remark: no marked difference of LD50 values observed with oral, s.c. or i.p. administration.
- 22-JUL-1997 (54)
- Type:
Remark: rat, single oral, i.p. or i.m. application of 0.1 to 0.2 ml: labored breathing, hypersalivation, pallor; paralysis after parenteral application; no symptoms after dermal application (purity not mentioned).
- 22-JUL-1997 (73)
- Type:
Remark: mice, i.p., 850 - 1000 mg/kg bw: narcosis, muscular paralysis
- 22-JUL-1997 (123)
- Type:
Remark: Reviews:
- Environmental Health Criteria 112, World Health Organization (1991)
- BIBRA Toxicity Profile (1991)
- Berufsgenossenschaft der chemischen Industrie. Toxikologische Bewertung Ausgabe 02/89, Nr. 170 (1989)
- 22-JUL-1997
Type:
Remark: rat: eye and nasal irritation after 1 hour exposure to atmospheric concentrations of 200 mg/l.
- 22-JUL-1997 (124)

5.11 Experience with Human Exposure

Remark:	some decrease in nonspecific esterase staining of monocytes in occupational exposed persons.	
04-NOV-1997		(125)
Remark:	skin penetration in vivo and in vitro: maximum steady state penetration rate 0.18 ug/cm ³ /min.	
22-JUL-1997		(126)
Remark:	workers exposed to 15 mg/m ³ of tributyl phosphate have complained of nausea and headache	
22-JUL-1997		(127)
Remark:	irritant effect on skin and mucous membranes (no further data).	
11-SEP-1997		(128)
Remark:	an abstract of a Soviet paper states that exposure to unspecified quantities during the production of scandium oxide may have been responsible (together with other compounds) for skin rashes in workers (no further information)	
22-JUL-1997		(129)

6. REFERENCES

- (1) Safety Data Sheet Bayer AG 08.09.1987
- (2) ABC Laboratories. Vapor Pressure of Tributyl Phosphate. ABC Project No. 38557. (1990) (At the request of Synthetic Organic Chemical Manufacturers Association Inc.)
- (3) Bayer AG data
- (4) THOR database Pomona 89, MedChem Software 1989. Daylight Chemical Information Systems, Claremont, CA 91711, USA
- (5) Calculation UWS-Produktsicherheit, Bayer AG 1991
- (6) Saeger, V.W. et al., Environ. Sci. Technol. 13 (7), 840-844 (1979)
- (7) Ishikawa, S. et al., Suishitsu Odaku Kenkyo Tokyo 8, 799-807 (1985)
- (8) ABC Laboratories. Hydrolysis of ¹⁴C-Tributyl Phosphate as a Function of pH at 25 degrees C. ABC Lab. Report No. 38559. (at the request of the Synthetic Organic Chemical Manufacturers Association).
- (9) FMC Study No. I90-1176.
- (10) BUA report (in press)
- (11) Monsanto study MO-77-615A. Biodegradation of Phosphate Esters. (1977)
- (12) 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
- (13) Monsanto study MO-77-615. Biodegradation of Phosphate Esters. (1977)
- (14) Monsanto study MO-77-615B. Biodegradation of Phosphate Esters. (1977)
- (15) Sasaki, K. et al., Bull. Environ. Contam. Toxicol. 27, 775-782 (1981)
- (16) 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
- (17) Sasaki, K. et al., Bull. Environ. Contam. Toxicol. 28, 752-759 (1982)

6. REFERENCES

- (18) Kawai, S. et al., Annu. Rep. Osaka City Inst. Public Health Environ. Sci. 49, 160-166 (1986)
- (19) Bowman, J.H. und Schrier, L., Acute Flow-Through Toxicity of Tributyl Phosphate to Rainbow Trout *Oncorhynchus mykiss*. June 21, 1990, ABC Laboratories No. 38552, Columbia, Missouri, USA. (at the request of the Synthetic Organic Chemical Manufacturers Association).
- (20) Dave, G. et al., Toxicity of 8 Solvent Extraction Chemicals and of Cadmium to Water Fleas, *Daphnia Magna*, Rainbow Trout, *Salmo Gairdneri*, and Zebrafish, *Brachydanio Rerio*. Comp. Biochem. Physiol. 69C (1), 83-98 (1981)
- (21) Juhnke, I. und Luedemann, D., Z. Wasser-Abwasser-Forschung 11 (5), 161-164 (1978)
- (22) ABC Laboratories. Acute Toxicity of TBP to Rainbow Trout. Study ID: AB-78-1384337-1d. Monsanto study AB-78-0386. (1978)
- (23) Dave, G. und Lidmann, U., Hydrometallurgy 3, 201-216 (1978)
- (24) ABC Laboratories. Acute Toxicity of TBP to Fathead Minnows. Study ID: AB-78-1384337-1c. Monsanto study AB-78-0386. (1978)
- (25) Dave, G. et al., J. Chem. Technol. Biotechnol. 29 (4), 249-257 (1979)
- (26) Yoshioka, Y. and Ose, Y., Environmental Toxicology and Water Quality: An International Journal 8(1), 87-101 (1993)
- (27) Yoshioka, Y. et al., Ecotox. Environ. Saf. 12 (3), 206-212 (1986)
- (28) Geiger, D.L. et al., Acute Toxicities of Organic Chemicals to Fathead Minnows (*Pimephales promelas*) Volume III. Center of Wisconsin-Superior Environmental Studies, University of Wisconsin-Superior ISBN 0-9614968-2-7 (1986)
- (29) Dave, G. et al., Comp. Biochem. Physiol. 69C (1), 83-98 (1981)
- (30) ABC Laboratories. Acute Toxicity of TBP to *Daphnia Magna*. Study ID: AB-78-1384337-1a. Monsanto study AB-79-0150. (1978)
- (31) Bringmann, G. und Kuehn, R., Z. Wasser-Abwasser-Forschung 15(1), 1-6 (1982)
- (32) Bringmann, G. und Kuehn, R., Z. Wasser-Abwasser-Forschung 10(5), 161-166 (1977)
- (33) Wakabayashi, M. et al., Tokyo-to Kankyo Kagaku Kenyusho Nempo, 126-128 (1988)

6. REFERENCES

- (34) Kuehn, R. et al., UFOPLAN Nr. 106 03 052 des BMU, Maerz 1988
- (35) ABC Laboratories. Acute Flow-Through Toxicity of TBP to *Daphnia Magna*. ABC Report No. 38553. (at the request of the Synthetic Organic chemical Manufacturers Association).
- (36) England, D.C. und Cramer, D., Acute Flow-Through Toxicity Exposure of Tributyl Phosphate to *Gammarus pseudolimnaeus*. September 23, 1991, ABC Laboratories No. 39499, Columbia, Missouri, USA. (at the request of the Synthetic Organic Chemical Manufacturers Association).
- (37) England, D.C. und Schrier, L., Acute Flow-Through Toxicity of Tributyl Phosphate to the Gammarid *Hyaella azteca*. June 18, 1990, ABC Laboratories No. 38555, Columbia, Missouri, USA. (at the request of the Synthetic Organic Chemical Manufacturers Association).
- (38) Bringmann, G. und Kuehn, R., Mitt. Internat. Verein. Limnol. 21, 275-284 (1978)
- (39) Bringmann, G. und Kuehn, R., Mitt. Internat. Verein. Limnol. 21, 275-284 (1978) and
Bringmann, G. und Kuehn, R., Z. Wasser-Abwasser-Forschung 10 (3/4), 87-89 (1997)
- (40) Kuehn, R. und Pattard, M., Water Research 24 (1), 31-38 (1990)
- (41) Burgess, D. und Wirth, J.N., Acute Toxicity of Tributyl Phosphate to *Selenastrum capricornutum* Printz. June 21, 1990, ABC Laboratories No. 38554, Columbia, Missouri, USA (at the request of the Synthetic Organic Manufacturers Association).
- (42) Blanck, H. et al., Ecotox. Environ. Saf. 8, 339-351 (1984)
- (43) Bringmann, G. und Kuehn, R., Z. Wasser-Abwasser-Forschung 10 (3/4), 87-89 (1977)
- (44) ABC Laboratories, Inc., Early Life-Stage Toxicity of Tributyl Phosphate to Rainbow Trout (*Oncorhynchus mykiss*) in a Flow-Through System, Project No. 38550, December 19, 1991 (at the request of the Synthetic Organic Chemical Manufacturers Association)
- (45) ABC Laboratories, Inc., Chronic Toxicity of Tributyl Phosphate (TBP) to *Daphnia magna* Under Flow-Through Test Conditions, Project No. 38556, September 18, 1991 (at the request of the Synthetic Organic Chemical Manufacturers Association).
- (46) IPC-Environmental Health Criteria 112, p. 40, Tri-n-butyl phosphate, WHO, Geneva 1991

6. REFERENCES

- (47) Bringmann, G. und Kuehn, R., gwf-wasser/abwasser 122, 308-313 (1981)
- (48) Ramm: Bayer AG data: Untersuchung zur akuten oralen Toxizitaet an maennlichen und weiblichen Wistar-Ratten, April 9 (1986)
- (49) Eastman Kodak Co. data from 1959 and 1968, NTIS Doc. No. 86860000118, Michrofiche OTS0510265 (1986)
- (50) Smyth & Carpenter; J. Ind. Hyg. Toxicol. 26, 269-273 (1944)
- (51) Johannsen et al., Toxicol. Appl. Pharmacol. 41, 291-304 (1977)
- (52) Kalinina, Gig. Tr. Prof. Zabol. 15, 30-33 (1971)
- (53) Mitomo et al., J. Tox. Sci. 5, 270-271 (1980)
- (54) Mitomo et al., J. Tox. Sci 5, 270-271 (1980)
- (55) Enslein, K. et al.: QSAR envir. Toxic. Proc. 11, 91 (1987) cited in BIBRA Toxicity Profile (1991)
- (56) Mac Kellar, D.G.: Food and Drug Research Lab., Report No. ICD/T-76-16, January 30 (1976) at the request of FMC
- (57) Carrington et al., Toxicol. Ind. Hyg. 6, 415-423 (1989)
- (58) Monsanto Comp. data, TSCA 8d submission 86860000103 (1986) cited in Chem. Reg. Reporter 11-13-87, 1244-1322 (1987)
- (59) Fassett & Irish (ed.), Patty's Industrial Hygiene and Toxicology, sec. ed. (1963)
- (60) FMC Corp. data (1976), EPA OTS 86860000114 cited in BIBRA Toxicity Profile (1991)
- (61) Bayer AG data, Report No. 19466, August 30 (1990)
- (62) FMC Corp. Data, TSCA 8d Submission 86860000116 (1976) cited in Chem. Reg. Reporter 11-13-87, 1244-1322 (1987) and cited in BIBRA Toxicity Profile (1991).
- (63) Eller, H.; Dissertation: Beitrag zur Toxikologie Technischer Weichmacher (1937)
- (64) Rohm & Haas Comp. data, FYI-OTS-0385-0380 (1985) cited in Chem. Reg. Reporter 11-13-87, 1244-1322 (1987)
- (65) Vandekar, M., Nature 179, 154-155 (1957)
- (66) Bayer AG data, Report No. 14478, March 26 (1986)
- (67) I.G.W. Elberfeld data, August 1936

6. REFERENCES

- (68) FMC Corp. data, TSCA 8d submission 86860000107 (1981) cited in Chem. Reg. Reporter 11-13-87, 1244-1322 (1987)
- (69) FMC Corp. data prepared for the US EPA (1985) cited in Environmental Health Criteria 112, World Health Organization (1991)
- (70) Dow Chemical Co. data, EPA OTS 86860000127 (1956) cited in BIBRA Toxicity Profile (1991)
- (71) MacKellar, D.G.: Food and Drug Research Lab., Report No. ICD/T-76-16, January 30 (1976) at the request of FMC
- (72) Du Pont, E.I. du Pont de Nemours & Co. data, EPA OTS 86860078 (1953) cited in BIBRA Toxicity Profile (1991)
- (73) Sabine & Hayes; Arch. Ind. Hyg. Occup. Med. 6, 174-177 (1952)
- (74) FMC Corp. data, Study no. I89-1102, March 12 (1990) (at the request of Synthetic Organic Chemical Manufacturers Association)
- (75) Monsanto Chemical Comp. data (1980), submitted to the US EPA cited in BIBRA Toxicity Profile (1991)
- (76) Cascieri et al. Subchronic Toxicity Study with Tributyl Phosphate in Rats. Toxicologist 5, 97 (1985) and

FMC Corp. data (1985) EPA OTS 86860000106 cited in BIBRA Toxicity Profile (1991)
- (77) Oishi et al.; Toxicology Lett. 6, 81-85 (1980)
- (78) Oishi et al.; Toxicology Lett. 13, 29-34 (1982)
- (79) Laham et al., J. Appl. Toxicol. 4, 150-154 (1984)
- (80) Laham et al., Arch. Environ. Health 40, 301-306 (1985) and

Laham et al., Toxicologist 4, 139 (1984)
- (81) Laham et al., Drug Chem. Toxicol. 6, 363-377 (1983)
- (82) Bio/dynamics Inc. 1990. A Four-week Range-finding Study of Tributyl Phosphate in the Mouse via Dietary Administration. Project No. 89-3530. December 20, 1990. (at the request of the Synthetic Organic Chemical Manufacturers Association)
- (83) Biodynamics Inc. data, Project No. 89-3531, July 29 (1991) (at the request of Synthetic Organic Chemical Manufacturers Association) and

Auletta, C.S., W.L. Wooding, and L.A. Kotkoskie. (1997). Subchronic Dietary Toxicity Study with Tributyl Phosphate in the Mouse. Fund. Appl. Toxicol. Suppl. The Toxicologist 36, No. 1, 173.

6. REFERENCES

- (84) Pupysheva, G.J. & Peresedov, V.P. (1970) cited in Berufsgenossenschaft der chemischen Industrie. Toxikologische Bewertung Ausgabe 02/89, Nr. 170 (1989)
- (85) Zyabbarova & Teplyakova (1968) cited in Berufsgenossenschaft der chemischen Industrie. Toxikologische Bewertung Ausgabe 02/89, Nr. 170 (1989)
- (86) Watanabe, K. Sakamoto, K and Sasaki, T. (1996). Comparisons on chemically-induced mutagenicity among four bacterial strains, Salmonella typhimurium TA102 and TA2638, and Escherichia coli WP2/pKM101 and WP2 uvrA/pKM101: Collaborative study. Mutation Research 361, 143-155.
- (87) Bayer AG data, Report No. 13805, September 10 (1985)
- (88) Hanna & Dyer, Mutat. Res. 28, 405-420 (1975)
- (89) FMC Corp. (1978), EPA OTS 86860000112 cited in BIBRA Toxicity Profile (1991) and cited in Chem. Reg. Reporter 11-13-87, 1244-1322 (1987)
- (90) Gafieva, Z.A. and Chudin, V.A.: Gig. Sanit 9, 81 (1986)
- (91) Blevins, R.D.: Envir. Mutagen. 9, 17 (1987) cited in BIBRA Toxicity Profile (1991) and
Pancorba, O.C. et al.: Arch. Envir. Hyg. ASS. J. 41, 220 (1980) cited in BIBRA Toxicity Profile (1991)
- (92) Microbiological Associates Inc., Chromosome Aberrations in chinese Hamster Ovary (CHO) Cells, Study No. T9145.337, July 17 (1990) (at the request of Synthetic Organic Chemical Manufacturers Association Inc.). and
Batt, K.J., Healy, C.E., Kniess, J.J., Putnam, D.L., Jacobson-Kram, D., Weiner, M.L., Fletcher, M.J. (1992). Genotoxicity Testing of Tributyl phosphate. 23rd Scientific Meeting of the Environmental Mutagen Society, March 15-19, 1992.
- (93) Mueller et al.; Health Physics 53, 667-671 (1987)
- (94) Microbiological Associates Inc., CHO/HGPRT Mutation Assay. Study No. T9145.332, July 18 (1990) (At the request of Synthetic Organic Chemical Manufacturers Association Inc.). and
Batt, K.J., Healy, C.E., Kniess, J.J., Putnam, D.L., Jacobson-Kram, D., Weiner, M.L., and Fletcher, M.L. (1992). Genotoxicity testing of tributyl phosphate, 23rd Scientific Meeting of the Environmental Mutagen Society, March 15-19, 1992.
- (95) Microbiological Assoc. data, Project No. T9145.105011, August 20 (1991) (At the request of Synthetic Organic Chemical Manufacturers Association Inc.) and

6. REFERENCES

- Batt, K.J., Healy, C.E., Kniess, J.J., Putnam, D.L., Jacobson-Kram, D., Weiner, M.L., and Fletcher, M.L. (1992). Genotoxicity of tributyl phosphate, 23rd Scientific Meeting of the Environmental Mutagen Society, March 15-19, 1992.
- (96) Auletta, C.S., Weiner, M.L., and Richter, W.R. (1998). A Dietary Oncogenicity Study of Tributyl Phosphate in the Rat. *Toxicology* 128, 125-134. and
Pharmaco. 1994. An Oncogenicity Study of Tributyl Phosphate in the Rat Via Dietary Administration. Bio/Dynamics Inc. East Millstone, NJ. Project No. 89-3533.
- (97) Auletta, C.S., Kotkoskie, L.A., Saulog, T., and Richter, W.R. (1998). A Dietary Oncogenicity Study of Tributyl Phosphate in the Mouse. *Toxicology* 128, 135-141. and
Pharmaco. 1994. An Oncogenicity Study of Tributyl Phosphate in the Mouse Via Dietary Administration. Project No. 89-3532. (at the request of Synthetic Organic Chemical Manufacturers Association Inc.)
- (98) Research Triangle Institute, Project No. 60C-4652, August 10 (1992) (at the request of the Synthetic Organic Chemical Manufacturers Association) and
Tyl, R.W., Gerhart, J.M., Myers, C.B., Marr, M.C., Brine, D.R., Seely, J.C., Henrich, R.T. (1997). Two Generation Reproductive Toxicity Study of Dietary Tributyl Phosphate in CD Rats. *Fund. Appl. Toxicol.* 40, 90-100.
- (99) Biodynamic Inc., Project No. 89-3534, January 24 (1991) (at the request of the Synthetic Organic Chemical Manufacturers Association Inc.)
- (100) Noda, T. Yamano, T. Shimizu, M and S. Morita. (1994). Effects of Tri-n-Butyl Phosphate on Pregnancy in Rats. *FD. Chem. Toxic.*, 32, No.11, 1031-1036.
- (101) Biodynamic Inc., A Developmental Toxicity Study in Rabbits with Tributyl Phosphate. Project No. 89-3537, January 24 (1991) (at the request of Synthetic Organic Chemical Manufacturers Association Inc.). and
Schroeder, R.E., Gerhart, J.M. and Kneiss, J. (1991). Developmental Toxicity studies of Tributyl Phosphate (TBP) in the Rat and Rabbit. *Teratology* 43, 455.
- (102) Biodynamic Inc., A Range-Finding Study to Evaluate the Toxicity of Tributyl Phosphate in the Pregnant Rabbit. Project No. 89-3536, January 24 (1991) (at the request of Synthetic Organic Chemical Manufacturers Association Inc.).
- (103) Roger et al.; *Biochem. Pharmacol.* 18, 373-392 (1969)

6. REFERENCES

- (104) Biodynamic Inc., A Developmental Toxicity Study in Rats with Tributyl Phosphate, Project No. 89-3535, January 24 (1991) (at the request of the Synthetic Organic Chemical Manufacturers Association Inc.) and
- Schroeder, R.E., Gerhart, J.M. and Kneiss, J. (1991). Developmental Toxicity Studies of Tributyl Phosphate (TBP) in the Rat and Rabbit. *Teratology* 43, 455.
- (105) Claeys et al., *Med. Hypoth.* 27, 145-146 (1988) and
- Edwards et al., *Vox Sang.* 52, 53-59 (1987) and
- Michalski et. al., *Vox Sang* 55, 202-210 (1988)
- (106) Ekwall, B. et al.: *Toxicology* 24, 199-210 (1982)
- (107) Suzuki et al.; *J. Agric. Food Chem.* 32, 1278-1283 (1984)
- (108) Suzuki et al.; *J. Agric. Food Chem.* 32, 603-610 (1984)
- (109) Suzuki et al.; *J. Pharm.* 26, 881-885 (1977)
- (110) La Du, B.N. et al.: *Fundamentals of drug metabolism and drug disposition.* Williams & Wilkins Co., Baltimore (1971)
- (111) Khalturin, G.V. and Androyushkeeva, N.I.: *Gig i. Sanit.* 2, 87 (1986) cited in *Environmental Health Criteria 112*, World Health Organization (1991)
- (112) Jones, A.R.: *Experienta* 26, 492-493 (1970) cited in *Environmental Health Criteria 112*, World Health Organization (1991)
- (113) Sasaki, K. et al.: *Bull. environ. Contam. Toxicol.* 33, 281-288 (1984) cited in *Environmental Health Criteria 112*, World Health Organization (1991)
- (114) Midwest Research Institut, MRI Project 9526-F, Preliminary report, October 22, 1992 (at the request of Synthetic Organic Chemical Manufacturers Association)
- (115) Bio Research Lab. data, Project No. 97053, August 9 (1991) (at the request of Synthetic Organic Chemical Manufacturers Association)
- (116) Carrington, C.D., Lapadula, D.M., Othman, M., Farr, C., Nair, R.S., Johannsen, F., and Abou-Donia, M.B. (1990). Assessment of delayed neurotoxicity of tributylphosphate, tributoxyethylphosphate, and dibutylphenylphosphate., *Toxicol. Ind. Health* 6, 415-432. Monsanto study DU-84-433.
- (117) Industrial Bio-Test Lab. Neurotoxicity Study with TBP in Chickens. Study ID: J2157. Monsanto Study BT-72-70.

6. REFERENCES

- (118) Healy, C.E., Beyrouy, P.C., and Broxup, B.R. (1995). Acute and subchronic neurotoxicity studies with tri-n-butyl phosphate in adult Sprague-Dawley rats. *AIHAJ.*, 56:349-355 and
Beyrouy, P., Washer, G., Noveroske, J.W. 1991. A 3-Month Study of the Potential Effects of Orally Administered Tributyl Phosphate on Behavior and Neuromorphology in Rats. Bio Research Laboratories LTD. Canada. Project No. 97045 (at the request of Synthetic Organic Chemical Manufactures association)
- (119) Metabolism of Tributyl Phosphate in Yucatan Minipigs following Intravenous and Dermal Exposure: Part II MRI 12/18/92; 4/14/94 9526 - F(02); 9526-02 (at the request of the Synthetic Organic Chemical Manufacturers Association Inc.)
- (120) Carrington, C.D. Lapadula, D.M., Othman, M., Farr, C., Nair, R.S., Johannsen, F., and Abou-Donia, M.B. (1990). Assessment of delayed neurotoxicity of tributylphosphate, tributoxyethylphosphate, and dibutylphenylphosphate., *Toxicol. Ind. Health* 6, 415-423. and
Duke University Medical Center. Studies in the Delayed Toxicity of TBP. Monsanto Study DU-84-433. (1984)
- (121) Healy, C.E., Beyrouy, P.C., and Broxup, B.R. (1995). Acute and subchronic neurotoxicity studies with tri-n-butyl phosphate in adult Sprague-Dawley rats. *AIHA J.*, 56: 349-355. and
Bio Research Lab., An acute study of the potential neurotoxic effects of tributyl phosphate in rats. Project No. 97044, December 20, 1990 (at the request of Synthetic Organic chemical Manufacturers Association).
- (122) Arnold, L.A., Cohen, S.M., Christensen, R., Cano, M., St. John, H., and Wahle, B.S. (1997). Tributyl Phosphate (TBP) Effects on Urine and Bladder Epithelium in Male Sprague-Dawley Rats. *Fund. Appl. Toxicol. Suppl. The Toxicologist* 36, No. 1, 173.
- (123) Chambers & Casida; *Tox. Appl. Pharm.* 10, 105-118 (1967)
- (124) FMC Corp. data (1976), EPA OTS 86860000116 cited in BIBRA Toxicity Profile (1991)
- (125) Mandel et al., *Am. J. Ind. Med.* 15, 207-212 (1989)
- (126) Marzulli, et al., *J. Invest. Derm.* 44, 339-341 (1965)
- (127) Mastromateo, E.; Personal communication to TLV Committee (1964) cited in ACGIH, Documentation of TLV values (1980=

6. REFERENCES

- (128) Anon.: Pestic. toxic. Chem. News 14, 24 (1986) cited in
BIBRA Toxicity Profile (1991) and

Stauffer, 1984 cited in environmental Health Criteria 112,
Worlds Health Organization (1991)
- (129) Feigein, B.G.: Gig. Tr. Prof. Zabol. 4, 39 (1985) cited in
Chem. Abst. 1985, 102, 225323g, cited in BIBRA Toxicity
Profile (1991)

**Robust Summary
for
Tributyl Phosphate**

MELTING POINT

TEST SUBSTANCE

Tributyl phosphate

METHOD

Guideline Followed OECD Guideline 102

Test Type: Melting Point Determination

GLP: Unknown

Year: 1987

Remarks: The melting point of tributyl phosphate was reported by Bayer AG on their 1987 MSDS to be -70°C.

Conclusion: The melting point was determined to be -70°C.

Data Quality: Reliable without restriction. Key study.

Reference: Bayer AG MSDS dated September 8, 1987.

**Robust Summary
for
Tributyl Phosphate**

BOILING POINT

TEST SUBSTANCE

Tributyl phosphate

METHOD

Guideline Followed: OECD Guideline 103

Test Type: Boiling Point Determination

GLP: Unknown

Year: 1987

Remarks: The boiling point of tributyl phosphate was reported by Bayer AG on their 1987 MSDS to be 130°C @ 5 hPa.

Conclusion: The boiling point was determined to be 130°C @ 5 hPa.

Data Quality: Reliable without restriction. Key study.

Reference: Bayer AG MSDS dated September 8, 1987.

**Robust Summary
for
Tributyl Phosphate**

VAPOR PRESSURE

TEST SUBSTANCE

Tributyl phosphate

METHOD

Guideline Followed U.S. EPA Guideline 796.1950

Test Type: Vapor Pressure Determination

GLP: Yes

Year: 1990

Remarks: The vapor pressure of tributyl phosphate was determined at 25°C using the gas saturation technique. The average vapor pressure at 25°C was determined by averaging the results of three separate tests using high (about 10 ml/minute) and low (about 5 ml/minute) flow rates.

Results: The results of the analyses gave a mean vapor pressure for tributyl phosphate at at 25°C of 0.00000346 hPa (2.6×10^{-6} mm Hg).

Conclusion: Vapor pressure was determined to be: 0.00000346 hPa (2.6×10^{-6} mm Hg).

Data Quality: Reliable without restriction. Key study.

Reference: ABC Laboratories, Inc., Vapor Pressure of Tributyl Phosphate. Study conducted for SOCMA TBP Task Force, 1990.

**Robust Summary
for
Tributyl Phosphate**

OCTANOL/WATER PARTITION COEFFICIENT

TEST SUBSTANCE

Tributyl phosphate

METHOD

Guideline Followed U.S. EPA Guideline 796.1550

Test Type: Octanol/Water Partition Coefficient, Shake Flask Method

GLP: No

Year: 1979

Remarks: The octanol/water partition coefficient was measured for two concentrations of tributyl phosphate. The test material was placed in 100 ml of 1-octanol, which was then added to 500 ml of purified water which was shaken for 48 hours. The mixture was then held for one week in a separatory funnel, after which aliquots of the aqueous phase were removed and extracted twice with methylene chloride. The extracts were analyzed for tributyl phosphate using gas chromatography.

Results: The octanol/water partition coefficient for tributyl phosphate was determined to be Log Kow = 4

Conclusion: Octanol/Water Partition Coefficient: Log Kow = 4

Data Quality: Reliable without restriction. Key study.

Reference: Saeger, V., Hicks, O., Kaley, R., Paul, M., Mieure, J. and Tucker, E. Environmental Fate of Selected Phosphate Esters. Environmental Science & Technology 13:840-844, 1979.

**Robust Summary
for
Tributyl Phosphate**

WATER SOLUBILITY

TEST SUBSTANCE

Tributyl phosphate

METHOD

Guideline Followed OECD Guideline 105

Test Type: Water Solubility Determination

GLP: Unknown

Year: 1987

Remarks: The water solubility of tributyl phosphate was reported by Bayer AG on their 1987 MSDS to be 0.4 g/l @ 20°C.

Conclusion: The water solubility was determined to be 0.4 g/l @ 20°C.

Data Quality: Reliable without restriction. Key study.

Reference: Bayer AG MSDS dated September 8, 1987.

**Robust Summary
for
Tributyl Phosphate**

PHOTODEGRADATION

TEST SUBSTANCE

Tributyl phosphate

METHOD

Guideline Followed Unknown

Test Type: Degradation by UV Light

GLP: Unknown

Year: 1985

Remarks: The stability of tributyl phosphate was determined in the presence of Ultraviolet light using low and high pressure mercury lamps. The exposure period was one hour.

Results: The photodegradation was 85% after 1 hour.

Conclusion: Under UV light, tributyl phosphate degrades about 85% in 1 hour.

Data Quality: Reliable with restriction. Key study.

Reference: Ishikawa, S., Yasuda, K., Shigezumi, K., and Shigemori, N. Behaviors of organophosphate esters in several water treatment processes. Suishitsu Odaku Kenkyo Tokyo 8:799-807, 1985.

**Robust Summary
for
Tributyl Phosphate**

STABILITY IN WATER

TEST SUBSTANCE

Tributyl phosphate, Lot #9B125, with a purity of 99.7%, was obtained from FMC Corporation
¹⁴C-Tributyl phosphate, with a purity of 97.6%, was obtained from Wizard Laboratories

METHOD

Guideline Followed EPA Guideline 796.3500

Test Type: Hydrolysis as a function of pH

GLP: Yes

Year: 1990

Remarks: A 30 day hydrolysis study was conducted in buffered solutions at pH 3, 7, and 11 under dark conditions at 25°C. The test substance was radiolabeled with ¹⁴C. The test solutions were prepared at a nominal concentration of 10 ppm. Duplicate test samples were collected and analyzed after days 0, 1, 7, 14, 22, and 30 days. The samples were analyzed for total radioactivity using liquid scintillation counting and for degradation of tributyl phosphate with thin layer chromatography (TLC). A 1 ml subsample from each of the 30 day samples was analyzed for microbial activity. The half life of the test substance was calculated at the 3 pH.

Results: The radioactivity in all of the samples was shown to be greater than 90% tributyl phosphate. Unknown products were detected at insignificant levels and appears constant at all time points and pH. No microbial contamination was observed in any of the samples. There was no evidence of significant hydrolytic degradation of tributyl phosphate at any of the 3 pH. The substance proved stable at all 3 pH and a decline curve could not be established for any of the buffered systems. The ¹⁴C mass balance ranged from 101.9% to 116.0% of the initial test solution with a mean of 108%. THC plate recoveries ranged from 67.5% to 96.4% with a mean recovery of 85.6%.

Conclusion: Tributyl phosphate was hydrolytically stable at pH 3, 7, and 11.

Data Quality: Reliable without restriction. Key study.

**Robust Summary
for
Tributyl Phosphate**

STABILITY IN WATER

Page 2

Reference: Wildlife International Ltd. Report no. 38559 entitled, Hydrolysis of ¹⁴C-Tributyl Phosphate as a Function of pH at 25°C. Study conducted for the SOCMA TBP Task Force, 1990.

**Robust Summary
for
Tributyl Phosphate**

BIODEGRADATION

TEST SUBSTANCE

Tributyl phosphate

METHOD

Guideline Followed OECD Guideline 301E

Test Type: Ready Biodegradability: Modified OECD Screening Test

GLP: No

Year: 1985

Remarks: Domestic activated sludge from a sewage treatment plant was placed in glass vessels with 1.5 liters of operating volume. Tributyl phosphate was added to vessels in the amount of either 3 or 13 mg/l and stirred with magnetic stirrers for 24 hour cycles, for up to 21 weeks. To measure degradation, a sample was drawn from each vessel immediately after mixing the samples and again once a week. The tributyl phosphate was extracted with hexane and quantified using gas chromatography. The efficiency of the extraction and analytical methods was determined prior to the conduct of the experimental part of the study. To confirm that the biodegradation was more than a slight modification of the parent molecule, a CO₂ evolution study was conducted. By measuring the amount of carbon dioxide produced and comparing that to the theoretical yield based on carbon content and weight of the ester, an indication of the total biodegradation of the molecule was obtained. The evolution study utilized 19.4 mg tributyl phosphate per liter of incubate.

Results: The activated sludge biodegraded tributyl phosphate, when added at the rate of 3 mg/l, 96% in 13 weeks. When added at 13 mg/l, the biodegradation was 56% ± 21% in 21 weeks. In the CO₂ evolution study, the % of the theoretical carbon dioxide was 30.4% in 7 days and 90.8% in 28 days, confirming the molecule is completely biodegraded.

Data Quality: Reliable with restriction. Key study.

Reference: Saeger, V., Hicks, O., Kaley, R., Mieure, J., and Tucker, E. Environmental Fate of Selected Phosphate Esters. Environmental Science & Technology 13:840-44, 1979

**Robust Summary
for
Tributyl Phosphate**

DISTRIBUTION (FUGACITY)

TEST SUBSTANCE

Tributyl phosphate

METHOD

Guideline Followed: No Guideline Available

Test Type: Mackay Level III Model

GLP: No

Year: 2001

Remarks: The distribution of tributyl phosphate was estimated using the Mackay Level III Model. The input values used in the model are as follows:

Molecular Weight: 266.32
 Water Solubility: 0.4 g/l at 20 degrees C
 Vapor Pressure: 0.000347 Pa at 25 degrees C
 Log Kow: 4
 Melting Point: -70 degrees C

Results:

<u>Emissions</u>	<u>Percent Distribution In</u>			
	<u>Air</u>	<u>Water</u>	<u>Soil</u>	<u>Sediment</u>
Air only – 1000 kg/hour	0.67	<0.3	99	0
Water only – 1000 kg/hour	0	63	23	14
Soil only – 1000 kg/hour	0	0	100	0
Combined – 1000 kg/hour (air, water, and soil compartments)	0	1	99	0

Data Quality: Reliable without restriction. Key study.

Reference: Level III Fugacity-Based Environmental Equilibrium Model, Trent University, 1999, based on Mackay, Donald, Multimedia Environmental Models: The Fugacity Approach, Lewis Publishers, CRC Press, Boca Raton, 1991

**Robust Summary
for
Tributyl Phosphate**

ACUTE TOXICITY TO FISH

TEST SUBSTANCE

Tributyl phosphate, lot number 9B125, 99.7% pure, was provided by FMC Corporation.

METHOD

Guideline Followed: U.S. EPA 40 CFR 797 Guideline 797.1400

Test Type: Acute 96-hour flow-through toxicity test of tributyl phosphate to the rainbow trout (*Oncorhynchus mykiss*)

GLP: Yes

Year: 1990

Species/Strain/Supplier: Rainbow trout (*Oncorhynchus mykiss*), Mt. Lassen Trout Farm, Red Bluff, California

Analytical Monitoring: Yes

Exposure Period: 96 Hours

Statistical Methods: Stephan et al. LC50 program, U.S. EPA, 1985.

Remarks: One hundred and forty fish were divided into groups of 10 fish per vessel. They had a mean weight of 0.91 grams and a mean standard length of 41 mm when measured at the end of the test. A proportional dilution system was used to introduce tributyl phosphate solutions into the flow-through system. The test substance was diluted with dimethylformamide (DMF) to achieve nominal concentrations of 1.3, 2.5, 5.0, 10, and 20 mg/l. The solvent control group received 0.1 ml/l of DMF. Two replicate vessels per dose group were used (20 fish per dose). Temperature, dissolved oxygen and pH were measured at 0, 48, and 96 hours. The concentration of the test substance was measured in the vessels at 0, 48, and 96 hours. The test substance samples were analyzed using gas-liquid chromatography and a nitrogen phosphorus detector.

Results: Water conditions determined during the conduct of this test were: hardness, 44-46 mg/l as CaCO₃, alkalinity, 58 mg/l as CaCO₃, pH 7.4-7.8, and total organic carbon, < 1 mg/l. The mean measured concentrations of tributyl phosphate were

**Robust Summary
for
Tributyl Phosphate**

ACUTE TOXICITY TO FISH

Page 2

1.2, 2.1, 4.3, 9.3, and 19 mg/l which yielded about 90% of the nominal target concentrations. Measurements of tributyl phosphate in the diluter stock solutions showed the chemical to very stable for the duration of the test. The temperature was maintained at 13°C and the dissolved oxygen was 8.2 to 9.0 mg/l. The 24, 48, and 96 hour LC50 was determined to be 13 mg/l. Complete mortality was observed at the dose of 19 mg/l. There was no mortality in the lower dose groups. Sublethal behavioral effects were observed in the 9.3 mg/l dose group as loss of equilibrium, erratic swimming, labored respiration, quiescence, and surfacing. The no-observable-effect level (NOEL) was determined to be 4.3 mg/l.

Conclusion: The measured 96-hour LC50 concentration to rainbow trout is 13 mg/l.

Data Quality: Reliable without restriction. Key study.

Reference: ABC Laboratories, Inc., Acute Flow-through Toxicity of Tributyl Phosphate To Rainbow Trout (*Oncorhynchus mykiss*). Study conducted for SOCMA TBP Task Force, 1990.

**Robust Summary
for
Tributyl Phosphate**

ACUTE TOXICITY TO AQUATIC INVERTEBRATES

TEST SUBSTANCE

Tributyl phosphate, lot number 9B125, 99.7% pure, was provided by FMC Corporation.

METHOD

Guideline Followed: U.S. EPA 40 CFR 797 Guideline 797.1300

Test Type: Acute 48-hour flow-through toxicity test of tributyl phosphate to *Daphnia magna*

GLP: Yes

Year: 1990

Species/Strain/Supplier: *Daphnia magna* obtained from an in-house daphnid culture maintained at ABC Laboratories since 1977.

Analytical Monitoring: Yes

Exposure Period: 48 Hours

Statistical Methods: Stephan et al. EC50 program, U.S. EPA, 1985.

Remarks: The test system consisted of seven sets of four replicate one liter test chambers, each containing five daphnids. The seven sets were identified as either the negative control, solvent control, or one of the five dose levels of tributyl phosphate. The test substance was diluted with the solvent dimethylformamide (DMF) to achieve nominal test concentrations of 0.48, 0.96, 2.0, 4.0, and 8.0 mg/l. The concentration of tributyl phosphate was measured at 0, 24, and 48 hours. The load factor was about 1 daphnid per 200 ml water. Water quality measurements were made for the water used in the study. The solvent control group received 0.1 ml/l of DMF. Temperature, dissolved oxygen and pH were measured at 0, 24, and 48 hours. The test chambers were maintained at 20°C. The concentration of the test substance was measured at 0, 24, and 48 hours. The water samples containing the test substance were analyzed using gas-liquid chromatography and a nitrogen phosphorus detector.

Results: Water conditions determined during the conduct of this test were: hardness, 174-178 mg/l as CaCO₃, alkalinity, 200-202 mg/l as CaCO₃, pH 8.2-8.4, and total organic

**Robust Summary
for
Tributyl Phosphate**

ACUTE TOXICITY TO AQUATIC INVERTEBRATES

Page 2

carbon, < 1 mg/l. The light cycle was 16 hours on, 8 hours off, with 30 minute transition periods. The mean measured concentrations of tributyl phosphate at 0, 24, and 48 hours were 0.32, 0.75, 1.8, 3.5, and 7.8 mg/l. These results yielded an average of $84 \pm 12\%$ of the nominal target concentrations of 0.48, 0.96, 2.0, 4.0, and 8.0 mg/l. The 4, 24, and 48 hour EC50 values were >7.8, >7.8, and 2.6 mg/l, respectively. The no observable effect concentration based on lack of immobility and other abnormal signs was 0.75 mg/l at 48 hours. One mortality was observed in the solvent control during this study. The dissolved oxygen concentration during the study was 8.7 to 8.9 mg/l, which were considered adequate and no supplemental aeration was necessary. Measurements of tributyl phosphate in the diluter stock solutions showed the chemical to very stable for the duration of the test.

Conclusion: The measured 48-hour EC50 concentration to the daphnid is 2.6 mg/l (95% confidence limits of 2.2 and 3.1) and the no observable effect level is 0.75 mg/l.

Data Quality: Reliable without restriction. Key study.

Reference: ABC Laboratories, Inc., Acute Flow-through Toxicity of Tributyl Phosphate To *Daphnia magna*. Study conducted for SOCMA TBP Task Force, 1990.

**Robust Summary
for
Tributyl Phosphate**

ACUTE ORAL TOXICITY

TEST SUBSTANCE

Tributyl phosphate, lot number 3471, > 99% pure, was provided by Stauffer Chemical Co.

METHOD

Guideline Followed Acute Oral Toxicity Test Guideline

Test Type: Acute Oral Toxicity Test in Rats

GLP: No

Year: 1973

Species/Strain: Sprague-Dawley Rats

Analytical Monitoring: No

Exposure Period: Single Exposure

Statistical Methods: Not identified

Remarks: Five male Sprague-Dawley rats, weighting from 210 to 230 grams, were assigned to each of four dose groups. The doses administered were 464, 1000, 2150, and 4640 mg/kg. Each animal received a single oral dose by gavage. The animals were observed daily for clinical signs of toxicity for 14 days after treatment. All animals underwent necropsy and gross examination.

Results: All 5 animals in the high dose group died by study day four. There was no mortality in any of the other 3 treatment groups. Clinical signs included slight to severe depression and excessive urination. No treatment-related gross lesions were found at necropsy. The acute oral LD50 in male rats was determined to be 3160 mg/kg with confidence limits of 2150-4639.

Conclusion: The acute oral LD50 in male rats is 3160 mg/kg (2150-4639)

Data Quality: Reliable with restriction. Female animals not used. Documentation weak.

Reference: Stauffer Chemical Company study no. T-4245, 1973.

**Robust Summary
for
Tributyl Phosphate**

REPEATED DOSE TOXICITY IN MAMMALS

TEST SUBSTANCE

Tributyl phosphate, lot number 2B-131, > 99% pure, was provided by FMC Corporation.

METHOD

Guideline Followed U.S. EPA TSCA Subchronic Oral Toxicity Test Guideline

Test Type: Thirteen Week Oral (Dietary) Study in Rats

GLP: Yes

Year: 1985

Species/Strain/Supplier: Sprague-Dawley Rats from Taconic Farms, Germantown, NY

Analytical Monitoring: Yes

Exposure Period: 13 Weeks

Statistical Methods: Equality of means were evaluated using one-way analysis of variance (ANOVA) for body weight, food consumption, hematology, and clinical chemistry data; Bartlett's test was performed to determine group variances; Dunnett's test was used to determine significant differences;

Remarks: This study was conducted to determine the effects of repeated exposure to tributyl phosphate on mortality, body weights, food consumption, hematology, clinical chemistry, and tissue morphology. Male and female rats were 30 days old at receipt, and were quarantined for one week prior to being placed in the study. Fifteen male and 15 female rats were randomly allocated to each of six groups. Tributyl phosphate was administered daily by blending it into the diet to achieve dietary concentrations of either 8, 40, 200, 1000, or 5000 ppm. The control group received just rodent diet. Five male and female rats from each group were sacrificed after 45 days, at which time blood was collected for hematological evaluation and for measuring clinical chemistry parameters. Tissues were taken for histopathology. The animals were maintained at 60-76°F with the humidity ranging between 35-72%. Water was available ad libitum. The actual concentration of the test substance in the diet was verified by analysis. All animals were observed daily for appearance and behavior, and for mortality.

Robust Summary for Tributyl Phosphate

REPEATED DOSE TOXICITY IN MAMMALS

Page 2

Body weights and food consumption were determined weekly. Blood parameters were determined pre-test, at 45 days and at the end of the in-life phase (90 days). Hematology parameters measured include hematocrit, hemoglobin, erythrocyte count, leukocytes (total and differential), platelet count, mean corpuscular volume, and prothrombin time. Clinical chemistry parameters measured include alkaline phosphatase, blood urea nitrogen, total bilirubin, SGPT, SGOT, SGGT, sodium, creatinine, phosphorus, potassium, albumin, total protein, and cholesterol. Brain, plasma, and erythrocyte cholinesterase activity was measured.

At the end of 90 days, all remaining animals were necropsied and examined for gross lesions. The following tissues were taken from each animal for examination: brain, spinal cord (3 levels), pituitary, thyroid with parathyroids, thymus, trachea, lungs, heart, liver, spleen, pancreas, kidneys, adrenals, muscle, eyes, prostate, mammary gland, skin, testes, ovaries, uterus, aorta, esophagus, stomach, duodenum, jejunum, ileum, colon, rectum, urinary bladder, and sciatic nerves. All tissues were examined from the control and high dose animals. In addition, the livers and urinary bladders were examined from all other groups.

Results: No animals died during this study. Significant depression of body weight gain was seen only in the males and females in the high dose group (5000 ppm), occurring throughout the study, when compared to the body weights of control animals (25% and 30% depression for males and females, respectively). A significant decrease in food consumption was seen in the high dose animals during certain weeks, but not consistently. Measured dietary concentrations were 7.6, 39.2, 196, 980, and 4790 ppm, representing 95%, 98%, 98%, 98%, and 96% of the theoretical (nominal) concentrations. At the interim sacrifice, platelet counts were significantly increased in the 40 ppm males and 5000 ppm females. Mean corpuscular hemoglobin values were significantly decreased in the 1000 ppm females. None of these findings were considered treatment-related. At termination, mean activated partial thromboplastin time was significantly elevated in the 5000 ppm males and this was considered treatment related.

Of the interim clinical chemistry measurements, the potassium value was lower in the 40 ppm males and plasma cholinesterase levels were higher in the 8 ppm females. Neither change was considered treatment related. Mean SGPT for the 5000 ppm males and SGGT values for the 1000 ppm and 5000 ppm males and 5000 ppm females were significantly elevated. This is considered treatment-related. At terminal sacrifice, SGOT values in the 8 ppm males and brain

**Robust Summary
for
Tributyl Phosphate**

REPEATED DOSE TOXICITY IN MAMMALS

Page 3

cholinesterase values in the 200 and 1000 ppm males was elevated, neither being treatment-related. Mean SGGT values for the 5000 ppm males and females, and mean albumin and calcium values for the 5000 ppm males were significantly elevated and these changes were considered treatment related. The only treatment-related histopathological finding was generalized transitional cell hyperplasia of the urinary bladders in the 1000 and 5000 ppm males and 5000 ppm females. There were no other treatment-related tissue changes in this study. The no observable adverse effect level (NOAEL) was 200 ppm (13.8 mg/kg/day) for males and 1000 ppm (80.9 mg/kg/day) for females. The lowest observed adverse effect level (LOAEL) for tributyl phosphate in this study was 1000 ppm (68.2 mg/kg/day) for males and 5000 ppm (423.2 mg/kg/day) for females.

Conclusion: The NOAEL for males was 200 ppm (13.8 mg/kg/day) and for females was 1000 ppm (80.9 mg/kg/day).

Data Quality: Reliable without restriction. Key study.

Reference: FMC Toxicology Laboratory, Thirteen Week Feeding Study of Tributyl Phosphate in Rats. 1985. Study provided by FMC to SOCMA TBP Task Force.

**Robust Summary
for
Tributyl Phosphate**

GENETIC TOXICITY: GENE MUTATION

TEST SUBSTANCE

Tributyl phosphate, highest purity available, was provided by Tokyo Kasei

METHOD

Guideline Followed: None

Test Type: Microbial Mutagenicity Test

GLP: No

Year: 1996

Species/Strain/Supplier: *Salmonella typhimurium* strains TA102 and TA 2638 and
Escherichia coli strains WP2/pKM101 and WP2 uvrA/pKM101

Analytical Monitoring: No

Exposure Period: Varied according to organism

Statistical Methods: Statistical significance was determined using a linear regression test.

Remarks: A collaborative study was conducted in which 20 participating laboratories evaluated the mutagenic activity of 29 chemicals, including tributyl phosphate. The objective was to determine the consistency of the interlaboratory results and the sensitivity of the four bacterial strains. Tributyl phosphate was evaluated in *Salmonella typhimurium* strains TA102 and TA 2638 and in *Escherichia coli* strains WP2/pKM101 and WP2 uvrA/pKM101, using the plate incorporation method, with and without metabolic activation. The activation system was prepared from rat livers induced by phenobarbital and 5,6-benzoflavone. The plates were incubated at 37°C for 48 hours after which colonies were quantified by an automated colony counter. The test included 5 dose levels and replicates of 3 plates per dose. The doses of tributyl phosphate used in all of the tests were 5000, 2500, 2000, 1250, 1000, 625, 500, 313, 250, 125, 78, 31.3, and 0 ug/plate. Positive controls, included in each test, were mitomycin C, 2-aminoanthracene, and 2-(2-furyl)-3-(5-nitro-2-furyl) acrylamide.

**Robust Summary
for
Tributyl Phosphate**

GENETIC TOXICITY: GENE MUTATION

Page 2

- Results:** Tributyl Phosphate was consistently found to be without mutagenic activity in each of the four strains in which it was evaluated, at all of the dose levels used, with and without metabolic activation, at all of the participating facilities at which it was evaluated.
- Conclusion:** Tributyl phosphate was not mutagenic in any of the four bacterial strains in which it was tested, with or without metabolic activation.
- Data Quality:** Reliable without restriction. Key study.
- Reference:** Watanabe, K., Sakamoto, K., and Sasaki, T. Comparisons on chemically induced mutagenicity among four bacterial strains, *Salmonella typhimurium* strains TA102 and TA 2638 and in *Escherichia coli* strains WP2/pKM101 and WP2 vrA/pKM101, collaborative study I. *Mutation Research* 361:143-155, 1996.

**Robust Summary
for
Tributyl Phosphate**

GENETIC TOXICITY: CHROMOSOME

TEST SUBSTANCE

Tributyl phosphate, lot number 2B-131, 99.5% pure, was provided by FMC Corporation.

METHOD

Guideline Followed: U.S. EPA TSCA Test Guideline 798.5385

Test Type: In Vivo Mammalian Bone Marrow Cytogenetics: Chromosome Analysis

GLP: Yes

Year: 1991

Species/Strain/Supplier: Sprague-Dawley Rats from Charles River Breeding Laboratories

Analytical Monitoring: Yes

Exposure Period: Single dose

Statistical Methods: Fisher's exact test was used to compare the percent of aberrant cells between treatment and control groups. The Cochran-Armitage test was used to evaluate dose-response.

Remarks: This study was conducted to determine the ability of tributyl phosphate to induce structure chromosomal aberrations in rats after a single exposure. Fifteen males and fifteen females, about 6 to 8 weeks of age, were assigned to each of the 5 test groups. Single oral tributyl phosphate doses were 300, 600, or 1200 mg/kg. The positive control group received a single 20 mg/kg dose of cyclophosphamide. The vehicle control group received corn oil in the amount of 10 ml/kg. The animals were housed at $74 \pm 6^\circ\text{F}$ with relative humidity at $50 \pm 20\%$. Five male and five female animals from each group were sacrificed either 12, 24, or 36 hours after dose administration. Immediately after sacrifice by carbon dioxide, the femur was exposed, and bone marrow was aspirated into a syringe. The bone marrow cells were processed and prepared on glass slides (stained with Giemsa) for microscopic examination. At least 3 slides were prepared from each animal. Slides were coded and scored "blind." A minimum of 50 metaphase cells containing 40 ± 2 centromeres were examined from each animal and scored for

**Robust Summary
for
Tributyl Phosphate**

GENETIC TOXICITY: CHROMOSOME

Page 2

chromatid type and chromosome-type aberrations.

Results: One male and four females died in the high dose group and were replaced with treated animals from a replacement group run in parallel. Clinical signs, observed in just a few animals, included diarrhea and irregular breathing. The total number of aberrations such as gaps, breaks, and rearrangements, were tabularized for each group. In addition, chromatid-type breaks and exchanges were tabularized. The percent of chromosomal damage was not significantly increased in the tributyl phosphate treated animals, regardless of sex, dose, or sacrifice time. In contrast, the positive control chemical, cyclophosphamide, induced a significant increase in cells containing one or more aberrations. In this test, tributyl phosphate did not induce chromosomal damage in rat bone marrow cells.

Conclusion: Tributyl phosphate did not induce chromosomal aberrations in this test.

Data Quality: Reliable without restriction. Key study.

Reference: Microbiological Associates, Inc., Study No. T9145.105011, 1991. Study conducted for the SOCMA TBP Task Force.

**Robust Summary
for
Tributyl Phosphate**

CHRONIC TOXICITY/CARCINOGENICITY STUDY

TEST SUBSTANCE

Tributyl phosphate, 99.7% pure, was provided by FMC Corporation.

METHOD

Guideline Followed U.S. EPA TSCA Guideline No. 798.3320

Test Type: 24-Month Oral (Dietary) Toxicity/Carcinogenicity Study in Rats

GLP: Yes

Year: 1996

Species/Strain/Supplier: Sprague-Dawley Rats from Charles River, Kingston, NY

Analytical Monitoring: Yes

Exposure Period: 24 Months

Statistical Methods: Bartlett's test was performed at the 1% two-sided risk level, to evaluate variance. Analysis of variance (ANOVA) was then performed, using parametric procedures in cases of unequal variance. Parametric procedures consisted of a one-way ANOVA using the F-distribution to assess significance and Dunnett's test to determine differences from control. Standard regression techniques with tests for trend and lack of fit were used to evaluate dose-related trends. Non-parametric procedures were those described by Hollander and Wolfe and consisted of the Kruskal-Wallis test for significance. Dunn's summed rank test and Jonckheere's test were also applied.

Remarks: This study was conducted to determine the toxicity and carcinogenic potential of tributyl phosphate after daily exposure for 24 months. Male and female rats were 4 weeks old at receipt, and were quarantined for two weeks prior to being placed in the study. Fifty male and 50 female rats were randomly allocated to each of four groups. Tributyl phosphate was administered daily in the diet, at levels of either 200, 700, or 3000 ppm. A control group received just rodent diet. Body weights and food consumption were measured weekly for the first 13 weeks and monthly thereafter. Hematologic evaluations were performed at 12, 18, and 24 months. Hematology parameters measured include hematocrit, hemoglobin,

Robust Summary for Tributyl Phosphate

CHRONIC TOXICITY/CARCINOGENICITY STUDY

Page 2

erythrocyte count, leukocytes (total and differential), platelet count, mean corpuscular volume, and prothrombin time. Urine analysis occurred at 3 weeks and at 3, 6, 12, and 18 months. All animals were euthanized after 24 months of exposure to tributyl phosphate, and underwent examination for gross lesions during necropsy.

The following tissues were taken from each animal for examination: brain, spinal cord (3 levels), pituitary, thyroid with parathyroids, thymus, trachea, lungs, heart, liver, spleen, pancreas, kidneys, adrenals, muscle, eyes, prostate, mammary gland, skin, testes, ovaries, uterus, aorta, esophagus, stomach, duodenum, jejunum, ileum, colon, rectum, urinary bladder, and sciatic nerves. All tissues were examined from the control and high dose animals. In addition, the liver, kidney, and urinary bladder were examined from all animals in the other groups. Urinary bladders were examined for the presence of calculi. If calculi were observed, the bladder was inflated with fixative and allowed to fix for five minutes prior to having the calculi removed. Any urinary calculi found at necropsy were saved and analyzed for calcium, magnesium, and phosphorus.

Results: Chronic exposure to tributyl phosphate did not affect survival. The primary clinical sign observed was red discoloration of the urine, in 2/50, 3/50, 3/50 and 14/50 males and 0/50, 0/50, 1/50 and 2/50 females in the 0, 200, 700, and 3000 ppm groups, respectively. The discoloration occurred most frequently between weeks 46 and 104. Food consumption was unaffected. Body weight gain in the high dose animals was significantly lower than in the corresponding control animals. Hematology and urinalysis parameters were unaffected by treatment. A dose-related increase in the incidence and severity of urinary bladder hyperplasia and the incidence of urinary bladder papillomas was observed in both male and female animals in the mid and high dose groups. Transitional cell carcinomas of the urinary bladder were present in 6 of 49 males and in 2 of 50 females in the high dose group, and a single squamous cell carcinoma was present in 1 of the 49 high dose males. The oncogenic effects showed a clear threshold of 700 ppm in the diet. The NOEL for chronic toxicity was 200 ppm. The mean intake of tributyl phosphate for the high dose male and female animals was 143 and 182 mg/kg/day. The consistently negative mutagenicity tests indicate that the urinary bladder tumors are induced by a nongenotoxic (epigenetic) mechanism.

Conclusion: The NOAEL for chronic toxicity was 200 ppm (9mg/kg/day for males and 12 mg/kg/day for females). Chronic exposure to the highest dose, 3000 ppm, resulted in an increased incidence of transitional cell tumors of the urinary

**Robust Summary
for
Tributyl Phosphate**

CHRONIC TOXICITY/CARCINOGENICITY STUDY

Page 3

bladder. A significant increase in urinary bladder hyperplasia was observed in the mid dose animals.

Data Quality: Reliable without restriction. Key study.

Reference: Huntingdon Life Sciences, A 24-Month Toxicity/Carcinogenicity Study of Tributyl Phosphate in Rats. 1996. Study conducted for the SOCMA TBP Task Force.

**Robust Summary
for
Tributyl Phosphate**

18-MONTH CARCINOGENICITY STUDY

TEST SUBSTANCE

Tributyl phosphate, 99.7% pure, was provided by FMC Corporation.

METHOD

Guideline Followed U.S. EPA TSCA Guideline No. 798.3300

Test Type: 18-Month Oral (Dietary) Carcinogenicity Study in Mice

GLP: Yes

Year: 1996

Species/Strain/Supplier: CD-1 Mice from Charles River, Kingston, NY

Analytical Monitoring: Yes

Exposure Period: 18 Months

Statistical Methods: Bartlett's test was performed at the 1% two-sided risk level, to evaluate variance. Analysis of variance (ANOVA) was then performed, using parametric procedures in cases of unequal variance. Parametric procedures consisted of a one-way ANOVA using the F-distribution to assess significance and Dunnett's test to determine differences from control. Standard regression techniques with tests for trend and lack of fit were used to evaluate dose-related trends. Non-parametric procedures were those described by Hollander and Wolfe and consisted of the Kruskal-Wallis test for significance. Dunn's summed rank test and Jonckheere's test were also applied.

Remarks: This study was conducted to determine the carcinogenic potential of tributyl phosphate after daily dietary exposure for 18 months. Male and female mice were 4 weeks old at receipt, and were quarantined for two weeks prior to being placed in the study. Fifty male and 50 female mice were randomly allocated to each of four groups. Tributyl phosphate was administered daily in the diet, at levels of either 150, 1000, or 3500 ppm. A control group received just rodent diet. Body weights and food consumption were measured weekly for the first 13 weeks and monthly thereafter. Hematologic evaluations were performed at 12, and 18 months. Hematology parameters measured include hematocrit, hemoglobin,

**Robust Summary
for
Tributyl Phosphate**

18 MONTH CARCINOGENICITY STUDY

Page 2

erythrocyte count, leukocytes (total and differential), and platelet count. All animals were euthanized after 18 months of dietary exposure to tributyl phosphate, and underwent examination for gross lesions during necropsy.

The following tissues were taken from each animal for examination: brain, spinal cord (3 levels), pituitary, thyroid with parathyroids, thymus, trachea, lungs, heart, liver, spleen, pancreas, kidneys, adrenals, muscle, eyes, prostate, mammary gland, skin, testes, ovaries, uterus, aorta, esophagus, stomach, duodenum, jejunum, ileum, colon, rectum, urinary bladder, and sciatic nerves. All tissues were examined from the control and high dose animals. In addition, the liver, kidney, and urinary bladder were examined from all animals in the other groups.

Results: Dietary exposure for 18 months to tributyl phosphate did not affect survival. Clinical signs and hematology parameters were also unaffected by treatment. Food consumption was unaffected. Body weight gain in the high dose animals was significantly lower than in the corresponding control animals. A significant dose-related increase in absolute and relative liver weights was observed in the mid and high dose male and female animals. The incidence of hepatocellular adenomas was significantly increased in male mice in the high dose group (3/50 in control mice vs. 10/50 in the high dose mice). Historical control data from the laboratory shows indices as high as 10 hepatocellular adenomas in 60 males, which indicates the results in this study may not be biologically significant. No other tumors were observed in any of the groups in this study. The NOEL for chronic toxicity was 150 ppm (28.9 mg/kg/day for females and 24.1 mg/kg/day for males). The mean intake of tributyl phosphate for the high dose male and female animals was 585 and 711 mg/kg/day.

Conclusion: The NOAEL for chronic toxicity was 150 ppm in the diet. Exposure for 18 months to the mid and high doses resulted in an increase in benign liver tumors.

Data Quality: Reliable without restriction. Key study.

Reference: Huntingdon Life Sciences, An 18-Month Carcinogenicity Study of Tributyl Phosphate in Mice. 1996. Study conducted for the SOCMA TBP Task Force.

**Robust Summary
for
Tributyl Phosphate**

REPRODUCTIVE TOXICITY

TEST SUBSTANCE

Tributyl phosphate, lot number 9B-125, 99.7% pure, was provided by FMC Corporation.

METHOD

Guideline Followed U.S. EPA TSCA Reproduction and Fertility Effects Guideline 798.4700

Test Type: Two-Generation Reproductive Toxicity Study

GLP: Yes

Year: 1991-92

Species/Strain/Supplier: Sprague-Dawley Rats from Charles River Laboratories

Analytical Monitoring: Yes

Exposure Period: 13 Weeks F0 Generation, 11 Weeks F1 Generation

Statistical Methods: Parametric and nonparametric statistical programs were applied.

Parametric evaluations include general linear models (SAS Institute Inc.), analysis of variance (ANOVA), arcsine-square root transformation, and Bartlett's test for homogeneity. Other tests employed include Dunnett's test was used to determine significant differences and the nonparametric Kruskal-Wallis test and Mann-Whitney U test for individual comparisons.;

Remarks: This study was conducted to determine the effects of repeated exposure to tributyl phosphate on reproduction and fertility. The animals were 7 weeks old upon arrival and were held for a one week quarantine before being incorporated in the study. Thirty weanling rats per sex per dose (the F0 generation) were administered tributyl phosphate in the diet for 10 weeks. Dietary concentrations were 0, 200, 700, and 3000 ppm. The animals were observed daily for clinical signs and mortality. Body weights and food consumption were measured weekly. At the 10 weeks of exposure, each female was mated with a single male from the same dose group for 3 weeks, with continued dietary exposure to tributyl phosphate. Observations of vaginal sperm and/or copulation plugs were

Robust Summary for Tributyl Phosphate

REPRODUCTIVE TOXICITY

Page 2

considered evidence of a successful mating. The date of insemination was identified as gestation day 0. Dams were weighed and food consumption recorded on gestation days 0, 7, 14, and 20. Exposure was continued through gestation and weaning. The date of parturition was designated postnatal day 0. Pups were individually counted, examined, and sexed and were weighed individually on postnatal days 1, 4, 7, 14, and 21. At weaning, 30 F1 weanlings /sex/dose group were randomly selected to be parents of the F2 generation. Ten F1 pups/sex/group were randomly selected for necropsy. The selected F1 weanlings were exposed via the diet to the same doses of tributyl phosphate for 11 weeks and then mated. The F1 dams and F2 litters were handled as described above for the F0 dams and F1 offspring.

F0 and F1 animals underwent necropsy, gross examination, with retention of the following organs: pituitary, ovaries, testes, vagina, uterus, epididymides, seminal vesicles, prostate, urinary bladder, kidneys, and liver. All of the listed tissues from the high dose and control animals were processed through histology and examined microscopically for treatment-related changes. In addition, the kidneys, livers, and urinary bladders were examined from all the animals in all dose groups.

Results: Adult toxicity was observed in both sexes and generations in the 700 and 3000 ppm dose groups. In the 3000 ppm group, there was no mortality and no treatment-related clinical observations in either male or female animals. Both sexes in both generations exhibited consistent reductions in body weights, weight gains, and food consumption. There were no gross lesions associated with treatment in the 3000 ppm males and females, but histologically the F0 and F1 males and females exhibited urinary bladder epithelial hyperplasia. In addition, animals from this dose group showed hepatic centrilobular hypertrophy. There were no effects on any other organ or tissue in the high dose animals. There was no mortality or clinical observations in the 700 ppm animals. Reductions in body weights and weight gains were observed only in the F1 females. There were no gross findings at necropsy. Histologically, the 700 ppm male and female F0 and F1 animals showed urinary bladder hyperplasia, and the females of both generations displayed hepatic centrilobular hypertrophy. The 200 ppm also displayed urinary bladder hyperplasia but the hepatic changes observed in the animals that received the higher doses were absent in these animals.

There were no effects on reproductive parameters at any dose level in either the F0 or F1 generations, including mating and fertility indices, and length of gestation. There were no treatment-related lesions in the reproductive organs of

**Robust Summary
for
Tributyl Phosphate**

REPRODUCTIVE TOXICITY

Page 3

the F0 and F1 male and female animals at any dose level. Further, there were no treatment-related effects at any dose level on any parameter measured in the offspring, including litter size, sex ratio, and pre- or postnatal loss. F0 and F1 pup body weights were consistently and significantly reduced in the 3000 ppm offspring. Occasional body weight reductions were observed in the 700 ppm pups. A no observable adverse effect level (NOAEL) for adult toxicity could not be established. However, an NOAEL for reproductive toxicity was at least 3000 ppm. The results of this study confirm that tributyl phosphate is not a reproductive toxicant.

Conclusion: Tributyl phosphate did not cause reproductive toxicity or adversely affect fertility in this study.

Data Quality: Reliable without restriction. Key study.

Reference: Research Triangle Institute, Study No. 60C-4652, 1992. Study conducted for the SOCMA TBP Task Force.

**Robust Summary
for
Tributyl Phosphate**

DEVELOPMENTAL TOXICITY

TEST SUBSTANCE

Tributyl phosphate, lot number 9B-125, 99.7% pure, was provided by FMC Corporation.

METHOD

Guideline Followed: U.S. EPA TSCA Developmental Toxicity Guideline 798.4900

Test Type: Developmental Toxicity Study

GLP: Yes

Year: 1990-91

Species/Strain/Supplier: Sprague-Dawley Rats from Charles River Laboratories

Analytical Monitoring: Yes

Exposure Period: Days 6-15 of Gestation

Statistical Methods: The following statistical methods were used to identify significant differences: Chi-square analysis of Snedecor and Cochran, Fisher Exact Test, Bonferroni Inequality Test, and Armitage's Test.

Remarks: This study was conducted to determine the effects of repeated exposure to tributyl phosphate on the pregnant rat and the developing fetuses. Tributyl phosphate was administered daily by oral gavage to 24 pregnant female rats per group, during gestation days 6-15. Dosing solutions were prepared fresh weekly and were analyzed to confirm concentration. Dose levels were 188, 375, and 750 mg/kg/day. Since the test substance was diluted with corn oil for dosing, a corn oil control group was included in the study. The animals were observed twice daily for mortality and morbidity, and for clinical signs of toxicity. The pregnant animals were weighed on days 0, 6, 9, 12, 16, and 20 of gestation and food consumption was determined for days 0-6, 6-11, 11-16, and 16-20 of gestation. The dams were sacrificed on gestation day 20 and subjected to gross examination. The liver and gravid uterus from each animal were weighed. The number of

Robust Summary for Tributyl Phosphate

DEVELOPMENTAL TOXICITY

Page 2

fetuses and resorptions sites were determined. The ovaries were removed and the number of corpora lutea per ovary was recorded. The fetuses were removed, sexed, weighed, and examined for external malformations. Litter size was documented. One-half of the fetuses in each litter were processed for visceral evaluation, using the Staples' micro-dissection procedure. The remaining fetuses were stained with Alizarin Red S and evaluated for skeletal malformations and ossification variations.

Results: Pregnancy rates for the control, low, mid, and high dose animals were 95.7%, 100%, 95.8%, and 95.8%, respectively. Food consumption was not reduced in the low dose group but was reduced in the mid and high dose groups. There was no effect on mean number of corpora lutea, number of pups per litter, or mean number of resorptions sites per pregnant female. Dams that received 750 mg/kg/day exhibited serious maternal toxicity, expressed as significant mortality (7 of 24 females died, 29.2%) and lower mean body weights on days 9, 12, 16, and 20, during which time the animals actually lost weight. While there was no embryotoxicity in the pups of this group, there was a significant reduction in mean fetal weight. The relative liver weight in these animals was significantly higher than control relative weights when compared to the respective body weights. Dams in the 188 and 375 mg/kg/day groups showed reduced body weights at gestation days 16 and 20, and a reduction in weight gain during days 1-16, but there was no mortality in these groups. No embryotoxicity was observed in the pups from the 188 and 375 mg/kg/day dams. The number of fetuses with visceral malformations for the control, low, mid, and high dose groups were 0.6% (1/181 fetuses), 0.5% (1/193 fetuses), 1.1% (2/189 fetuses) and 0.7% (1/134 fetuses). The incidence of skeletal malformations for these groups were 0% (168 fetuses) evaluated), 0.06% (1/177 fetuses), 0% (0/173 fetuses), and 1.6% (2/124 fetuses), respectively. The incidence on a per fetus or per litter basis did not differ significantly between treated and control groups. External, visceral, and skeletal examination of the fetuses recovered from female rats in the treated groups on gestation day 20 revealed no teratogenic response at any of the dose levels evaluated in this study.

Conclusion: Tributyl phosphate was maternally toxic at all 3 dose levels but did not cause a teratogenic response in the fetuses of any treatment group in this study.

Data Quality: Reliable without restriction. Key study.

Reference: Biodynamics Inc. study No. 89-3535 1992. Study was conducted for the SOCOMA TBP Task Force.

**Robust Summary
for
Tributyl Phosphate**

REPEATED DOSE NEUROTOXICITY TEST

TEST SUBSTANCE

Tributyl phosphate, lot number 92B-125, was provided by FMC Corporation.

METHOD

Guideline Followed U.S. EPA TSCA Subchronic Neurotoxicity Screening Battery, as identified in Subpart G, Guidelines 798.6050, 798.6200, and 798.6400

Test Type: Thirteen Week Oral (Gavage) Study in Rats

GLP: Yes

Year: 1991

Species/Strain/Supplier: Sprague-Dawley Rats from Charles River, Constant, Quebec

Analytical Monitoring: Yes

Exposure Period: 13 Weeks

Statistical Methods: Group variances for body weight, food consumption, grip strength, hindlimb splay, and brain measurements were tested using Bartlett's test. Since differences between group variances were not significant, a one-way analysis of variance (ANOVA) was performed. Dunnett's test was used to compare the control and treated groups.

Remarks: This study was conducted to assess the potential neurotoxicity of tributyl phosphate using a functional observation battery, motor activity battery, and a neuropathological examination. Body weights and food consumption were measured weekly. Twelve male and 12 female rats were randomly allocated to each of four groups. Tributyl phosphate was administered daily by oral gavage at doses of 32.5, 100, or 325 mg/kg/day. A control group received just corn oil (vehicle). The animals were evaluated with a functional observation battery prior to the first dose, at 1, 6, and 12 hours after the first dose, and prior to dosing on days 7, 14, 35, 63, and 91. Motor activity evaluations were performed prior to the first dose and on study days 28, 62, and 90. At the completion of the in-life phase of the study, 6 animals per sex per group were randomly selected for perfusion and neuropathological evaluation. Neurological tissues examined

**Robust Summary
for
Tributyl Phosphate**

REPEATED DOSE NEUROTOXICITY TEST

Page 2

include forebrain, midbrain, cerebellum, medulla oblongata, pons, cervical and lumbar spinal cord, sural nerve, tibial nerve, and certain ganglia. Many other tissues were collected from each animal and preserved for possible future examination. During the study, all animals were observed daily for appearance, behavior, and mortality.

Results: Two males and 1 female in the mid-dose group and 3 males and 4 females in the high dose group died during the study. Male and female rats in the high dose group showed a higher incidence of muzzle staining, urogenital staining, and alopecia on their limbs and body. Body weight loss was observed in the males (beginning on day 14) and females (beginning on day 35) of the high dose group. Body weights of the mid and low dose animals were comparable to that of the control animals. A significant decrease in food consumption was seen only in the high dose animals during the first week of dosing.

Qualitative functional observation battery evaluations (body position, locomotor activity, bizarre behavior, tremors, etc.) and quantitative functional observation battery measurements (grip strength, hind limb splay, etc.) did not reveal any treatment-related differences. There were no significant differences in motor activity test results between the treated and control animals. Microscopic examination of the nervous system did not find any treatment-related neuropathology. Brain weight, length, and width measurements showed no treatment-related differences.

Conclusion: The NOAEL for male and female rats is greater than 325 mg/kg/day, the highest dose administered in this study.

Data Quality: Reliable without restriction. Key study.

Reference: Bio-Research Laboratories Ltd. A 3-Month Study of the Potential Effects of Orally Administered Tributyl Phosphate on Behavior and Neuromorphology in Rats. 1991. Study conducted for the SOCMA TBP Task Force.