FOREWORD INTRODUCTION

2,4,6-TRIBROMOPHENOL

CAS N°: 118-79-6

SIDS Initial Assessment Report

For

SIAM 17

Arona, Italy, 11-14 November 2003

1.	**Chemical Name:**	2,4,6-Tribromophenol
2.	**CAS Number:**	118-79-6
3.	**Sponsor Country:**	Japan
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4.	**Shared Partnership with:**	Mr. Kenji Miyazawa Manac Inc. E-mail: miyazawa@manac-inc.co.jp
5.	**Roles/Responsibilities of the Partners:**	See below
•	Name of industry sponsor /consortium	Manac Inc., DSBG/Bromine Compounds Ltd. (Israel)
•	Process used	The document was written by Mitsubishi Chemical Safety Institute LTD.
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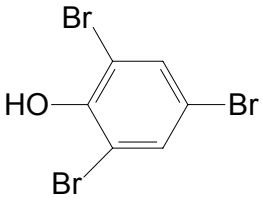
11.	**Comments:**	None

SIDS INITIAL ASSESSMENT PROFILE

CAS No.	118-79-6
Chemical Name	2,4,6-tribromophenol
Structural Formula	

SUMMARY CONCLUSIONS OF THE SIAR

Human Health

2,4,6-Tribromophenol is rapidly absorbed from the gastro-intestinal tract and is rapidly excreted via urine and feces.

The acute oral LD_{50} in rats is 1,486 mg/kg bw. The acute inhalation LC_{50} in rats is greater than 50,000 mg/m^3. The acute dermal LD_{50} in rats is greater than 2,000 mg/kg bw.
This substance is considered to be non-irritating to the skin, but irritating to the eye. This substance is considered to be a sensitiser in guinea pigs.

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test [OECD TG 422] was conducted in SD rats administered by gavage at the doses of 0 (vehicle), 100, 300 and 1,000 mg/kg/day. At 1,000 mg/kg/day, body weight gain suppression, and increase of absolute and relative liver weight were observed in both sexes and increases of total protein, albumin, A/G and ALP in blood were observed in male rats. At 300 mg/kg/day, salivation was observed in both sexes and increase in blood creatinine was observed in male rats. The NOAEL for the repeat dose toxicity is considered to be 100 mg/kg/day in rats of both sexes.

Two independent *in vitro* gene mutation studies in bacteria [OECD TG 471] were negative. One *in vitro* chromosomal aberration test [OECD TG 473] was positive with and without metabolic activation. In one *in vivo* micronucleus assay up to MTD (maximum tolerance dose) [OECD TG 474] by intraperitoneal injection, no evidence of genotoxicity was observed.

In the above described combined repeated dose toxicity study with the reproduction/developmental toxicity screening test [OECD TG 422], SD (Crj: CD) rats received gavage doses of 0 (vehicle), 100, 300 and 1,000 mg/kg/day. No adverse effects were observed on estrous cycle, copulation index, fertility index and duration of gestation period, number of corpora lutea, and delivery findings as well as number of implants, number of total pups and live pups born, implantation index and delivery index in any of the substance-treated groups. Neonatal viability on day 4 of lactation and neonatal body weights on days 0 and 4 of lactation in the 1,000 mg/kg/day group were lower than those in the control group (about 50% for neonatal viability in the treated group). In maternal animals at the same dose, body weight was reduced by about 8 % and liver weight was increased by about 15 %. In conclusion, the oral NOAEL for reproduction/developmental toxicity is considered to be 300 mg/kg/day.

Environment

2,4,6-Tribromophenol is a white to almost white crystalline powder, which is slightly soluble in water (59 mg/L at 25 °C). Melting point, boiling point, vapour pressure, and partition coefficient are 93.9 °C, 244 °C, 0.042 Pa (25 °C), and log Kow = 3.89 (25 °C), respectively. This substance is abiotically not hydrolyzed regardless of the pH. Direct photolysis by UV indicated a half-life of 4.6 hours. This substance is biodegradable (BOD = 49 % after 28 days) [similar to OECD TG 301C] and the most conservative measured bioconcentration factor in fish is

BCF = 513. A Mackay level III fugacity model shows that if this substance is released to water and soil, it is unlikely to be distributed into other compartments. When this substance is released to air, 29.2 % stays in air and 21.4 % is transported to water and 47.8 % is transported to soil.

This substance has been tested using aquatic species (algae, invertebrates and fish). An acute toxicity test with algae (*Selenastrum capricornutum*), resulted in a 72-h EC_{50} and a 72-h NOEC (biomass) of 0.76 and 0.22 mg/L, and a 24-72h EC_{50} and a 24-72h NOEC (growth rate) of 1.6 and 1.0 mg/L, respectively [OECD TG 201]. A 48-h EC_{50} for daphnids (*Daphnia magna*) was 0.26 mg/L [OECD TG 202 part 1]. A 96-h LC_{50} for fish (*Cyprinus carpio*) was 1.1 mg/L [OECD TG 203]. A chronic toxicity test was performed with daphnids (*Daphnia magna*) [OECD TG 211]. The 21-d NOEC for reproduction was reported to be 0.1 mg/L. A test with protozoae (*Tetrahymena pyriformis*) was performed and a 60h-IGC50 (50%inhibitory growth concentration) of 2.95 mg/l was reported.

Exposure

The production volume of 2,4,6-tribromophenol was estimated at approximately 2,500 t/year in Japan and 9,500 t/year worldwide in 2001. This substance is industrially produced in a closed system in Japan. This substance is used almost entirely as a chemical intermediate to make a flame retardant or directly as a flame retardant. The way to use this substance as a flame retardant is called "capping" i.e. the terminal -OH group of a polymer is capped with 2,4,6-tribromophenol. The reaction occurs during polymerization of oxirane to form 2,4,6-tribromophenoxy-ether. Consequently, the resulting polymer becomes flame retardant/resistant. From the use pattern of the substance, it has been suggested that it is released to the environment through various waste streams. There are some available monitoring data on environmental concentrations of this substance in Japan and over the world. The causes are ascribed to the fact that this substance is known to occur naturally through biosynthesis by benthic animals along with various bromophenols. The intake of this substance by food and water may happen because of the indirect exposure.

During production and use of this substance, occupational exposure is possible by inhalation and by the dermal routes. The workplace exposures during manufacturing processes are controlled. This chemical is normally transported from the producer to the downstream user in form of pellets in Japan. Workers normally wear protective gear such as masks, rubber gloves and goggles to prevent exposure.

RECOMMENDATION

The chemical is a candidate for further work.

RATIONALE FOR THE RECOMMENDATION AND NATURE OF FURTHER WORK RECOMMENDED

The chemical possesses properties indicating a hazard for the human health (sensitisation, irritation and uncertainty regarding reproductive toxicity in a screening test) and the environment. It is recommended to investigate the industrial exposure in down stream application and the possible use as a germicide. If necessary a risk assessment should be performed. Countries may desire to investigate any exposure scenarios that were not presented by the Sponsor country.

SIDS Initial Assessment Report

1 IDENTITY

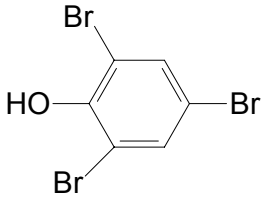
1.1 Identification of the Substance

CAS Number: 118-79-6

IUPAC Name: 2,4,6-Tribromophenol

Molecular Formula: $C_6H_3Br_3O$

Structural Formula:



Molecular Weight: 330.80

Synonyms: Tribromophenol
TBP
Bromkal Pur 3
Bromol
FR-613

1.2 Purity/Impurities/Additives

Purity: 99.0 - 99.7 % (w/w)

Impurity: other brominated phenols (2,3,4-tribromophenol and 2,3,5-tribromophenol) < 1.0 (w/w)
polybromated dibenzofuran and dibenzodioxin < detection limit

1.3 Physico-Chemical properties

Table 1 Summary of physico-chemical properties

Property	Value	Reference
Physical state	Solid	Nacalai Tesque, MSDS, 2001
Melting point	93.9 °C	CITI Japan, 1999
Boiling point	244 °C	Merck Index, 2001
Relative density	2.55 g/cm^3 (20 °C)	Merck Index, 2001
Vapour pressure	4.2 X 10^{-2} Pa (25 °C)	CITI Japan, 1999
Water solubility	59 mg/L (25 °C)	CITI Japan, 1999
pKa	5.97	CITI Japan, 1999
Partition coefficient n-octanol/water (log value)	3.89 (25 °C)	CITI Japan, 1999
Henry's law constant	4.77 X 10^{-8} atm–m^3/mole	HENRYWIN version 1.90, Syracuse Research Co.
Appearance	White to almost white (pale pink-brown) crystalline powder, with acrid odor like phenol	Nacalai Tesque, MSDS, 2001

2 GENERAL INFORMATION ON EXPOSURE

2.1 Production Volumes and Use Pattern

The production volume of 2,4,6-tribromophenol was estimated at approximately 2,500 t/year in Japan and 9,500 t/year world-wide in 2001. This substance is produced in a closed system. This substance is used almost entirely as a chemical intermediate to make a flame retardant or directly as a flame retardant. The way to use this substance as a flame retardant is called "capping" i.e. the terminal -OH group of a polymer is capped with 2,4,6-tribromophenol which is then covalently bound to the polymer. The reaction occurs during polymerization of oxirane to form 2,4,6-tribromophenoxy-ether. Consequently, the resulting polymer becomes flame retardant/resistant. The presence of the free substance itself in the polymer would give the resin a stinking odor because of the sublimating property of the substance and the resin would not be of commercial value. The potential for release of this substance from resins "capped" with it are not higher than the potential for release of 2,4,6-tribromophenol from polymers added with flame retardants derived from this substance. Other than that, antiseptic and germicide use (e.g., in pharmaceutical prepns) is reported [Danish EPA, 2000]. However, the amount is too small to be detected by the producer of the chemical.

2.2 Environmental Exposure and Fate

2.2.1 Sources of Environmental Exposure

It is known that this substance occurs naturally through production by benthic animals that are known to biosynthesize this chemical together with other bromophenols. The capitellid polychaete *Notomastus lobatus* produces and excretes large amount of bromophenols without an obvious

dietary source of these compounds [Higa et al., 1980]. It has been demonstrated that the synthesis occurs utilizing inorganic Br- anion as one source. The existence of the enzyme involved (peroxidase) in various species had been reported [Chen et al., 1991].

This substance industrially produced may be released to the environment through various waste streams, caused by the use of flame retardant. The intake of this substance by food and water may happen through indirect exposure. .

2.2.2 Photodegradation

Direct photolysis by UV light in air indicated a half-life of 4.6 hours [Velsicol Chemical Corp., 1978].

2.2.3 Stability in Water

Abiotically this substance is considered to be stable in water and not hydrolyzed regardless of pH [CITI Japan, 1999].

2.2.4 Transport between Environmental Compartments

The Mackay level III fugacity model was employed to estimate the environmental distribution of this substance in air, water, soil and sediment.

The results show that if this substance is released into soil, 99.9 % stays in soil and it is unlikely to migrate into other compartments. When this substance is released to water, 92.9 % stays in water, and 7.1 % is transported to the sediment compartments. If released into air, 29.2 % stays in air, 21.4 and 47.8 % are transported to water and soil, respectively. In the calculation process, the halflife time in soil was set at a default value of 1200 hours. However, because of the dissociation property (pKa of 5.97), Koc (1186; calculated by PCKOCWIN) is very sensitive to pH and, accordingly the halflife time may vary significantly with pH.

Table 2 Estimated distribution under three emission scenarios

Compartment	Release: 100 % to air	Release: 100 % to water	Release: 100 % to soil
Air	29.2 %	0.0 %	0.0 %
Water	21.4 %	92.9 %	0.1 %
Soil	47.8 %	0.0 %	99.9 %
Sediment	1.6 %	7.1 %	0.0 %

2.2.5 Biodegradation

This substance is biodegradable but not classifiable as readily biodegradable under aerobic condition (BOD = 49 % after 28 days) in a method similar to OECD TG 301C [CITI, 1981]. Nevertheless some biodegradation is expected under environmental conditions.

2.2.6 Bioaccumulation

Four bioaccumulation results have been reported, namely 20 (experimental), 83 (experimental), 120 (calculation) and 513 (experimental). The experimental result of 20 obtained from bluegills (Lepomis macrochirus) is reliable, because measurements were conducted using C14. However, the most conservative measured bioconcentration factor in fish is BCF = 513 [Butte et al., 1987 considered and reevaluated by Devillers et al., 1996].

2.2.7 Other Information on Environmental Fate

In Japan this substance was monitored in water and sediment. The highest concentration of this substance was 2.7 x 10^{-4} mg/L and 0.036 mg/kg in river water in 1996 [Saitama prefecture, Japan, 1997] and in upper-river sediments in 1981-1983 [Watanabe I. et al., 1991], respectively. The wastewater from the only industrial plant in Japan (Manac Inc., Hiroshima Japan) is treated at the sewage plant. This substance was not detected in the treated water [Manac, 2003].

In other parts of the world this substance was monitored in air, water and sediment. This substance was detected in the gas from refuse incineration in a Swedish hazardous waste incinerator, located at Norrtorp [Oeberg T. et al., 1987]. The highest concentration in the flue gas was 3.8 x 10^{-4} mg/m^3. Raw water and treated water at 40 potable water treatment plants across Canada were analysed for this substance. The highest concentration of raw water and treated water were 1.3 x 10^{-5} mg/L and 2.2 x 10^{-5} mg/L, respectively [Sithole B.B and Williams D.T., 1986]. This substance was also detected in estuarine sediments in France with a maximum concentration of 3.69 mg/kg (in dry wt basis).

Whitfield reported the content of bromophenols (2-BP, 4,BP, 2,4diBP, 2,6diBP, 2,4,6triBP(BP; for bromophenol)) in various aquatic organisms in Australia [Whitfield F.B. et al., 1992, 1995, 1997, 1998]. The content spectrum of the homologue chemicals and the extent of content varied widely among species. The highest concentrations of this substance contained in algae, bryozoa, hydroid, sponge, prawn, fish and fish gut were 0.068, 0.027, 0.029, 0.0034, 0.17, 0.012 and 0.23 mg/kg, respectively. The origin of bromophenols is considered by some authors to be benthic animals that are known to biosynthesize bromophenols [Higa et al., 1980].

Table 3 Environmental concentration of 2,4,6-tribromophenol

Media		Monitoring data	Country	Year	Remark	Reference
Air	Flue gas from hazardous waste incinerator	<1.4 x 10^{-5} mg/m^3	Norrtop, Sweden		The incinerator was fed chlorinated (mainly solvents) and brominated waste (tetrabutylammonium bromide).	Oeberg T. et al. (1987)
		3.8 x 10^{-4} mg/m^3				
		2.6 x 10^{-4} mg/m^3				
		4 - 5 x 10^{-6} mg/m^3			The incinerator was fed municipal waste.	
		<5 x 10^{-6} - 6 x 10^{-5} mg/m^3			The incinerator was fed peat.	
Water	River water	2.7 x 10^{-4} mg/L (max. conc.)	Saitama pref., Japan	1996	TBP was detected in 4 out of 6 rivers.	Saitama pref., Japan (1997)
	Industrial liquid waste	7.6 x 10^{-5} mg/L (max. conc.)			TBP was detected in 3 out of 6 waste water	
		7.8 x 10^{-5} mg/L (max. conc.)		1997	TBP was detected in 2 out of 8 waste water	Saitama pref., Japan (1998)
	Raw water	2.0 x 10^{-7} - 1.3 x 10^{-5} mg/L	Canada	1984-1985	Water samples were collected once each season at 40 potable water treatments plants across Canada.	Sithole B.B and Williams D.T. (1986)
	Treated water	2.0 x 10^{-7} - 2.2 x 10^{-5} mg/L				
Sediment	Non-industrial site	0.0015 - 0.004 ppm	Japan	1986	TBP was detected in 1 out of 11 sediment sites.	EA, Japan (1998)
	Upper river	8.0 x 10^{-4} - 0.036 mg/kg (in dry wt basis)	Osaka pref., Japan	1981-1983	TBP was detected in 10 out of 12 sediment sites.	Watanabe I. et al. (1991)
	Estuarine sediment	0.026 - 3.69 mg/kg (in dry wt basis)	Rhone estuary, France	1987-1988	Sediment samples were collected from 5 sites and TBP was detected in all samples.	Tolosa I. et al. (1991)
Organism	Algae	0.0045 - 0.068 mg/kg	Gutters region of Exmouth Gulf, Western Australia	1990	TBP was detected in 8 out of 8 algae.	Whitfield F.B. et al. (1992)
	Bryozoa	0.024 - 0.027 mg/kg			TBP was detected in 2 out of 2 bryozoa.	
	Hydroid	0.029 mg/kg			One hydroid was investigated.	
	Sponge	2.2 x 10^{-4} - 0.0034 mg/kg			TBP was detected in 8 out of 8 sponges.	
	Fish (whole gut)	0.0057 - 0.17 mg/kg	Eastern coast of Australia	1992	TBP was detected in 8 whole guts among 10 fishes	Whitfield F.B. et al. (1995)
	Fish (carcasses)	1.0 x 10^{-4} - 0.0034 mg/kg			TBP was detected in 6 carcasses among 10 fishes	
	Fish (gut)	4.0 x 10^{-4} - 0.23 mg/kg	Australia	1994-1995	32 species of ocean fish supplied by the state department of New South Wales Fisheries and caught off the coast of New South Wales. TBP was detected in 22 guts among 32 fishes.	Whitfield F.B. et al. (1998)
	Fish (fresh)	1.0 x 10^{-4} - 0.012 mg/kg			32 species of ocean fish supplied by the state department of New South Wales Fisheries and caught off the coast of New South Wales. TBP was detected in 19 among 32 fishes.	
	Prawn (natural)	7.0 x 10^{-5} - 0.17 mg/kg	Eastern coast of Australia	1993-1996	TBP was detected in 28 samples among 30 samples of 9 species of prawns (shrimp).	Whitfield F.B. et al. (1997)
	Prawn (cultivated)	1.3 - 5.3 x 10^{-4} mg/kg				

TBP: 2,4,6-tribromophenol

2.3 Human Exposure

2.3.1 Occupational Exposure

Occupational exposure at production sites may occur by inhalation and the dermal route. This substance is produced in a closed system. This substance is normally transported from the producer to the downstream user in form of pellets in Japan. The workplace exposures during manufacturing are controlled with personal protective equipment. Workers normally wear protective gear such as a mask, rubber gloves and goggles to prevent exposure. The atmospheric concentration was measured at one production site [JISHA, 2002]. The monitored data are shown in Table 4. The workplace exposure at downstream users in Japan has not been, to the knowledge of the lead company, surveyed systematically however. The downstream users belong to polymer industries or chemical industries.

NIOSH (NOES Survey 1981-1983) has statistically estimated that 1427 workers (734 of these are female) are potentially exposed to this substance in the US [NIOSH, 1983].

The TLV (Threshold Limit Values) for this substance is not established. The 5 mg/m^3 as TWA value is a company recommendation [BDBG/BCL].

Table 4 Work place monitoring data for 2,4,6-tribromophenol

Operation	Monitoring data mg/m^3	Frequency time/day	Working time hrs/day
Recovery work I (recovering residue on transfer pipes)	1.357	2	0.33
Recovery work II (recovering residue on solidification equipments)	6.280	1	0.25
Drum filling	1.243	10	1.67
Filling machine operation	0.600	10	1.67
Analysis work	<0.019	1	0.17

[Monitoring method] Air sample was suctioned at the breathing zone of the worker at the suction rate of 0.4 L/min. for 5 min. and adsorbed through a collection can and analyzed by GC.

2.3.2 Consumer Exposure

Since this substance is mainly used for flame retardant synthesis or covalently bound to polymer matrix, the consumer exposure can be considered to be low. Intake of this substance in food may happen because it is naturally occurring and somewhat bio-accumulative. However, the contribution of man made chemical is unknown.

3 HUMAN HEALTH HAZARDS

3.1 Effects on Human Health

3.1.1 Toxicokinetics, Metabolism and Distribution

The available data are limited. Two available reports were reviewed and summarized below.

Studies in Animals

In vivo Studies

2,4,6-Tribromophenol was rapidly absorbed from the gastro-intestinal tract [Clayton et al., 1981]. The absorption, distribution, and elimination of this substance were examined in male or female Eolzman's albino rats after a single oral administration at doses from 4.04 to 5.34 mg/kg. This substance was rapidly absorbed in rats. The bulk of the radioactivity (77 %) was readily excreted via urine and 2 to 14 % were eliminated in the feces, within 48 hours. The pharmacokinetics of this substance in rats appeared to follow a one compartment open model system. The rate constant for elimination (Ke) was 0.3 and the half-life in the blood was 2.03 hours. Based on the results of this study, this substance should neither be persistent nor accumulative in mammalian systems [GLCC, 1977].

Conclusion

This substance was rapidly absorbed from the gastro-intestinal tract and was rapidly excreted via urine and feces.

3.1.2 Acute Toxicity

There are various studies on the acute toxicity by oral, inhalation or dermal routes. Five reports on the acute toxicity via oral, inhalation or dermal routes to rats or rabbits were reviewed and summarised below.

Studies in Animals

Inhalation

Only one report was available which was considered reliable [GLCC, 1974a]. Because this study was described in detail, it was identified as the key study. Five male and five female Spartan albino rats were exposed to 50,000 mg/m^3 micronized 2,4,6-tribromophenol for 4 hours in a dynamic air chamber. A decreased motor activity, eye squint, slight dyspnea, erythema, ocular porphyrin discharge, and diarrhoea were observed. No changes in mortality rate or body weight gain were found. Necropsy of all rats following the 14-day observation period did not reveal any compound related findings. The lethal concentration for acute inhalation toxicity of this substance would be greater than 50,000 mg/m^3.

Dermal

Two reports were available. One study on rats by DSBG/BCL and another study on rabbits by GLCC, these were well-organized studies. The rat study by DSBG/BCL was conducted in accordance with OECD TG 402 in compliance with GLP and is identified as the key study [DSBG/BCL, 1997a].

Five male and 5 female rats were given a single 24 hours, semi-occlusive dermal application to intact skin at a dose level of 2,000 mg/kg bw. There were no deaths, no sign of systemic toxicity, no sign of irritation observed during and after 14 days. Also no abnormalities were noted at necropsy.

The LD50 in rats is considered to be greater than 2,000 mg/kg bw.

GLCC reported that the LD50 in New Zealand White rabbits was greater than 8,000 mg/kg bw [GLCC, 1974b].

Oral

Two reports are available. Both of them seemed well-organized studies: [MHW Japan, 1999] and [DSBG/BCL, 1985a]. The MHW study was identified as the key study because this study was well conducted according to OECD TG 401 in compliance with GLP. The LD50 value in this study was the lowest (the severest) of all reported values reviewed. The details of this study were as follows. The purity of test substance was 99.8 %. CD (SD) rats (5 animal/dose/sex) were administrated by gavage at doses of 0 (vehicle), 1,000, 1,300, 1,690, 2,197, and 2,856 mg/kg/day. The animals died at 1,300 mg/kg and higher. The death occurred within one day after administration in both sexes. The mortality by dose was identical for both gender (1,300 mg/kg: 2/5, 1,690 and 2197 mg/kg: 4/5, 2,856 mg/kg: 5/5). At 1,300 mg/kg and higher, hypoactivity, salivation, chronic convulsions, or tremors were observed. The body weight of surviving animals in these groups increased steadily on day 7 and 14 after administration. At autopsy, no macroscopic abnormalities were observed in dead and surviving animals. LD50 value determined by the probit method was 1,486 mg/kg for males or females.

Conclusion

Based on the results of the studies summarized in Table 5, acute toxicity by each exposure route was concluded as follows;

(Oral toxicity) The acute oral LD50 value in rats for this substance is 1,486 mg/kg bw.

(Inhalation toxicity) The acute inhalation LC50 in rats for this substance is considered to be greater than 50,000 mg/m^3.

(Dermal toxicity) The LD50 in rats is considered to be greater than 2,000 mg/kg. The acute dermal LD50 in rabbits is considered to be greater than 8,000 mg/kg bw.

Table 5 Acute toxicity of 2,4,6-tribromophenol in experimental animals

Route	Animals	Values	Type	References
Oral	Rat	1,486 mg/kg bw for both sexes or combined.	LD_{50}	MHW Japan, 1999
Oral	Rat	> 5,000 mg/kg bw for both sexes	LD_{50}	DSBG/BCL, 1985a
Inhalation/ 4 hrs	Rat	> 50,000 mg/m^3 for both sexes	LC_{50}	GLCC, 1974a
Dermal	Rat	> 2,000 mg/kg bw for both sexes	LD_{50}	DSBG/BCL, 1997a
Dermal	Rabbit	> 8,000 mg/kg bw for both sexes	LD_{50}	GLCC, 1974b

3.1.3 Irritation

Skin Irritation

Studies in Animals

Two available reports for skin irritation were reviewed and summarized in Table 6.

Among the two reports, the report by DSBG/BCL is identified as the key study because it was conducted in accordance with OECD TG 404 in compliance with GLP. The potential of this substance to cause skin irritation was tested at one dosage at 0.5 g of this substance which was applied for 4 hours to the intact and the abraded skin of rabbits under occluded conditions. No vehicle was used. Reactions of the test sites were scored according to the criteria of Draize (1959). No sign of skin irritation were observed at any of the test sites.

The result was classified as "not irritating" to skin [DSBG/BCL, 1985b].

Table 6 The skin irritation of 2,4,6-tribromophenol

Animals	Method	Result	Reference
Rabbit	OECD TG 404 One dosage (0.5 g), 4 hours	Not irritating	DSBG/BCL, 1985b
Rabbit	No data One dosage (0.5 g), 24 hours	Not irritating Primary irritation score: 0.3	GLCC, 1974c

Eye Irritation

Studies in Animals

Two available reports of eye irritation were reviewed and summarized in Table 7.

Among two reports, the report by DSBG/BCL is identified as the key study because it was conducted according to OECD TG 405 in compliance with GLP [DSBG/BCL, 1997b]. A single application of the test substance to the non-irrigated eye of three rabbits produced diffuse corneal opacity, iridial inflammation and moderate conjuctival irritation. No vehicle was used. The test material produced a maximum group mean score of 27.0. The result was classified as a "moderate irritant" to eye.

Table 7 The eye irritation of 2,4,6-tribromophenol

Animals	Method	Result	Reference
Rabbit	OECD TG 405 One dosage (100 mg)	Moderately irritating	DSBG/BCL, 1997b
Rabbit	No data One dosage (100 mg)	Irritating	GLCC, 1974d

Conclusion

This substance is moderately irritant to the eye, but not irritating to the skin.

3.1.4 Sensitisation

Studies in Animals

Skin

Two available study reports are summarised in Table 8. The study by DSBG/BCL was conducted according to OECD TG 406 with the principles of GLP and was identified as the key study [DSBG/BCL, 1997c]. The summary of this study was as follows;

Twenty test and ten control guinea pigs were used for the main study. Based on the results of sighting tests, the concentration of the test material for the induction and challenge phases were selected as follows: intradermal induction; 10 % w/v in arachis oil BP, topical induction; 50 % w/w in arachis oil BP, topical challenge; 75 % and 50 % w/w in arachis oil BP. The test material produced a sensitising rate of 75 % (15/20). This substance was classified as a strong sensitiser to guinea pig skin.

Table 8 The result of the sensitisation test of 2,4,6-tribromophenol

Type	Animal	Method	Result	Reference
Skin sensitising	Guinea pig	OECD TG 406	Sensitising	DSBG/BCL, 1997c
Skin sensitising	Guinea pig	no data	Sensitising	GLCC, 1974e

Conclusion

This substance is considered to be a sensitiser in guinea pigs.

3.1.5 Repeated Dose Toxicity

Only one oral administration study was available. The study by MHW was identified as the key study, because it was conducted according to OECD TG 422 in compliance with GLP [MHW Japan, 1999].

According to the OECD test guidelines for combined repeated dose toxicity study with the reproduction/developmental toxicity screening test [OECD TG 422], SD (Crj: CD) rats were administrated by gavage at doses of 0 (vehicle; corn oil), 100, 300, and 1,000 mg/kg/day (12 animal/dose/sex). The dosing period for males was 48 days starting from 14 days before mating, and for females was 41 to 45 days starting, from 14 days before mating to the day 3 of lactation. For females which did not succeed to mate, the dosing period was 48 days.

At 1,000 mg/kg/day, salivation, significant suppression of body weight gain, decrease of food consumption, increases of absolute and relative liver weight, increase of relative kidney weight were observed in both sexes. Significant increases in total protein, albumin, A/G and ALP, decreases in total bilirubin and potassium in blood, significant decrease of absolute thymus weight, enlargement, incidence of hepatocyte hypertrophy increase, and decrease of fatty change in liver, renal papillary necrosis, dilatation of tubules, lymphocytes infiltration, basophilic tubular epithelium and hyaline casts in kidney were observed in males at 1,000 mg/kg/day. No biochemical or histopathological changes were found in females at 1, 000 mg/kg/day.

At 300 mg/kg/day, salivation was observed in both sexes and significant increase in creatinine in blood was observed in males. At 100 mg/kg/day, no adverse effect was observed in both sexes. The NOAEL for the repeat dose toxicity is considered to be 100 mg/kg/day for both sexes.

Conclusion

The NOAEL for repeated oral toxicity in rats is considered to be 100 mg/kg/day in both sexes.

3.1.6 Mutagenicity

Genetic Toxicity

Four reports were available and summarised in Table 9. These were two bacterial in vitro test reports, one non-bacterial in vitro test report and one genotoxic in vivo test report.

Table 9 Summary of genotoxicity studies of 2,4,6-tribromophenol

Type of test	Test system	Dose	Result	Reference
Bacterial *in vitro* test				
Reverse mutation OECD TG 471	*S. typhimurium* (strains TA100, TA1535, TA98, TA1537) *E. coli* WP2 *uvr*A	Up to 5,000 ug/plate	Negative for all strains at all doses with and without MA	MHW Japan, 1999
Reverse mutation OECD TG 471	*S. typhimurium* (strains TA1535, TA1537, TA1538, TA98 and TA100)	Up to 1,500 ug/plate	Negative for all strains at all doses with and without MA	DSBG/BCL, 1996
Non Bacterial *in vitro* test				
Chromosomal aberration test OECD TG 473	CHL/IU cells	Up to 1.6 mg/mL	Positive (with and without MA)	MHW Japan, 1999
Genetic *in vivo* test				
Micronucleus Test OECD TG 474	Mouse, bone marrow	75, 150, 300 mg/kg bw Intraperitoneal	Negative	DSBG/BCL, 2002

* MA: Metabolic activation

In vitro Studies

Bacterial test

Two studies were reviewed. The results of both studies were negative for gene mutation. These two studies [MHW Japan, 1999], [DSBG/BCL, 1996] were reliable because these were conducted according to OECD TG 471 in compliance with GLP. The MHW study [MHW Japan, 1999] was identified as the key study because the details were fully available.

1) MHW Japan, 1999:

This substance was not mutagenic in Salmonella typhimurium TA 100, TA 1535, TA 98, TA 1537 and Escherichia coli WP2 urvA, with and without an exogenous metabolic activation system. This substance did not induce gene mutation in any strains. Toxicity was observed above 500 ug/ plate

(TA 100, TA 1535, TA 98, TA 1535), above 2500 ug/plate (WP2 urvA) without an S9 mix and above 1,000 ug/plate (TA 98), and above 2,500 ug/plate (WP2 urvA) with an S9 mix.

2) DSBG/BCL, 1996:

DSBG/BCL reported that this substance was negative in of S. typhimurium TA 1535, TA 1537, TA 1538, TA 98 and TA 100 at doses of 5 to 500 ug/plate in the confirmation test.

Non-bacterial in vitro test

Only one study was available. A chromosomal aberration study was conducted in cultured Chinese hamster lung cells according to OECD TG 473 in compliance with GLP [MHW Japan, 1999]. This study was identified as the key study.

In the short-term treatment, this substance induced structural chromosomal aberration at doses of 0.050 mg/mL and 0.10 mg/mL, with and without metabolic activation systems. No polyploidy was induced. Cells with structural chromosomal aberrations were apparently increased at the two higher doses in the short-term treatment with and without metabolic activation (frequencies: 10.5 % at 0.050 mg/mL and 23.5 % at 0.10 mg/mL). Polyploidy was not induced. Cytogenetic effects were observed at 0.050 mg/mL in the short-term treatment without metabolic activation and at 0.10 mg/mL in the short-term treatment with metabolic activation.

In vivo Study

Only one study on the in vivo micronucleus assay was available. This study was conducted according to OECD TG 474 in compliance with GLP. This study was identified as the key study [DSBG/BCL, 2002]. The summary of this study is shown below.

A micronucleus assay was conducted with bone marrow in NMRI mice (5 animal/dose/sex). Animals received a single intraperitoneal injection at 75, 150 and 300 mg/kg. An MTD (maximum tolerance dose) was 300 mg/kg. Cyclophosphamide was used as positive control. No increase of erythrocytes with micronuclei was observed in any group.

Conclusion

Two independent in vitro gene mutation studies in bacteria [OECD TG 471] were negative. One in vitro chromosomal aberration test [OECD TG 473] was positive with and without metabolic activation. In one in vivo micronucleus assay up to MTD (maximum tolerance dose) [OECD TG 474] by intraperitoneal injection, no evidence of genotoxicity was observed.

3.1.7 Carcinogenicity

There is no available information.

3.1.8 Toxicity for Reproduction

Two studies were available, an oral study [MHW Japan, 1999] and an inhalation study [Lyubimov et al., 1998]. The latter study was omitted from evaluation because experimental conditions, especially those related to exposure, were not reported.

Studies in Animals

Effects on Fertility

Oral Study:

The combined repeated dose toxicity study with the reproduction/developmental toxicity screening test [MHW Japan, 1999] was conducted according to OECD TG 422 in compliance with GLP. SD (Crj: CD) rats received gavage doses of 0 (vehicle), 100, 300 and 1,000 mg/kg/day. Males were dosed for 48 days starting from 14 days before mating and females were dosed for 41 to 45 days from 14 days before mating to day 3 of lactation. No adverse effects were observed in estrous cycle, copulation index, fertility index and duration of gestation period, number of corpora lutea, and delivery findings as well as number of implants, number of total pups and live pups born, implantation index and delivery index in any of this substance-treated groups. Neonatal viability on day 4 of lactation and neonatal body weights on days 0 and 4 of lactation in the 1,000 mg/kg/day group were lower than those in the control group (about 50% for neonatal viability in the treated group). In conclusion, the NOAEL for reproduction/developmental toxicity is considered to be 300 mg/kg/day.

Inhalation Study:

Pregnant Wistar rats were exposed to this substance by whole body inhalation (0, 0.03, 0.1, 0.3, 1.0 mg/m^3, 24 hr/day, 7 days/week from day 1 to 21 of gestation) [Lyubimov et al., 1998]. The authors reported that pre-implantation and post-implantation embryo losses were significantly increased in a dose-dependent manner and were seen in all treated groups except the lowest concentration (0.03 mg/m^3 equivalent to an oral dose of 0.015 mg/kg/day) group and that changes were observed in various behavioural, neuro-toxicological or immuno-toxicological parameters. However, the method for generating airborne substance, proof of ambient air concentration (analysis) or physical state of the test substance (vapour / dust) were not provided in the publication to convey confidence that the exposure was properly achieved. Thus, this Russian study was omitted from evaluation.

Developmental Toxicity

See the section of "Effects on Fertility"

Conclusion

In the oral study, neonatal viability on day 4 of lactation and neonatal body weights on days 0 and 4 of lactation in the 1,000 mg/kg/day group were lower than those in the control group. The oral NOAEL for reproduction/developmental toxicity is considered to be 300 mg/kg/day.

3.2 Initial Assessment for Human Health

This substance is rapidly absorbed from the gastro-intestinal tract and is rapidly excreted via urine and feces.

The acute oral LD50 in rats is 1,486 mg/kg bw. The acute inhalation LC50 in rats is greater than 50,000 mg/m^3. The acute dermal LD50 in rats is greater than 2,000 mg/kg bw.

This substance is considered to be non-irritating to the skin, but irritating to the eye. This substance is considered to be a sensitiser in guinea pigs.

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test [OECD TG 422] was conducted in SD rats administered by gavage at the doses of 0 (vehicle), 100, 300 and 1,000 mg/kg/day. At 1,000 mg/kg/day, body weight gain suppression, and increase of

absolute and relative liver weight were observed in both sexes and increases of total protein, albumin, A/G and ALP in blood were observed in male rats. At 300 mg/kg/day, salivation was observed in both sexes and increase in blood creatinine was observed in male rats. The NOAEL for the repeat dose toxicity is considered to be 100 mg/kg/day in rats of both sexes.

Two independent in vitro gene mutation studies in bacteria [OECD TG 471] were negative. One in vitro chromosomal aberration test [OECD TG 473] was positive with and without metabolic activation. In one in vivo micronucleus assay up to MTD (maximum tolerance dose) [OECD TG 474] by intraperitoneal injection, no evidence of genotoxicity was observed.

In the above described combined repeated dose toxicity study with the reproduction/developmental toxicity screening test [OECD TG 422], SD (Crj: CD) rats received gavage doses of 0 (vehicle), 100, 300 and 1,000 mg/kg/day. No adverse effects were observed on estrous cycle, copulation index, fertility index and duration of gestation period, number of corpora lutea, and delivery findings as well as number of implants, number of total pups and live pups born, implantation index and delivery index in any of the substance-treated groups. Neonatal viability on day 4 of lactation and neonatal body weights on days 0 and 4 of lactation in the 1,000 mg/kg/day group were lower than those in the control group (about 50% for neonatal viability in the treated group). In maternal animals at the same dose, body weight was reduced by about 8 % and liver weight was increased by about 15 %. In conclusion, the oral NOAEL for reproduction/developmental toxicity is considered to be 300 mg/kg/day.

4 HAZARDS TO THE ENVIRONMENT

4.1 Aquatic Effects

The reliable toxicity data of aquatic organisms are summarized in Table 10. All of these toxicity tests were performed with GLP and in accordance with OECD test guidelines. The substance concentrations in the testing media were monitored during the course of the experiments.

Table 10 Summary of effects of 2,4,6-tribromophenol on aquatic organisms

Organism	Test duration	Result (mg/L)	Reference
Algae			
Green algae (*Selenastrum capricornutum*)	72 h (op)	EC_{50} (bms, 0-72 h) = 0.76 NOEC (bms, 0-72 h) = 0.22 EC_{50} (gr, 24-48 h) = 1.1 EC_{50} (gr, 24-72 h) = 1.6 NOEC (gr, 24-72 h) = 1.0	EA, Japan 2000a
Invertebrates			
Water flea (*Daphnia magna*)	48 h (op, s)	EC_{50} (imm) = 2.2 EC_0 (imm) = 1.0	EA, Japan 2000b
	48 h (s)	EC_{50} (imm) = 0.26 EC_0 (imm) = 0.1	DSBG/BCL, 1988b
	21 d (op, ss)	NOEC (rep) = 0.10	EA, Japan 2000c
Fish			
Medaka (*Oryzias latipes*)	96 h (op, ss)	LC_{50} = 1.5 LC_0 = 1.0 LC_{100} = 3.2	EA, Japan 2000d
Carp (*Cyprinus carpio*)	96 h (op, s)	LC_{50} = 1.1	DSBG/BCL, 1998a
Fathead minnow (*Pimephales promelas*)	96 h (op, ft)	LC_{50} = 6.5 - 6.8	Phipps, 1981
	96 h (op, ft)	LC_{50} = 6.25	Broderius, 1995

op: open system, s: static, ss: semi-static, bms: biomass, gr: growth rate, ft: flow through, imm: immobilization, rep: reproduction rate, These values were calculated based on measured concentrations, because measured concentration were within ± 20 % of nominal concentration.

Acute toxicity data have been reported for aquatic species from three trophic levels (algae, invertebrates and fish) by the Environmental Agency of Japan [E.A., Japan, 2000a, b, d], DSBG/BCL [DSBG/BCL, 1998a and b] and others. One growth inhibition test for algae was performed in accordance with OECD TG 201 using *Selenastrum capricornutum*. EA, Japan (2000a) estimated EC50s for algae based on biomass and growth rate. The EC50 (biomass; 0-72 h) was 0.76 mg/L and the EC50 (growth rate; 24-72 h) was 1.6 mg/L. EA, Japan (2000b) and DSBG/BCL (1998b) performed an acute toxicity test for daphnid (*Daphnia magna*) according to OECD TG 202 part 1. The 48-h EC50s for daphnids was 2.2 mg/L or 0.26 mg/L respectively. And two acute toxicity tests for fish were performed according to OECD TG 203 by EA, Japan (2000d) and DSBG/BCL (1998a). EA, Japan (2000d) used Medaka (*Oryzias latipes*) in the acute toxicity test for fish and its 96-h LC50 was 1.5 mg/L, while DSBG/BCL (1998a) used Carp (*Cyprinus carpio*) and its 96-h LC50 was 1.1 mg/L. Additionally, two acute toxicity tests for Fathead minnow (*Pimephales promelas*) were found and their 96-h LC50 were 6.25 and 6.8 mg/L [Phipps et al., 1981 and Broderius et al., 1995] respectively. The most sensitive acute toxicity of this substance has been reported as 48-h EC50 of 0.26 mg/L in daphnids (DSBG/BCL, 1998b).

Chronic Toxicity Test Results

EA, Japan (2000a) estimated NOECs for algae based on biomass and growth rate. The NOEC (biomass; 0-72 h) was 0.22 mg/L and the NOEC (growth rate; 24-72 h) was 1.0 mg/L. Chronic

toxicity test for daphnid (*Daphnia magna*) on reproduction was performed according to OECD TG 211. The 21-d NOEC was 0.1 mg/L, the highest tested concentration (EA, Japan, 2000c).

4.2 Terrestrial Effects

There is no available information.

4.3 Other Environmental Effects

One test for protozoa (*Tetrahymena pyriformis*) was performed. The 60-h IGC50 (50% inhibitory growth concentration, aquatic) was 2.95 mg/L (Schultz and Riggin, 1985).

4.4 Initial Assessment for the Environment

This substance is a white to almost white crystalline powder, which is slightly soluble in water (59 mg/L at 25 °C). Melting point, boiling point, vapour pressure, and partition coefficient are 93.9 °C, 244 °C, 0.042 Pa (25 °C), and log Kow = 3.89 (25 °C), respectively. This substance is abiotically not hydrolyzed regardless of the pH. Direct photolysis by UV indicated a half-life of 4.6 hours. This substance is biodegradable (BOD = 49 % after 28 days) [similar to OECD TG 301C] and the most conservative measured bioconcentration factor in fish is BCF = 513. A Mackay level III fugacity model shows that if this substance is released to water and soil, it is unlikely to be distributed into other compartments. When this substance is released to air, 29.2 % stays in air and 21.4 % is transported to water and 47.8 % is transported to soil.

This substance has been tested using aquatic species (algae, invertebrates and fish). An acute toxicity test with algae (*Selenastrum capricornutum*), resulted in a 72-h EC50 and a 72-h NOEC (biomass) of 0.76 and 0.22 mg/L, and a 24-72h EC50 and a 24-72h NOEC (growth rate) of 1.6 and 1.0 mg/L, respectively [OECD TG 201]. A 48-h EC50 for daphnids (*Daphnia magna*) was 0.26 mg/L [OECD TG 202 part 1]. A 96-h LC50 for fish (*Cyprinus carpio*) was 1.1 mg/L [OECD TG 203]. A chronic toxicity test was performed with daphnids (*Daphnia magna*) [OECD TG 211]. The 21-d NOEC for reproduction was reported to be 0.1 mg/L.

A test with protozoa (*Tetrahymena pyriformis*) was performed and a 60h-IGC50 (50%inhibitory growth concentration) of 2.95 mg/L was reported.

5 RECOMMENDATIONS

The chemical is a candidate for further work.

The chemical possesses properties indicating a hazard for the human health (sensitisation, irritation and uncertainty regarding reproductive toxicity in a screening test) and the environment. It is recommended to investigate the industrial exposure in down stream application and the possible use as a germicide. If necessary a risk assessment should be performed. Countries may desire to investigate any exposure scenarios that were not presented by the Sponsor country.

6 REFERENCES

Broderius, S.J., M.D. Kahl, and M.D. Hoglund. (1995). Use of Joint Toxic Response to Define the Primary Mode of Toxic Action for Diverse Industrial Organic chemicals., Environ. Toxicol. Chem., 14, 9:1591-1605

Butte., W., Fox., K., Zauke., G. P. (1987). Bioaccumulation of phenol in zebrafish determined by a dynamicflow through test. In, QSAR in EnvironmentalToxicology-II (K.L.E. Kaiser, Ed.). Recdel Publishing Company, Dordrecht, 43-53

Chen, Y. P., Lincoln, D. E., Woodin, S. A., Lovell, C, R. (1991), Purification and properties of a unique flavin-containing chloroperoxidase from the capitellid polychaete, Notomastus lobatus., J. Biol. Chem., 266, 23909-23915

CITI, Japan. (1999). Report No. 80492K, Chemical Inspection and Testing Institute, unpublished data

CITI, Japan. (1981). Report No. 20492, Chemical Inspection and Testing Institute, unpublished data

Clayton et al. (1981). Patty's Industrial Hygienes and Toxiology 3rd. ed., 2A: 2615-2616

Danish EPA. (2000). Bromited flame retardant; Toxicity and ecotoxicity, Evironmental project No. 568 2000 Miljøprojekt

Devillers, J., Bintein, S. and Domine, D. Comparison of BCF models based on log P. (1996). Chemosphere, 33:1047-65

DSBG/BCL. (1985a). Acute Oral Toxicity in the Rat; unpublished study of DSBG/Bromine Compounds Ltd.

DSBG/BCL. (1985b). Primary Skin Irritation Study in Rabbits: unpublished study of DSBG/Bromine Compounds Ltd.

DSBG/BCL. (1996). Reverse Mutation Assay "Ames Test" Using Salmonella Typhimurium: unpublished study of DBSG/Bromine Compounds Ltd.

DSBG/BCL. (1997a). Acute Dermal Toxicity (limit test) in Rat: unpublished study of DSBG/ Bromine Compounds Ltd.

DSBG/BCL. (1997b). Acute Eye Irritation Test in the Rabbit: unpublished study of DSBG/Bromine Compounds Ltd.

DSBG/BCL. (1997c). Magnusson and Kligman Maximisation Study in the Guinea Pig: unpublished study of DSBG/ Bromine Compounds Ltd.

DSBG/BCL. (1998a). 96-hour Acute Toxicity Study in carp with 2,4,6-Tribromophenol (FR-613), (STATIC), unpublished study of DSBG/Bromine Compounds Ltd.

DSBG/BCL. (1998b). Acute Toxicity Study in Daphnia Magna with 2,4,6-Tribromophenol (FR-613), (STATIC), unpublished study of DSBG/Bromine Compounds Ltd.

DSBG/BCL. (2002). Micronucleus Test in Bone Marrow Cells of the Mouse with Tribromophenol: unpublished study of DSBG/Bromine Compounds Ltd.

DSBG/BCL. (2002). MSDS, Revision 4.

Ed. Sweetman J A; Simmons M S. (1980). The production of bromophenols resulting from chlorination of waters containing bromide ion and phenol. Water Res. Vol.14, No. 3, p. 287-290.

Environ. Mutagen. (1987). Salmonella mutagenicity tests: Results from the testing of 255 chemicals. 9 (Suppl. 9), 1-109

EA (Environmental Agency), Japan. (2000a). Ecotoxicity testing report (unpublished), Test Number; 10031, Growth inhibition Test to Algae (*Selenastrum capricornutum*), Japan Food Research Laboratories.

EA (Environmental Agency), Japan. (2000b). Ecotoxicity testing report (unpublished), Test Number; 10032, Acute Toxicity to Daphnid (*Daphnia magna*), Japan Food Research Laboratories.

EA (Environmental Agency), Japan. (2000c). Ecotoxicity testing report (unpublished), Test Number; 10033, Reproduction Test to *Daphnia Magna*; Japan Food Research Laboratories.

EA (Environmental Agency), Japan. (2000d). Ecotoxicity testing report (unpublished), Test Number; 10034, Acute Toxicity to Himedaka (*Orizas lapties*), Japan Food Research Laboratories.

EA, Japan. (1998). Chemicals in the Environment. Environmental Health and Safety Division, Environmental Health Department, Environment Agency of Japan p.568

EPA/OTS, Doc #88-7800198. (1978). Ntis Order No; NTIS/OTS0200382. nc 88-7800198.

GLCC. (1977). Pharmacokinetic Study of 2,4,6-Tribromophenol in Rats, Velsicol Chemical Corp., (EPA/OTS, Doc #86-900000322): unpublished report of Great Lakes Chemical Corp.

GLCC. (1974a). Acute inhalation toxicity in the Albino rat by International Research and Development Corporation for Michigan Chemical Corporation (EPA/OTS; Doc #86-900000305): unpublished report of Great Lakes Chemical Corp.

GLCC. (1974b). Acute dermal toxicity in Male and Female Albino Rabbits by International Research and Development Corporation for Michigan Chemical Corporation, (EPA/OTS; Doc #86-900000306): unpublished report of Great Lakes Chemical Corp.

GLCC. (1974c). Primary skin irritation study in Albino Rabbits by International Research and Development Corporation for Michigan Chemical Corporation, (EPA/OTS; Doc #86-900000303): unpublished report of Great Lakes Chemical Corp.

GLCC. (1974d). Eye irritation study in Albino Rabbits by International Research and Development Corporation for Michigan Chemical Corporation, (EPA/OTS; Doc #86-900000304): unpublished report of Great Lakes Chemical Corp.

GLCC. (1974e). Dermal Sensitization Study in the Albino Guinea Pig by International Research and Development Corporation for Michigan Chemical Corporation, (EPA/OTS; Doc#86-900000308): unpublished report of Great Lakes Chemical Corp.

Higa, T., Fujiyama, T., Scheuer, P.J. (1980). Halogenated phenol and indole constituents of acorn worms, Comp. Biochem. Physiol., 65B, 525-530

HPV Challenge Program. (2002). 201-14177A JISHA. (2002). Japan Industrial Safety and Health Association, unpublished data

Lyubimov, Alexander V; Babin, Vadim V; Kartashov Alex, I. (1998). Developmental neurotoxicity of 2,4,6-Tribromophenol in Wistar rats, Neurotoxicology, 19(2), 303-312,

Manac Inc., unpublished data

Manac Inc. (2003). Water Quality Report, unpublished data

Mar. Ecol. Prog. Ser. (1997). Biogenic bromophenols as negative recruiment cues. 157, p.303-306.

Marine Pollution Bulletin. (1991). Identification and occurrence of brominated and nitrated phenols in estuarine sediments. Vol. 22, No. 12 pp. 603-607.

Merck Index (Budavari, S. (ed.). (2001) The Merck Index - An Encyclopedia of Chemicals, Drugs, and Biologicals.) Whitehouse Station, NJ, Merck and Co., Inc., No. 9687

Meylan, W.M. and P.H. Howard. (1993). Computer estimation of the atmospheric gas-phase reaction rate of organic compounds with hydroxyl radicals and ozone. Chemosphere, 26, 2293-2299

MHW (Ministry of Health and Welfare), Japan. (1999). Toxicity Testing Reports of Environmental Chemicals, 7, 387-421

NIOSH. (1983). National Occupational Exposure Survey (NOES)

Nacalai Tesque. (2001). MSDS (MSDS No.34514)

Oeberg T., Warman K. and Bergstroem J. (1987). Brominated aromatics from combustion; Chemosphere 16: 2451-65

Phipps, G.L., G.W. Holcombe, and J.T. Fiandt. (1981). Acute Toxicity of Phenol and Substituted Phenols to the Fathead Minnow, Bull. Environ. Contam. Toxicol. 26(5) 585-593

Polyhalogenated dibenzo-p-dioxins/dibenzofurans testing and reporting requirements under the toxic substances control act (TSCA). (1989). Chemosphere, 19(1-6), 849-52.

Saitama-prefecture White Paper on the Environment. (1997).

Saitama-prefecture White Paper on the Environment. (1998).

Schultz, T.W. and G.W. Riggin. (1985). Predictive Correlations for the Toxicity of Alkyl- and Halogen-Substituted Phenols, Toxicol. Lett. 25:47-54

Sithole B.B. and Williams DT. (1986). Halogenated phenols in water at forty canadian potable water treatment facilities, J Assoc Off Anal Chem 69: 807-10

Sithole B.B., Williams D.T., Lastoria C. And Robertson J.L. (1986). Determination of Halogenated Phenols in raw and potable water by selected ion gas chromatography-mass spectrometry; J Assoc Off Anal Chem 69: 466-73

Tolosa I., Bayona J.M. and Albaiges J. (1991). Identification and Occurrence of Brominated and Nitrated

Phenols in estuarine sediments; Marine Pollut Bull 22: 603-7

Velsicol Chemical Corp., Project#428148, report#4, June 22, (1978).

Wako Pure Chemical Industries, Ltd. (2002). MSDS No. JW200437

Watanabe I., Takahashi K. and Tatsukawa R. (1985). Brominated phenols and anisoles in river and marine sediments in Japan; Bull Environ Contam Toxicol 35: 272-78

Water Sci. Technol. (1995). The source of bromophenols in some species of Australian ocean fish, 31(11 off-Flavorous in the Aquatic Environment 1994, 113-20

Whitfield F.B., Helidoniotis F. Svoronos D., Shaw K.J. and Ford G.L. (1995). The source of bromophenols in some species of australian ocean fish; Wat. Sci. Tech. 31: 113-120

Whitfield F.B., Helidoniotis F., Shaw K.J. and Svoronos D. (1997). Distribution of bromophenols in Australian wild harvested and cultivated prawns (shrimp). Journal of Agricultural and Food Chemistry; 45(11), 4398-405

Whitfield F.B., Helidoniotis F., Shaw K.J. and Svoronos D. (1998). Distribution of bromophenols in Australian wild harvested and cultivated prawns (shrimp). Journal of Agricultural and Food Chemistry; 46(9) 3750-7

Whitfield F.B., Shaw K.J. and Walker D.I. (1992). The source of 2,6-dibromophenol: cause of an iodoform taint in australian prawns; Wat. Sci. Tech. 25: 131-138

S I D S

Dossier

Existing Chemical	:	ID: 118-79-6
CAS No.	:	118-79-6
EINECS Name	:	2,4,6-tribromophenol
EC No.	:	204-278-6
Molecular Weight	:	330.8
Molecular Formula	:	C6H3Br3O

Producer related part

Company	:	MITSUBISHI CHEMICAL SAFETY INSTITUTE LTD.
Creation date	:	06.05.2003

Substance related part

Company	:	MITSUBISHI CHEMICAL SAFETY INSTITUTE LTD.
Creation date	:	06.05.2003
Status	:	
Memo	:	SIAM 17 2,4,6-tribromophenol
Printing date	:	04.03.2005
Revision date	:	06.05.2003
Date of last update	:	04.03.2005
Number of pages	:	
Chapter (profile)	:	Chapter: 1, 2, 3, 4, 5
Reliability (profile)	:	Reliability: without reliability, 1, 2, 3, 4
Flags (profile)	:	Flags: without flag, confidential, non confidential, WGK (DE), TA-Luft (DE), Material Safety Dataset, Risk Assessment, Directive 67/548/EEC, SIDS

1.0.1 APPLICANT AND COMPANY INFORMATION

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25.07.2003

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02.12.2003

1.0.2 LOCATION OF PRODUCTION SITE, IMPORTER OR FORMULATOR

1.0.3 IDENTITY OF RECIPIENTS

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Cedex :
Email :
Homepage :

03.06.2003

1.0.4 DETAILS ON CATEGORY/TEMPLATE

1.1.0 SUBSTANCE IDENTIFICATION

1.1.1 GENERAL SUBSTANCE INFORMATION

Purity type :
Substance type : organic
Physical status : solid
Purity : = 99 % w/w
Colour :
Odour :

Remark : for commercial
Flag : Critical study for SIDS endpoint
02.12.2003 (13)

Purity type :
Substance type : organic
Physical status : solid
Purity : = 99.7 % w/w
Colour :
Odour :

Flag : Critical study for SIDS endpoint
04.08.2003 (6)

1.1.2 SPECTRA

1.2 SYNONYMS AND TRADENAMES

2,4,6-Tribromophenol

Flag : Critical study for SIDS endpoint

Bromkal Pur 3

Flag : Critical study for SIDS endpoint

Bromol

Flag : Critical study for SIDS endpoint

FR-613

Flag : Critical study for SIDS endpoint

TBP

Flag : Critical study for SIDS endpoint

Tribromophenol

Remark : Chemical LAND21 [on line]
Flag : Critical study for SIDS endpoint
10.06.2003

1.3 IMPURITIES

Purity :
CAS-No :
EC-No :
EINECS-Name : other brominated phenols
Molecular formula :
Value : < 1 % w/w

Flag : Critical study for SIDS endpoint
04.08.2003 (41)

Purity :
CAS-No :
EC-No :
EINECS-Name : 2,3,4-tribromophenol
Molecular formula :
Value :

Flag : Critical study for SIDS endpoint
03.06.2003

Purity :
CAS-No :
EC-No :
EINECS-Name : 2,3,5-tribromophenol
Molecular formula :
Value :

Flag : Critical study for SIDS endpoint
03.06.2003

Remark : polybromated dibenzofuran and dibenzodioxin < detection limit
Flag : Critical study for SIDS endpoint
02.12.2003 (49)

02.12.2003

1.4 ADDITIVES

1.5 TOTAL QUANTITY

Quantity : - tonnes produced in

Remark : Approximately 2500 tons/year in Japan, 9500 tons/ year in worldwide

Flag : Critical study for SIDS endpoint
04.08.2003 (49)

1.6.1 LABELLING

1.6.2 CLASSIFICATION

1.6.3 PACKAGING

1.7 USE PATTERN

Type of use : industrial
Category : Basic industry: basic chemicals

Remark : This substance is used almost entirely as a chemical intermediate to make a flame retardant or directly as a flame retardant. The way to use this substance as a flame retardant is called "capping" i.e. the terminal -OH group of a polymer is capped with 2,4,6-tribromophenol. The reaction occurs during polymerization of oxirane to form 2,4,6-tribromophenoxy-ether. Consequently, the resulting polymer becomes flame retardant/resistant. This substance is used almost entirely as a chemical intermediate to make the flame retardant. The existence of chemical species of this substance itself makes the resin stinking odor because of the sublimating property and the resin cannot be of commercial value. Risk to release this substance is not evident for the resins "capped" with this substance more than the one added with flame retardant derived from this substance.

Flag : Critical study for SIDS endpoint
02.12.2003

Type of use : use
Category : other:antiseptic and germicide (e.g., in pharmaceutical prepns)

Flag : Critical study for SIDS endpoint
02.12.2003 (10)

1.7.1 DETAILED USE PATTERN

1.7.2 METHODS OF MANUFACTURE

1.8 REGULATORY MEASURES

1.8.1 OCCUPATIONAL EXPOSURE LIMIT VALUES

Type of limit : other
Limit value : 5 mg/m3

Remark : The TLV for TBP has not been determined by ACGIH or OSHA(US), Netherlands, Germany or UK.
The manufacturer's recommendation is 5 mg/m3.
The TLV for TBP is not established.
Company recommendation [every thing] = 5 mg/m3
DSBG/Bromine Compounds Ltd.
Flag : Critical study for SIDS endpoint
19.06.2003

1.8.2 ACCEPTABLE RESIDUES LEVELS

1.8.3 WATER POLLUTION

1.8.4 MAJOR ACCIDENT HAZARDS

1.8.5 AIR POLLUTION

1.8.6 LISTINGS E.G. CHEMICAL INVENTORIES

1.9.1 DEGRADATION/TRANSFORMATION PRODUCTS

1.9.2 COMPONENTS

1.10 SOURCE OF EXPOSURE

Method : Revised ICCA HPV Guidance for initial risk assessment (1998)
Remark : EHE
Result : Occupational exposures at production sites may occur by inhalation and dermal route. This substance is produced in

a closed system. This substance is normally transported from the producer to the downstream user in form of pellets in Japan. The workplace exposures during manufacturing are controlled with personal protective equipment. Workers normally wear protective gear such as a mask, rubber gloves and goggles to prevent exposure. The atmospheric concentration was measured at one production site [JISHA, 2002].

Work place monitoring data for TBP

Operation	Monitoring Data (Maximum Concentration)	Frequency (time/day)	Working time (hrs/day)	Maximum EHEinh (mg/kg/day)
Recovery work I (recovering residue on transfer pipes)	1.357 mg/m3	2	0.33	8.08 x10-3
Recovery work II (recovering residue on solidification equipments)	6.280 mg/m3	1	0.25	2.80 x10-2
Drum filling	1.243 mg/m3	10	1.67	3.70 x10-2
Filling machine operation	0.600 mg/m3	10	1.67	1.79 x10-2
Analysis work	<0.019 mg/m3	1	0.17	5.65x10-5

Total 9.10 x 10-2 mg/kg/day
[Monitoring method]Air sample was suctioned at the breathing zone of the worker at the suction rate of 0.4 L/min. for 5 min. and adsorbed through a collection can and analyzed by GC. As shown in Table 2, the monitored exposure concentrations were <0.019 - 6.280 mg/m3 at the recovery work I, recovery work II, drum filling, filling machine operation and analysis work. The highest daily intake (respiratory EHEinh) for a worker (body weight; 70 kg, respiratory volume; 1.25 m3/hr) assigned to the drum filling work without protection is calculated as 0.037 mg/kg/day.

Flag : Critical study for SIDS endpoint
02.12.2003 (44)

Remark : NIOSH (NOES Survey 1981-1983) has statistically estimated that 1427 workers (734 of these are female) are potentially exposed to this substance in the US.
Probable Route of Human Exposure

Flag : Critical study for SIDS endpoint
02.12.2003 (56)

1.11 ADDITIONAL REMARKS

Memo : CAS NUMBER: 118-79-6

Flag : Critical study for SIDS endpoint
04.08.2003

Memo : EINECS NUMBER: 204-278-6

Flag : Critical study for SIDS endpoint
04.08.2003

Memo : NAME (IUPAC): 2,4,6-tribromophenol

04.08.2003

Memo : NAME (OECD): 2,4,6-tribromophenol

04.08.2003

Memo : MOLECULAR FORMULA & WEIGHT: C6H3Br3O, 330.80

Flag : Critical study for SIDS endpoint
04.08.2003 (2)

Memo : STRUCTUAL FORMULA: Oc(c(cc(c1)Br)Br)c1Br

04.08.2003

Memo : APPERANCE: white to almost white (pale pink-brown) crystalline powder, odor: acridity like phenol

Flag : Critical study for SIDS endpoint
04.08.2003 (55)

Memo : 14. Transportation information

Remark : -UN; No. 3077

-IMO; Proper shipping name: Environmentally hazardous substance, solid, n.o.s (Tribromophenol)
Class: 9-Miscellanous Dangerous Substance and Articles
Making: MARINE POLLUTANT
Label:9
Packing Group: III

-ADR/RID; Proper shipping name: Environmentally hazardous substance, solid, n.o.s (Tribromophenol)
Classification Code: M7
Danger Label Model No.:9
Packing Group: III
Hazard identification No.90

-ICAO/IATA; Class:9

-DOT; Proper shipping name: Environmentally hazardous substance, solid, n.o.s (Tribromophenol)
Class: 9-Miscellanous Hazardous Material
Label: 9
Making: MARINE POLLUTANT
Packing Group: III

Flag : Critical study for SIDS endpoint
04.08.2003 (13)

Memo : 15. Regulatory information

Remark : -EEC; Reported in EINECS (No. 2042786)
--Indication of danger; Dangerous for the environment, symbol required (N)
Irritant,symbol reguired (Xi)

--Risk Phrases; R 36:Irritanting to eyes.
R 43:May cause sensitization by skin contact.
R 50/53:Very toxic to aquatic organisms, may cause long-term adverse effects in the aqautic environment
-Safety Phrase; 24/25: Avoid contact with skin and eyes.
S 26:In case of contact with eyes, rinse immediately with plenty of water and seek medical advice.
S 60:This material and its container must be disposed of as hazardous waste.
S 61: Avoid release to the environment. Refer to special instructions/Safety data sheets.

-Australia; Listed in AICS

-USA; Reported in the EPA TSCA Inventory

-Canada; Listed in DSL

-Japan; Biodegradable substance. Listed in MITI(ENCS No. 3-959)

-Philippines; Listed in PICCS

-Switzerland; Listed in Giftliste 1 (G-3150)

Flag : Critical study for SIDS endpoint
04.08.2003 (13)

Memo : The dioxin testing of DSBG

Remark : FR-613
Polybrominated Dibenzodioxins and Dibenzofurans Contamination
Summary of Analysis
FR-613, 2,4,6-Tribromophenol produced by Dead Sea Bromine Group / Bromine Compounds Ltd., Beer-Sheva, Israel was analysed for polybrominated p-Dibenzodioxins and Dibenzofurans contamination at Institut Fresenius, Germany.

High resolution gas chromatography followed by high resolution mass-spectrometry was used for analysis of the polybrominated p-Dibenzodioxins and Dibenzofurans. The method of analysis included several chromatographic extraction and clean-up steps using silica gel and alumina columns.

Quantitation levels (in ppb's) were achieved by spiking the solutions with specified amounts of isotopically (13C12) labeled PBDD/PBDF standards. The internal standards used for recovery calculation, labeled HxDD, were added to the samples just prior to GC/MS analysis.

Recovery rates of 13C-labeled standards are within the EPA guidelines (50 - 150 %).

System performance criteria, sample preservation procedures and quality assurance requirements were in compliance with U.S. EPA and German regulations.
The attached results of analysis performed show below:
The levels of polybrominated p-Dibenzodioxins and Dibenzofurans found in FR-613 are far below the limits specified in the German Ordinance "Chemikalien -

Verbotsverordnung".
No polybrominated Dibenzodioxins and Dibenzofurans are present in FR-613 at a level higher than the limits of quantitation (LOQs) specified by US EPA Toxic Substance Control Act (TSCA) 40 CFR section 766.27.

Taunusstein, 10th November 1997

FR-613
Polybrominated Dibenzodioxins and Dibenzofurans
Contamination according to German Ordinance "Chemikalienverbotsverordnung"
Sample Description: FR-613
Date of Report: 29th August, 1991

	Measurement (ug/kg)	German Requirement (ug/kg)	Recovery Rate(%)
Chemikalienverbotsverordnung			
-Group IV			
2,3,7,8-TBrDD	0.03	---	88
2,3,7,8-TBrDF	0.37	---	80
1,2,3,7,8-PeBrDD	0.08	---	129
2,3,4,7,8-PeBrDF	< 0.05	---	86
-Sum of Group IV	< 0.53	1.0	---
-Group V			
1,2,3,4,7,8-HxBrDD	< 0.1	---	---
1,2,3,6,7,8-HxBrDD	< 0.1	---	---
1,2,3,7,8,9-HxBrDD	< 0.1	---	68
1,2,3,7,8-PeBrDF	0.09	---	86
Sum Group V	< 0.39	---	---
-Sum Group IV + V	< 0.92	---	5.0

Institut Fresenius Chemische und Biologische Laboratorien GmbH

FR-613
Polybrominated Dibenzodioxins and Dibenzofurans
Contamination according to TSCA
Sample Description: FR-613
Date of Report: 29th August, 1991

	Measurement (ug/kg)	EPA LOQs Requirement (ug/kg)	Recovery Rate(%)
-Polybrominated Dibenzodioxins			
2,3,7,8-TBrDD	0.03	0.1	88
1,2,3,7,8-PeBrDD	0.08	0.5	129
1,2,3,4,7,8-HxBrDD	< 0.1	2.5	---
1,2,3,6,7,8-HxBrDD	< 0.1	2.5	---
1,2,3,7,8,9-HxBrDD	< 0.1	2.5	68
1,2,3,4,6,7,8-HpBrDD	< 0.2	100	---
-Polybrominated Dibenzofurans			
2,3,7,8-TBrDF	0.37	1	80
1,2,3,7,8-PeBrDF	0.09	5	86
2,3,4,7,8-PeBrDF	< 0.05	5	86
1,2,3,4,7,8-HxBrDF	< 0.1	25	---
1,2,3,6,7,8-HxBrDF	< 0.1	25	---

1,2,3,7,8,9-HxBrDF	< 0.1	25	---
2,3,4,6,7,8-HxBrDF	< 0.1	25	---
1,2,3,4,6,7,8-HpBrDF	< 0.2	1000	---
1,2,3,4,7,8,9-HpBrDF	< 0.2	1000	---

Institut Fresenius Chemische und Biologische Laboratorien GmbH

04.08.2003 (19)

Memo : Transportation in Japan

Remark : This substance is normally transported from the producer to the downstream user in form of pellets in Japan.

Flag : Critical study for SIDS endpoint

02.12.2003 (49)

Remark : Disposal Considerations:The product can be disposed of by dissolving or mixing the material with a combustible solventand burning it in a chemical incinerator equipped with an afterburner.The disposal should comply with all federal,
state and local environmental regulations.

02.12.2003

1.12 LAST LITERATURE SEARCH

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

Remark : ACGIH
AQUIRE (CIS, STN)
BEILSTEIN (STN)
BIOSIS (STN, Dialog)
CHEMCATS (STN)
CHRIS (CIS, CHEM-BANK)
CSCHEM (STN)
ChemFinder
ECDIN
GMELIN (STN)
HODOC(STN)
HSDB (CIS, STN, DataStar, CHEM-BANK)
IARC
IRIS (CIS, CHEM-BANK)
IUCLIDMSDS-CCOHS (STN, Dialog)
MEDLINE (STN, Dialog, Datastar)
MSDS-OHS (STN)
NCI
NIOSHOHMTADS (CIS, CHEM-BANK)
NIOSHTIC(STN, Dialog)
PROMT(STN, Dialog)
REGISTRY (STN, Dialog)
RTECS(STN, CIS, Dialog, CHEM-BANK)
SPECINFO (STN)
SRC PhysPro Database(SRC: Syracuse Research Corporation)
TOXCENTER (STN)
TOXFILE (Dialog, Datastar)

TSCATS (CIS)

Date of the literature search: 15 July, 2003

02.12.2003

1.13 REVIEWS

2.1 MELTING POINT

Value : 93.9 °C

Remark : quotation: information of MSDS, Wako Pure Chemical Industry, Lot No.: JPH9500, purity = 99.7%
Reliability : (2) valid with restrictions
Flag : Critical study for SIDS endpoint
02.12.2003 (6)

Value : 94 - 96 °C

Reliability : (4) not assignable
04.08.2003 (2)

Value : 93 °C
Sublimation :
Method : other
Year : 1988
GLP : no
Test substance :

Remark : The product was examined in-house, according to method No- 410 developed by BCL R&D division.
Reliability : (4) not assignable
04.08.2003 (13)

2.2 BOILING POINT

Value : 282 - 290 °C at 994.585 hPa
Decomposition :
Method : other
Year : 1985
GLP : no data
Test substance :

Remark : TBP decomposes at 125 degrees C.
Reliability : (4) not assignable
04.08.2003 (8) (71)

Value : 290 °C at
Decomposition :
Method : other
Year :
GLP : no data
Test substance : other TS: Wako pure Chemical Industries, Ltd. purity = 98%

Reliability : (4) not assignable
04.08.2003 (74)

Value : = 244 °C at

Remark : quotation: The Merck Index - An Encyclopedia of Chemicals, Drugs, and Biologicals. Whitehouse Station, NJ, Merck and

Co., Inc., No. 9687 (2001)
Reliability : (2) valid with restrictions
Flag : Critical study for SIDS endpoint
02.12.2003 (2)

2.3 DENSITY

Type :
Value : = 2.55 g/cm³ at 20 °C

Remark : quotation: The Merck Index - An Encyclopedia of Chemicals, Drugs, and Biologicals. Whitehouse Station, NJ, Merck and Co., Inc., No. 9687 (2001)
Reliability : (2) valid with restrictions
Flag : Critical study for SIDS endpoint
02.12.2003 (2)

Type : relative density
Value : 2.55 g/cm³ at 20 °C
Method : other
Year : 1991
GLP : no data
Test substance :

Reliability : (2) valid with restrictions
02.12.2003 (9)

Type : relative density
Value : 2.55 g/cm³ at °C
Method : other
Year :
GLP : no data
Test substance : other TS: Wako pure Chemical Industries, Ltd. purity = 98%

Reliability : (2) valid with restrictions
02.12.2003 (74)

2.3.1 GRANULOMETRY

2.4 VAPOUR PRESSURE

Value : .00042 hPa at 25 °C
Decomposition :
Method : OECD Guide-line 104 "Vapour Pressure Curve"
Year : 1999
GLP : yes
Test substance : other TS

Method : n=3
rate of flow :20 - 40mL/min
collection vehicle: acetonitrile
carrier gas: N2 gas (99.99%)
test temperature: 40, 50, 60 degree C
Test substance : purchase: WAKO Chemical LTD
Purity: 99.7 %

Lot No. : K-492
Reliability : (2) valid with restrictions
Flag : Critical study for SIDS endpoint
02.12.2003 (6)

2.5 PARTITION COEFFICIENT

Partition coefficient :
Log pow : = 3.89 at 25 °C
pH value :
Method : OECD Guide-line 107 "Partition Coefficient (n-octanol/water), Flask-shaking Method"
Year : 1999
GLP : yes
Test substance : other TS: Wako Pure Chemical Industry, Ltd. Lot No.: JPH9500, purity = 99.7%

Method : Volume of test substance: 5.99mg

Condition to measure:
water(saturated)-1-octanol layer and
1-octanol(saturated)-waterlayer:
condition 1; 5 and 30
condition 2;10 and 25
condition 3; 20 and 15

25 plus or minus 1 degree, 20 cycle/minute, 5 minutes, n=2

Analysis: HPLC
Result : condition 1: 3.96
condition 2: 3.90
condition 3: 3.82
mean = 3.89
SD = 0.07

pH of water layer: 6.1 - 6.5
Reliability : (2) valid with restrictions
Flag : Critical study for SIDS endpoint
02.12.2003 (6)

Partition coefficient :
Log pow : = 3.7 at °C
pH value :
Method : OECD Guide-line 117 "Partition Coefficient (n-octanol/water), HPLC Method"
Year : 1992
GLP : yes
Test substance :

Method : -HPLC method:
Using 75/25 (v/v) methanol/phosphate buffer pH 2 as the mobile phase, a 125 mm LiChrospher 100 RP-18 column (Merck) and a spevtrophotometric detector set to read the absorbance at TBP. Pow = 4.6X10E3 (log Pow = 3.7). The temperarture fo the mobile phase was 23.5 plus or minus 0.5 degree C during the test.
Conclusion : The results of the Calculation method and the HPLC are not in agreement . Since the HPLC method is more accurate

method
than the Calculation method, the result of HPLC method is reported as the partition coefficient (n-octanol/water), Pow, TBP.

Reliability : (2) valid with restrictions
02.12.2003 (13)

Partition coefficient :
Log pow : = 4.3 at °C
pH value :
Method :
Year : 1992
GLP :
Test substance :

Remark : -Calculation method:
Rekker calculation method (Pow): From the structural formula of TBP, the Pow was calculated to be 2.2X10E4 (Log Pow = 4.3).
Perrin's calculation method (pKa): From the structural formula of TBP, the pKa value for the acidic group was calculated to be 6.3.
Reliability : (2) valid with restrictions
02.12.2003 (13)

Partition coefficient :
Log pow : = 4.18 at °C
pH value :
Method : other (calculated)
Year : 2003
GLP : no
Test substance :

Remark : calculated using: KOWWIN version 1.66 - 2000U.S. Environmental Protection Agency
Reliability : (2) valid with restrictions
02.12.2003

Partition coefficient :
Log pow : = 4.13 at °C
pH value :
Method : other (calculated)
Year :
GLP :
Test substance :

Reliability : (2) valid with restrictions
02.12.2003 (39)

2.6.1 SOLUBILITY IN DIFFERENT MEDIA

Solubility in :
Value : 59 mg/l at 25 °C
pH value :
concentration : at °C
Temperature effects :
Examine different pol. :

pKa : at 25 °C
Description :
Stable :
Deg. product :
Method : OECD Guide-line 105
Year : 1999
GLP :
Test substance : other TS: Wako Pure Chemical Industry, Ltd. Lot No.: JPH9500, purity = 99.7%

Remark : 25 degree plus or minus 1 degree
Result : 24h: 57 mg/L
48h: 61 mg/L
72h: 58 mg/L

Mean: 59 mg/L
Reliability : (1) valid without restriction
Flag : Critical study for SIDS endpoint
02.12.2003 (6)

Solubility in :
Value : at °C
pH value :
concentration : 10 mg/l at 25 °C
Temperature effects :
Examine different pol. :
pKa : 5.97 at 25 °C
Description :
Stable :
Deg. product :
Method : other: OECD Guide-line 112
Year : 1999
GLP :
Test substance : other TS: Wako Pure Chemical Industry, Ltd. Lot No.: JPH9500, purity = 99.7%

Remark : 25 degree plus or minus 1 degree
n=3
Result : pKa: 5.95, 5.97, 5.99
mean: 5.97
Reliability : (1) valid without restriction
Flag : Critical study for SIDS endpoint
02.12.2003 (6)

Solubility in :
Value : = 50 mg/l at 19 °C
pH value :
concentration : at °C
Temperature effects :
Examine different pol. :
pKa : at 25 °C
Description :
Stable :
Deg. product :
Method : OECD Guide-line 105
Year : 1998
GLP : yes
Test substance :

Reliability : (2) valid with restrictions

02.12.2003 (16)

Solubility in :
Value : at °C
pH value :
concentration : at °C
Temperature effects :
Examine different pol. :
pKa : 6 at 25 °C
Description :
Stable :
Deg. product :
Method :
Year : 1988
GLP : no data
Test substance :

Reliability : (4) not assignable
02.12.2003 (45)

Solubility in :
Value : = 70 mg/l at 15 °C
pH value :
concentration : at °C
Temperature effects :
Examine different pol. :
pKa : at 25 °C
Description :
Stable :

Reliability : (4) not assignable
02.12.2003 (81)

2.6.2 SURFACE TENSION

2.7 FLASH POINT

2.8 AUTO FLAMMABILITY

2.9 FLAMMABILITY

Result : non flammable
Method : other
Year : 1991
GLP : no
Test substance :

Remark : HAZARDLINE, Oct 1991, AN: 3670.
DSBG/ Bromine Compounds Ltd.

10.06.2003

2.10 EXPLOSIVE PROPERTIES

Remark : Not applicable on the basis of TBP structure and physical properties nor is it known to contribute explosive properties with other materials.

10.06.2003

2.11 OXIDIZING PROPERTIES

Remark : Not applicable due to the physical nature of the substance.

10.06.2003

2.12 DISSOCIATION CONSTANT

2.13 VISCOSITY

2.14 ADDITIONAL REMARKS

Memo : Henry's law constant

Result : 4.77 X 10E-8 atm-m3/mole
Method: Calculated
Calculated using HENRYWIN version 1.90 - 2000 U.S. Environmental Protection Agency, Syracuse Research Co.

Reliability : (2) valid with restrictions

Flag : Critical study for SIDS endpoint

11.07.2003

Remark : Soluble in most organic solvents:chloroform, diethyl ether, ethanol, glycerol.

(70)

Remark : Soluble in alcohol, chloroform, ether, and caustic alkaline solutions.

10.06.2003

(68)

3.1.1 PHOTODEGRADATION

Type	:	air
Light source	:	other: UV light (Chromato-Vue TLC viewing box, Ultra-Violet Products, Inc.)
Light spectrum	:	nm
Relative intensity	:	based on intensity of sunlight
DIRECT PHOTOLYSIS		
Halflife t1/2	:	= 4.6 hour(s)
Degradation	:	% after
Quantum yield	:	
Deg. product	:	
Method	:	other (calculated): not reported
Year	:	
GLP	:	no data
Test substance	:	other TS: 14-C 2,4,6-Tribromophenol.
Method	:	Photolysis of 14-C 2,4,6-tribromophenol was conducted on silica gel G TLC plates under UV light.
Remark	:	Deg. Product: 2,6-debromo-3,5-dihydroxy-p-quinoimine
Result	:	The half-life of tribromophenol under these conditions was 4.6 hours. A degradation product was tentatively identified as 2,6-dibromo-3,5-dihydroxy-p-quinoimine by mass spectrometry.
Source	:	U.S. EPA Challenge Program: 201-14177A (2002)
Reliability	:	(2) valid with restrictions
Flag	:	Critical study for SIDS endpoint

06.08.2003 (73)

Type	:	air
Light source	:	
Light spectrum	:	nm
Relative intensity	:	based on intensity of sunlight
INDIRECT PHOTOLYSIS		
Sensitizer	:	OH
Conc. of sensitizer	:	1500000 molecule/cm³
Rate constant	:	= .000000000000475 cm³/(molecule*sec)
Degradation	:	= 50 % after 22.5 day(s)
Deg. product	:	
Method	:	other (calculated)
Year	:	2003
GLP	:	no
Test substance	:	
Remark	:	calculated using: AOPWIN version 1.90 - 2000 U.S. Environmental Protection Agency
Reliability	:	(2) valid with restrictions

02.12.2003 (53)

3.1.2 STABILITY IN WATER

Type	:	abiotic
t1/2 pH4	:	at °C
t1/2 pH7	:	at °C
t1/2 pH9	:	at °C
Deg. product	:	
Method	:	OECD Guide-line 111 "Hydrolysis as a Function of pH"

Year : 1999
GLP :
Test substance : other TS: Wako Pure Chemical Industry, Ltd. Lot No.: JPH9500, purity = 99.7%

Method : -Preliminary Test
a) Water Temperature: 50 degree C
b) Nominal Concentration: ca. 20 mg/L
c) pH: pH4, 7 and 9
d) Number of Replicates: 2
e) Test Period: 5 days
f) Exposure Vessel Type: Glass Vial

Result : As a result of the preliminary test, this chemical was not hydrolyzed in 5 days on condition of 50 plus or minus 1 degree C, pH 4, 7 and 9.

Reliability : (2) valid with restrictions
Flag : Critical study for SIDS endpoint
02.12.2003 (6)

Remark : 2,4,6-Tribromophenol is not expected to undergo hydrolysis in the environment due to the lack of hydrolyzable functional groups.

Reliability : (4) not assignable
02.12.2003 (47)

3.1.3 STABILITY IN SOIL

3.2.1 MONITORING DATA

Remark : The other monitoring Data is described in 3.8 (Additional Remarks).
10.06.2003

Type of measurement : other
Media : other
Concentration :
Method : GLP

Result : The production site, purification center discharge underwater TBP after examining analysis, the TBP concentrations which are in the midst of the draining are measured. Manac Inc. Minooki Plant, Hiroshima, JapanAnalysis Results:

adoption date	Production Site discharge water			Purification center discharged water		
2002	11/30	12/13	12/26	11/30	12/13	12/26
TBPconcentration (ug/L)	6.1	33	5.2	BDL	BDL	BDL

BDL: below detection limit (less than 1ug/L)

Reliability : (1) valid without restriction
Flag : Critical study for SIDS endpoint
11.07.2003 (50)

3.2.2 FIELD STUDIES

3.3.1 TRANSPORT BETWEEN ENVIRONMENTAL COMPARTMENTS

3.3.2 DISTRIBUTION

Media : air - biota - sediment(s) - soil - water
Method : Calculation according Mackay, Level III
Year : 2002

Method : Distributions were calculated with following factors.
2,4,6-tribromophenol
Molecular Weight: 330.8
Melting Point [degree C]: 93.9
Vapor Pressure [Pa]: 0.042
Water Solubility [g/m3]: 59
log Kow: 3.89
half life [h] in air: 4.6
in water: 1,200
in soil: 1,200
in sediment: 3,600
Temp. [degree C]: 25

Remark : It was calculated using the default value according to the manual, presented by CITI Japan.

Result : The potential environmental distribution of 2,4,6-tribromophenol obtained from generic level III fugacity model under three emission scenarios is shown in table. The results show that if 2,4,6-tribromophenol is released into air and soil, this chemical is not transported into the other compartment. When TBP is released to water, 92.1% stays in water and 7.0% is transported to sediment.

Compartment	Amount %		
	Release 100% to air	Release 100% to water	Release 100% to soil
Air	29.2%	0.0%	0.0%
Water	21.4%	92.9%	0.1%
Soil	47.8%	0.0%	99.9%
Sediment	1.6%	7.1%	0.0%

Reliability : (2) valid with restrictions
Flag : Critical study for SIDS endpoint
02.12.2003

3.4 MODE OF DEGRADATION IN ACTUAL USE

3.5 BIODEGRADATION

Type : aerobic
Inoculum : predominantly domestic sewage, non-adapted

Contact time	:	
Degradation	:	49 (±) % after 28 day(s)
Result	:	
Deg. product	:	
Method	:	other: equivalent of OECD TG 301 C
Year	:	1981
GLP	:	
Test substance	:	other TS: Tokyo Kasei Kogyo Co., Ltd., purity >= 98%
Remark	:	The degradation curve was on the upward trend.
Result	:	Three replicated Value: 47, 66, 33 Mean: 49
Test condition	:	Inoculum added: 30 mg/l; BOD measurement. The inoculum was a mixture of activated sewage whose source was collected from ten different sites in Japan. Water Temperature: 25 plus or minus 1 degree C Test period: 28 days Activated Sludge Concentration: 30 ppm Test Substance Concentration: 100 ppm
Reliability	:	(2) valid with restrictions
Flag	:	Critical study for SIDS endpoint

02.12.2003 (5)

Type	:	
Inoculum	:	Pseudomonas sp. (Bacteria)
Concentration	:	200 mg/l related to Test substance related to
Deg. product	:	
Method	:	
Year	:	
GLP	:	
Test substance	:	as prescribed by 1.1 - 1.4
Remark	:	Degradation by pseudomonas sp. 200 mg/l at 30 celsius degree, 14% ring disruption in 120 hr by parent strain, 92% ring disruption by mutant in 42 hr.
Reliability	:	(4) not assignable

04.08.2003 (69)

Type	:	anaerobic
Inoculum	:	anaerobic bacteria
Deg. product	:	
Method	:	other
Year	:	1995
GLP	:	
Test substance	:	
Remark	:	AB: An anaerobic 2,4,6- Tribromophenol debrominating bacterium, strain DSL-1, was isolated from enrichment cultures inoculated with sediments from burrows of the bromoarom-producing marine hemichordates Balanoglossus aurantiacus and Saccoglossus Kowalewsky. DSL-1 preferentially removed ortho-position bromines, resulting in the transient appearance of 2,4- dibromophenol and accumulation of 4-bromophenol. Cell-free exts. and partially purified reductive debrominase prepns. from DSL-1 also debrominated 2,4,6- Tribromophenol, yielding 2,4-dibromophenol and 4-bromophenol. Both NADH and NADPH stimulated 2,4,6-Tribromophenol redn. by partially purified

debrominase. These data are consistent with a reductive debromination mechanism. The org. cosubstrate and specific electron donors used by DSL-1 in vivo are currently unknown.

Reliability : (2) valid with restrictions
02.12.2003 (66)

Type : anaerobic
Inoculum : anaerobic sludge
Deg. product :
Method :
Year :
GLP : no data
Test substance : as prescribed by 1.1 - 1.4

Remark : AB:Halogenated phenols were added to three anoxic marine sediments samples which were incubated under different conditions. The concentration of the halogenated phenols were monitored throughout the experiment in order to study their degradation. The results were the following:
1. The main degradation pathway was progressive dehalogenation.The dehalogenation order was ortho >para > meta.
2. Between 6 and 30 C the dehalogenation rate increase for all the substances, while a further increase in temperature resulted in a decrease of dehalogenation rate.
3. Bromophenols were degraded faster than chlorophenols.
4. Sediment which had been exposed to effluent water from a paper and pulp mill showed a higher dehalogenation potential.
5. The results indicate that microorganism associated to particles are responsible for the dehalogenation.

Reliability : (4) not assignable
02.12.2003 (11)

3.6 BOD5, COD OR BOD5/COD RATIO

3.7 BIOACCUMULATION

Species : Brachydanio rerio (Fish, fresh water)
Exposure period : at °C
Concentration :
BCF : 513
Elimination :
Method :
Year : 1996
GLP : no data
Test substance :

Reliability : (2) valid with restrictions
Flag : Critical study for SIDS endpoint
08.08.2003 (12)

Species : Petromyzon fluviatilis
Exposure period : 32 day(s) at 25 °C
Concentration :
BCF : 83
Elimination :

Method :
Year : 1980
GLP : no data
Test substance :

Reliability : (2) valid with restrictions
Flag : Critical study for SIDS endpoint
02.12.2003 (65)

Species : Lepomis macrochirus (Fish, fresh water)
Exposure period : 28 day(s) at °C
Concentration : .0092 mg/l
BCF : = 20
Elimination :
Method : other: not reported
Year :
GLP : no data
Test substance : other TS: 14-C 2,4,6-Tribromophenol.

Method : The bluegill sunfish, Lepomis macrochirus, was exposed 2,4,6-tribromophenol in a flow-through bioassay system. The compound was labeled with carbon-14 in the aromatic ring. Exposure was for a period of 28 days at 0.0092 ppm. This was followed by a 14 day withdrawal phase. Samples of water and both edible tissue and viscera of the fish were collected during the study for radiocarbon analysis.
Result : Bioaccumulation in the edible tissue was 20 fold over the 14-C concentration in the water while bioaccumlation in the viscera was 140 fold. These plateau levels in the both edible tissue and viscera were reached 3-7 days of beginning the exposure phase. Once the withdrawal phase had begun, the half-life for radiocarbon residues in the fish was less than 24 hours (both edible tissue and viscera).
Source : U.S. EPA Challenge Program: 201-14177A (2002)
Reliability : (2) valid with restrictions
Flag : Critical study for SIDS endpoint
02.12.2003 (67)

Elimination :
Method : other: calculated
Year : 2003
GLP :
Test substance :

Remark : calculated using: BCFWIN version 2.14 - 2000 U.S. Environmental Protection Agency
Result : Log BCF = 2.080, BCF = 120.3
Reliability : (2) valid with restrictions
Flag : Critical study for SIDS endpoint
02.12.2003

Elimination :
Method : other
Year :
GLP :
Test substance :

Remark : The carcass and gut contents of 10 species of fish caught along the eastern coast of Australia were analyzed by gas chromatograph multiple ion detection -mass spectrometry for

a range of bromophenols, including 2- and 4-bromophenol,2,4- and 2,6- dibromophenol and 2,4,6-Tribromophenol. These bromophenols, the cause of iodoform-like off-flavors in seafoods, were found in eight of the above species; the largest total concentration of bromophenols occurred in the com. important species Nemadactylus douglasii (40 ng/g). The concns. of bromophenols in another three species, were found to exceed 10 ng/g while in a further four species their concens. varied between 3 and 8 ng/g. The variations among fish diets suggest that the bromophenol content of individual fish can be explained by the relative contribution of benthic organisms and marine algae to the fish diet. Bromophenols were found in all of the benthic carnivores and diverse omnivores examd. but were not detected in pelagic carnivorous fish.

Reliability : (3) invalid
11.07.2003 (76)

3.8 ADDITIONAL REMARKS

Memo : Origin of Bromophenols in the natural Diets of Ocean Fish

Result : Four species (Platycephalus caeruleopunctatus, Centroberyx affnis, Platycephalus mamoratus, and Platycephalus arenarius) occasionally feed on polychaetes, benthic animals that are known to biosynthesize bromophenols.
Reliability : (2) valid with restrictions
Flag : Critical study for SIDS endpoint
05.08.2003 (4) (40)

Remark : AB: Endeavour prawns from Exmouth Gulf, Shark Bay, and Groote Elylandt, Australia, contained 2,4,6-tribromophenol at concentrations of 41 to 97, 7.8, and 8.5 ug/kg, respectively. Ten different species of fish, collected in August 1992 from the eastern coast of Australia, contained 2,4,6-tribromophenol at concentrations of <0.05 to 3.4 ng/g for the carcass and <0.05 to 170 ng/g for the whole gut (analysis of single fish from each species). Samples of ocean fish were supplied by the state department of New South Wales Fisheries and caught off the coast of New South Wales during August and September 1994 and 1995. Ocean fish were separated by species into pelagic carnivores, benthic carnivores, diverse omnivores and restricted omnivores; concentrations in the flesh ranged from <0.01 to 0.9 ng/g, <0.01 to 12 ng/g, <0.01 to 4.3 ng/g, and 0.1 to 1.4 ng/g, respectively, while concentrations in the gut ranged from <0.01 to 11 ng/g, <0.01 to 230 ng/g, 0.04 to 55 ng/g, and 7 to 45 ng/g, respectively. Thirty samples of 9 species of prawns, collected from the eastern coast of Australia from 1993 to 1996, contained 2,4,6-tribromophenol at concentrations of <0.01 to 170 ng/g. 2,4,6-Tribromophenol concentrations in cultivated prawns ranged from <0.01 to 0.53 ng/g.
Reliability : (2) valid with restrictions
Flag : Critical study for SIDS endpoint
10.06.2003 (77) (78) (79) (80)

Remark : AB: 2,4,6-Tribromophenol was monitored in 40 potable water treatment plants in Canada; mean concentrations for October/December 1984, February/March 1985, and May/June 1985 were 0.6 and 1.3 (raw water and treated water, respectively), 0.2 and 0.2, and 0 and 0.5 ng/l, respectively.
Reliability : (2) valid with restrictions
Flag : Critical study for SIDS endpoint
10.06.2003 (63)

Remark : AB: Raw water from water treatment plants in 6 Canadian cities and treated water from water treatment plants in 5 of 6 Canadian cities, collected in February 1985, contained 2,4,6-tribromophenol at concentrations below the quantitation limit; one sample of treated water contained 2,4,6-tribromophenol at 5 ng/l.
Reliability : (2) valid with restrictions
Flag : Critical study for SIDS endpoint
10.06.2003 (64)

Remark : AB: The raw flue gas from a Swedish hazardous waste incinerator, located at Norrtorp, and fed chlorinated (mainly solvents) and brominated waste (tetrabutylammonium bromide) contained 2,4,6-tribromophenol at <14, 380, and 260 ng/cu m over three tests; bromides were present initially at 32, 110, and 530 mg/cu m . Flue gas from this incinerator, fed municipal waste, contained 2,4,6-tribromophenol at 4-5 ng/cu m. Peat combustion released 2,4,6-tribromophenol at concentrations of <5 to 60 ng/cu m.
Reliability : (2) valid with restrictions
Flag : Critical study for SIDS endpoint
10.06.2003 (57)

Remark : AB: Upper river and marine sediment layers in Osaka Prefecture, Japan, collected in 1981 through 1983 at 12 different locations. 2,4,6-tribromophenol was detected in sediment in 10 sites at 0.8 - 36 ug/kg (dry weight basis).
Reliability : (2) valid with restrictions
Flag : Critical study for SIDS endpoint
10.06.2003 (75)

Remark : AB: Surficial sediments from the Rhone estuary, collected in 1987/1988, contained 2,4,6-tribromophenol at concentrations of 26 to 3690 ng/g, dry weight basis, from 5 sampling sites.
Reliability : (2) valid with restrictions
Flag : Critical study for SIDS endpoint
10.06.2003 (72)

Remark : AB: Concentrations of 2,4,6-tribromophenol were measured in brown algae (14 to 38 ug/kg wet weight), red algae (4.5 to 68 ug/kg), bryozoa (24 and 27 ug/kg), a hydroid (29 ug/kg), and sponges (0.22 to 240 ug/kg) collected from Exmouth Gulf,

Australia, in October 1990.
Reliability : (2) valid with restrictions
Flag : Critical study for SIDS endpoint
10.06.2003 (80)

Remark : AB: Saitama prefectural government have monitored 2,4,6-tribromophenol concentration in river water in Saitama prefecture, Japan. 2,4,6-tribromophenol was detected 4 of 6 rivers water in 1994 and the maximum concentration was at 0.27 ug/L. 2,4,6-tribromophenol was detected in 3 out of 6 industrial liquid waste in the Saitama prefecture in 1996 and 2 out of 8 industrial liquid waste in the Saitama prefecture in 1997 and the maximum concentration of 2,4,6-tribromophenol was 0.076 ug/L and 0.078 ug/L, respectively.
Reliability : (2) valid with restrictions
Flag : Critical study for SIDS endpoint
10.06.2003 (60) (61)

Remark : AB: 2,4,6-triboromophenol concentration in water and sedimetnt in 11 non-industrial sites in Japan was monitored in 1986 and 1996 by Environmental Agency of Japan. Sediment in 1 site, collected in 1986, contained 2,4,6-tribromophenol at 0.0015 - 0.004 ppm. 2,4,6-tribromopenol was not detected in the other samples.
Reliability : (2) valid with restrictions
Flag : Critical study for SIDS endpoint
10.06.2003 (3)

Remark : AB: The formation of 2,4,6-Tribromophenol results from the chlorination of water containing phenol and Br at pH 7.4. Direct bromination with hypobromous acid is compared with bromination by hypochlorous acid and Br-. Under conditions where HOCL is not limiting, a higher yield of Br substitution products can be expected from bromination by HOCL + Br- than by direct bromination by HOBr.
(26)

Remark : AB: Brominated and nitrated phenols were positively identified for the first time in estuarine sediments (Rhoneestuary -France). 2,4,-Dibromophenol, 2,4,6-Tribromophenol and 2- nitrophenol were the major components present, exhibiting concentrations in the range of 7-5850 ng g-1. The analysis of sediment extracts by CGC-MS in the negative ion chemical ionization (NICI) mode allowed also the identification of a series of bromochloro, dibromochloro, and bromodichloro-nitrophenol and their alkylated derivatives. The observed seaward negative gradient of concentrations, suggests a land -based discharge as the principal source, probably originated in automobile emissions which are wash-out to the riverine streams by urban runoff. However, their precise origin remains to be identified.
11.07.2003 (52)

Remark : AB: Synthetic bromophenols were added to natural sediments at field concns. and the responses of recently settled juveniles of 2 bivalve and 1 polychaete infaunal species were obsd. Fifty and 67% of the bivalve juveniles burrowed into this contaminated sediments . The arenicolid polychaete juveniles burrowed into the sediments, but the rate was slower than in control sediments.

(51)

4.1 ACUTE/PROLONGED TOXICITY TO FISH

Type	:	semistatic
Species	:	Oryzias latipes (Fish, fresh water)
Exposure period	:	96 hour(s)
Unit	:	mg/l
LC0	:	= 1
LC50	:	= 1.5
LC100	:	= 3.2
Limit test	:	
Analytical monitoring	:	yes
Method	:	OECD Guide-line 203 "Fish, Acute Toxicity Test"
Year	:	2000
GLP	:	yes
Test substance	:	other TS: Wako Pure Chemical Industries, Ltd., Lot. No.; JPH9500, Purity = 99.7 %

Method :

-Test Organisms:
a) Supplier: Test organisms(Lot. No.; F039811) were obtained from Takizawa Yougyo-jo (Fish Farm, Japan) and reproduced by the testing laboratory.
b) Size (length and weight): 2.2 cm (2.1 - 2.3 cm) in length; 0.15 g (0.12 - 0.20 g) in weight
c) Age: Not described
d) Any pretreatment: Acclimated for at least 7 days before testing, any groups showing < 5 % mortality were not used for testing. During acclimination, test fish were fed with TETRAMINE. These test organisms were not fed for 24 hours before the test started.

-Test Conditions:
a) Dilution Water Source: Dechlorinated tap water (Tokyo, Japan)
b) Dilution Water Chemistry: pH: = 7.7
Total hardness (as CaCO3): = 53 mg/L
c) Exposure Vessel Type: 3 L test solution in a 5 L Glass Tank
d) Nominal Concentrations: control, solvent control, 0.32, 0.56, 1.0, 1.8 and 3.2 mg/L
e) Stock Solutions Preparations and Stability: 2,4,6-tribromophenol was dissolved in Dimethyl Sulphoxide, polyoxyethylene sorbitan fatty acid ester solution.
f) Vehicle/Solvent and Concentrations: Dimethyl sulphoxide and polyoxyethylene sorbitan fatty acid ester were used for solvent. At the maximum, 32 mg/L solvent could be contained in the test solutions.
g) Number of Replicates: duplicate
h) Fish per Replicates: 5 fishes per replicate
i) Renewal Rate of Test Water: Every 24 hours
j) Water Temperature: 24±1ºC
k) Light Condition: 16:8 hours, light-darkness cycle
l) Feeding: None
m) Aeration : None

-Methods of Analysis:
About all concentration divisions, before an exposure start and exchange (24 hours after), proper quantity extraction of the sample was carried out from the examination tank (2/ concentration division) of each concentration division, and

equivalent mixture was carried out and it considered as the liquid for analysis of 100mL(s). It measured by HPLC It computed from the peak area ratio.

-Statistical Method:
a) Data Analysis: Binominal method for LC50
b) Method of Calculating Mean Measured Concentrations (i.e. arithmetic mean, geometric mean, etc.): Time-weighted mean

Result : - Measured Concentrations : The test concentrations were measured at the start and the 24th hour(before exchange of test solution). All of them, the deviation from the nominal were less than ± 20%.

Nominal Conc., mg/L	Measured Conc., mg/L			Percent of Nominal Conc.	
mg/L	0 Hour Fresh	24 Hours Old	Mean mg/L	0 Hour Fresh	24 Hours Old
Control	<0.002	<0.002	---	---	---
Solv. Cont.	<0.002	<0.002	---	---	---
0.32	0.332	0.267	0.300	104	83
0.56	0.571	0.477	0.523	102	85
1.0	1.10	0.891	0.992	110	89
1.8	1.87	1.68	1.77	104	93
3.2	3.37	3.16	3.26	105	99

Fresh: Start of renewal period
Old: End of renewal period
Mean: Time weighted mean

- Water chemistry (pH and DO) and temperature in test:
Water chemistry and temperature were measured for control and each concentration at the start of test and every 24 hours for fresh and old test solutions.
pH: 7.4 - 7.6
DO: 8.6 - 9.8 mg/L
Water Temperature: 23.3 - 24.3 degree C

-Effect Data(mortality):
LC50 (96hr) = 1.5 mg/L (nc)
LC0 (96hr) = 1.0 mg/L (nc)
LC100 (96hr) = 3.2 mg/L (nc)
nc: based on nominal concentration

- Cumulative Mortality: None of test organisms were killed during exposure period at control, solvent control, 0.32, 0.56 and 1.0 mg/L, however all test organisms were killed at 3.2 mg/L after 24 hours.

Nominal Conc.	Cumulative Number of Dead (Percent Mortality)			
mg/L	24hr	48hr	72hr	96hr
Control	0 (0)	0 (0)	0 (0)	0 (0)
Solv. Cont.	0 (0)	0 (0)	0 (0)	0 (0)
0.32	0 (0)	0 (0)	0 (0)	0 (0)
0.56	0 (0)	0 (0)	0 (0)	0 (0)
1.0	0 (0)	0 (0)	0 (0)	0 (0)

1.8 7 (70) 7 (70) 8 (80) 8 (80)
3.2 10 (100) 10 (100) 10(100) 10(100)

-Other Effect:Toxicological symptom was observed at 1.8mg/L (24, 48, 72 and 96 hour).

Nominal Conc. mg/L	Symptoms 24hr	48hr	72hr	96hr
Control	n	n	n	n
Solv. Cont.	n	n	n	n
0.32	n	n	n	n
0.56	n	n	n	n
1.0	n	n	n	n
1.8	le	le	le	le
3.2	a	---	---	---

n: No abnormalities are detected
le: Lethargy
a: No observation was made because all fish were died or killed.

- Calculation of toxic values: It was the nominal concentrations. The reason is that all deviations from the nominal were less than ± 20%.

Reliability : (1) valid without restriction
Flag : Critical study for SIDS endpoint
03.12.2003 (31)

Type : static
Species : Cyprinus carpio (Fish, fresh water)
Exposure period : 96 hour(s)
Unit : mg/l
NOEC : = .56 calculated
LC50 : = 1.1 calculated
NOEC : = .26 measured/nominal
LC50 : = 1.1 measured/nominal
Limit test :
Analytical monitoring : yes
Method : OECD Guide-line 203 "Fish, Acute Toxicity Test"
Year : 1998
GLP : yes
Test substance : as prescribed by 1.1 - 1.4

Remark : The purpose of the study was to evaluate the test substance for its ability to generate acute toxicity effects in Cyprinus carpio during an exposure period of 96 hours and, if possible, to determine the LC50 at all observation times. After a range-finding test, two definitive test were performed with carp exposed to concentrations ranging from 0.1 to 3.2 mg/l in a static system. Stock solutions were prepared in acetone and a solvent-control was included. Seven carp were exposed per concentration and a control test. During the first test aeration was introduced 24 hr of exposure, while the second study was performed without aeration. Samples for analysis were taken at the start and the end of the test. In the second samples were taken after 48 hr exposure. 2,4,6- Tribromophenol (FR-613) induced no effects in carp at or below nominal 0.56 mg/l.

Result :

parameter	First Study (mg/L) nomimal	First Study (mg/L) actual*	Second Study (mg/L) nomimal	Second Study (mg/L) actual*
LC50(24hr)	1.1(0.9-1.5)#	1.1	2.4	1.8
LC50(96hr)	1.1(0.9-1.5)#	1.1	1.3	1.0
NOEC	0.56	0.26	0.56	0.35

*: Average measured concentrations
#: Between brackets; 95 % confidence interval

Conclusion : Aeration of the test solutions in the first study did not induce a significant difference in mortality compared to non-aerated second study. Based on average measured concentrations the 96 hr - LC50 for carp exposed to TBP corresponded with ca. 1 mg/L.

Reliability : (2) valid with restrictions
Flag : Critical study for SIDS endpoint
16.07.2003 (14)

Type : flow through
Species : Pimephales promelas (Fish, fresh water)
Exposure period : 96 hour(s)
Unit : mg/l
LC50 : = 6.5 - 6.8
LC50(192hr) : = 4.5 - 4.9
LC50(48hr:static) : = 10
Method : other
Year : 1981
GLP : no data
Test substance : as prescribed by 1.1 - 1.4

Method : -Test Organisms:
a) Age: Laboratory-reared fathead minnows 30 - 35 days old were used.
b) Any pretreatment: Fish in the rearing system were fed live brine shrimp nauplii in excess until 12 - 24 th before testing.

-Test Conditions:
a) Dilution Water Source: Lake Superior water which was filtered through sand and then finally filtered by 5um cotton rope filters.
b) Exposure Vessel Type: 41L all glas aquaria
c) Dilution Factor: 0.6
d) Number of Replicates: duplicate
e) Fish per Replicates: 4 fish per tank
f) Renewal Rate of Test Water: Diluters were cycled at a rate sufficient to give 10 tank volumes/day.
g) Water Temperature: 25±2ºC
h) Light Condition: A constant 16-h photoperiod was used. Light was provided by a combination of fluorescent bulbs that produced 48 lumens at the water surface.
i) Feeding: None

-Methods of Analysis: The tested concentrations were measured daily by using the automated 3-methyl-2-benzothiazolone hydrazone method as modified by Gales (1975). Gales, M. E.: Analyst 100, 841 (1975).

-Statistical Method:
a) Data Analysis: Trimmed Spearman Karber method for LC50

Remark : Flow-through acute toxicity to fathead minnow was tested with a variety (12) of phenolic compds. including 2,4,6-Tribromophenol.

Result : (1st exp)
LC50 (96 hr) equal 6.5 mg/L, 5.0-8.3(95% confidence limits)
(2nd exp)
LC50 (96 hr) equal 6.8 mg/L, 4.7-9.8(95% confidence limits)
(1st exp)
LC50 (192 hr) equal 4.5 mg/L, 3.8-5.4(95% confidence limits)
(2nd exp)
LC50 (192 hr) equal 4.9 mg/L, 4.2-5.6(95% confidence limits)

These values were based on the nominal concentrations.

- Water chemistry (pH, DO, hardness and alkalinity) in test: Water chemistries were determined in each concentration at the beginning, middle and end of each 8-day test according to methods described by the American Public Health Association et al. (1971).
pH: 7.56 - 7.35
DO: 6.2 - 8.2 mg/L
hardness (as CaCO3): 43.3 - 48.5 mg/L
alkalinity (for control water as CaCO3): 38.0 - 44.3 mg/L

American Public Health Association, American Water Works Association and Water Pollution Control Federation: Standard method for the examination of water and wastewater. 13th ed. New York. 874p. (1971).

Reliability : (2) valid with restrictions
Flag : Critical study for SIDS endpoint
03.12.2003 (58)

Type : flow through
Species : Pimephales promelas (Fish, fresh water)
Exposure period : 96 hour(s)
Unit : mg/l
LC50 : = 6.25
Method :
Year : 1995
GLP : no data
Test substance : other TS: Aldrich Chemical Co. (Milwaukee, WI), purity >= 95%

Method : -Test Organisms:
a) Age: 26-34 day old (juvenile)

-Test substance: 2,4,6-tribromophenol
Purity: >=95 %

-Test Conditions:
a) Dilution Water Source: Lake Superior (sand filtration)
b) Dilution Water Chemistry: pH: = 7.8
Total hardness (as CaCO3): = 45 mg/L
Alkalinity (as CaCO3): = 42 mg/L
c) Nominal Concentrations: control and four or five concentrations
d) Number of Replicates: duplicate
e) Water Temperature: 25ºC

-Methods of Analysis: Toxicant concentrations in the test chambers were measured daily. Methods of chemical analysis included high-pressure liquid chromatography (HPLC) and

gas-liquid chromatography (GC).

Result : Mortalities were recorded daily, and estimates concentration of toxicant most likely to case 50% mortality (LC50) and their 95% cofidence limits were determined after 96 h of exposure from relationships fitted mathematically by the trimmed Spearman-Karber method.

Reliability : (2) valid with restrictions

Flag : Critical study for SIDS endpoint

03.12.2003 (1)

4.2 ACUTE TOXICITY TO AQUATIC INVERTEBRATES

Type : static
Species : Daphnia magna (Crustacea)
Exposure period : 48 hour(s)
Unit : mg/l
EC0 : = 1
EC50 : = 2.2
Analytical monitoring : yes
Method : OECD Guide-line 202
Year : 2000
GLP : yes
Test substance : other TS: Wako Pure Chemical Industries, Ltd., Lot. No.; JPH9500, Purity = 99.7 %

Method : - Test Organisms:
a) Age: < 24 hours old
b) Supplier/Source: Test organisms were obtained from National Institute for Environmental Studies (JAPAN) and had been reproduced in the testing laboratory for one year.
c) Any pretreatment: Parental daphnids were acclimated for at least 14 days on test condition before testing, any groups showing high mortality were not used for testing. During acclimination, test daphnids were fed with Chlorella vulgaris, 0.15 mg carbon/day/individual.

-Test Conditions:
a) Dilution Water Source: Dechlorinated tap water (Tsukuba city, Ibaraki, Japan).
b) Dilution Water Chemistry: pH: = 7.7
Total hardness (as CaCO3): = 72 mg/L
c) Exposure Vessel Type: 100 mL test solution in a 270 mL Vessel
d) Nominal Concentrations: control, solvent control, 1.0, 1.8, 3.2, 5.6, and 10 mg/L
e) Stock Solutions Preparations and Stability: 2,4,6-tribromophenol was dissolved in Dimethyl Sulphoxide, polyoxyethylene sorbitan fatty acid ester solution.
f) Vehicle/Solvent and Concentrations: Dimethyl sulphoxide and polyoxyethylene sorbitan fatty acid ester were used for solvent. At the maximum, 100 mg/L solvent could be contained in the test solutions.
g) Number of Replicates: 4
h) Individuals per Replicate: 5
i) Water Temperature: 20 plus or minus 1 degree C
j) Light Condition: 16:8 hours, light-darkness cycle
k) Feeding: None

-Methods of Analysis: Test concentrations were measured at

the start and the end of exposure (48 hours after).
Start of exposure: extraction of the sample (100 mL)
End of test: proper quantity extraction of the sample was carried out from the examination tank (2/concentration division) of each concentration division, and equivalent mixture was carried out and it considered as the liquid for analysis of 100mL(s).
It measured by HPLC It computed from the peak area ratio.

- Statistical Method:
a) Data Analysis: Binominal method for EC50
b) Method of Calculating Mean Measured Concentrations:Time-Weighted Mean

Result : - Measured Concentrations : The test concentrations were measured at the start and end of test. All of them, the deviation from the nominal were less than +/- 20%.

Nominal Conc., mg/L	Measured Conc., mg/L		Percent of Nominal Mean	
	0 Hour Fresh	48 Hours Old	0 Hour Fresh	48 Hours Old
Control	<0.002	<0.002	---	---
Solv. Cont.	<0.002	<0.002	---	---
1.0	1.12	1.03	1.07	112	103
1.8	1.87	1.87	1.80	104	96
3.2	3.44	3.18	3.31	108	99
5.6	6.08	5.88d	5.98	109	105d
10	10.6	10.1d	10.3	106	101d

Fresh: freshly prepared test solution
Old: test solution after 48 hours exposure
Mean: Mean mesured concentration (Time-weighted Mean)
d: Test solutions after 24 hours because all daphnids were dead at this period

- Water chemistry (pH and DO) and temperature in test:
Quality of test water and temperature were measured for control and each concentration at the start and end of the test.
pH: 7.6 - 7.7
DO: 8.8 - 9.0 mg/L
Water Temperature: 19.8 - 20.8 degree C

-Effect Data:
EC50 (24hr) = 3.9 mg/L (nc)
EC50 (48hr) = 2.2 mg/L (nc)
NOEC (48hr) = 1.0 mg/L (nc)
nc: based on nominal concentration

-Mortality or Immobility: No test organism was immobilized at control, solvent control, 1.0 and 1.5mg/L. The lowest concentration that the test organisms were affected was 1.9mg/L after 48 hours. All test organisms were affected at 3.2, 5.6 and 10.0 mg/L after 24th hour.

Nominal Conc.	Cumulative Number of Dead or Immobilized Daphnids (Percent Mortality or Immobility)

mg/L	24 Hour	48 Hour
Control	0 (0)	0 (0)
Solv. Cont.	0 (0)	0 (0)
1.0	0 (0)	0 (0)
1.8	0 (0)	4 (20)
3.2	3 (15)	20 (100)
5.6	20 (100)	20 (100)
10	20 (100)	20 (100)

- Calculation of toxic values: Based on the nominal concentrations. The reason is that all deviations from the nominal were less than +/- 20%.

Reliability : (1) valid without restriction
Flag : Critical study for SIDS endpoint
03.12.2003 (29)

Type : static
Species : Daphnia magna (Crustacea)
Exposure period : 48 hour(s)
Unit : mg/l
NOEC : = .1
EC50 : = .26 calculated
presolvent:acetone : < 100
Analytical monitoring : yes
Method : OECD Guide-line 202
Year : 1998
GLP : yes
Test substance : as prescribed by 1.1 - 1.4

Remark : Daphnia magna were exposed to 2,4,6-Tribromophenol for a maximum of 48 hours to a concentration ranging from 0.1 to 10 mg/l in a static system . Stock solutions were prepared in acetone and a solvent control was included. The test was performed in duplicate with 10 Daphnia per vessel. Samples for analyses were taken at 0.1, 1.0 and 10 mg/l at the start and at the end of the test. However, validity of statistical method employed for EC50 is questionable.

Result : concentration Number exposed Response: number immobile

mg/l		at 24 h	at 48 h
0	10	0	0
0	10	0	0
0 + acetone	10	0	0
	10	0	0
0.1	10	0	0
	10	0	0
0.22	10	0	0
	10	0	3
0.46	10	6	10
	10	1	10
1.0	10	7	10
	10	5	10

2.2	10	6	9	
	10	6	10	
4.6	10	10	10	
	10	9	10	
10	10	10	10	
	10	10	10	

.....

The 24h-EC50 was 1.0 mg/L (95% confidence interval between 0.6 and 1.9 mg/L).
The 48h-EC50 was 0.26 mg/L (95%confidence interval between 0.21 and 0.40 mg/L).
The 48h-NOEC was 0.10 mg/L and 24h-NOEC was 2.2 mg/L.

Test condition : Analytical recovery for nominal concentration for 0.1, 1, 10 mg/l were 115, 113, 96 % as averages of those at begining and the 48 hr after respectively. So nominal values were used through out the evaluation.
Reliability : (2) valid with restrictions
Flag : Critical study for SIDS endpoint
22.10.2004 (15)

Type : static
Species : Daphnia magna (Crustacea)
Exposure period : 48 hour(s)
Unit : mg/l
LC50 : = 1.31 measured/nominal
LC50 : = 1.14 calculated
Analytical monitoring : no
Method :
Year : 1975
GLP : no data
Test substance :

Method : - Test Organisms:
a) Age: 12±12 hours old

-Test Conditions:
a) Dilution Water Source: Non-filtered and non-chlorined Lake Superior water from the Duluth National Water Quality Laboratory was used for testing.
b) Exposure Vessel Type: 200 mL test solution in a Glass Beaker with a pane of glass.
c) Number of Replicates: 4
d) Individuals per Replicates: 20 daphnids per replicates (5 daphnids per beaker)
e) Water Temperature: 18±1ºC
f) Light Condition: 16:8 hours, light-darkness cycle
g) Feeding: Daphnia were fed a suspension of food (0.2mL/200mL) at the beginning of each test. The 48-h LC50 was estimated by using probit method.

Remark : The details are unknown.
Reliability : (4) not assignable
03.12.2003 (46)

4.3 TOXICITY TO AQUATIC PLANTS E.G. ALGAE

Species : Selenastrum capricornutum (Algae)
Endpoint : biomass

Exposure period	:	72 hour(s)
Unit	:	mg/l
NOEC	:	= .22
EC50	:	= .76
NOEC(gr,24-72h)	:	= 1
EC50(gr,24-48h)	:	= 1.1
EC50(gr,24-72h)	:	= 1.6
Limit test	:	
Analytical monitoring	:	yes
Method	:	OECD Guide-line 201 "Algae, Growth Inhibition Test"
Year	:	2000
GLP	:	yes
Test substance	:	other TS: Wako Pure Chemical Industries, Ltd., Lot. No.; JPH9500, Purity = 99.7 %

Method :

- Test Organisms:
a) Supplier/Source: Obtained from American Type Culture Collection
b) Method of Cultivation: Sterile
c) Stain Number: ATCC22622
d) Any pretreatment: Acclimated for 3 days before testing, any groups observed abnormal cells or cellular deformation were not used for testing.

- Test Conditions:
a) Medium: OECD medium
b) Exposure Vessel Type: 100 mL Medium in a 500mL Erlenmeyer flask with glass cap
c) Nominal Concentrations: control, solvent control, 0.10, 0.22, 0.46, 1.0, 2.2, 4.6 and 10mg/L
d) Vehicle/Solvent and Concentrations: Dimethyl sulphoxide and polyoxyethylene sorbitan fatty were used for solvent. 100 mg/L solvent was contained in each concentration.
e) Stock Solution: 2,4,6-tribromophenol was dissolved in Dimethyl Sulphoxide, polyoxyethylene sorbitan fatty solution.
f) Number of Replicates: 3
g) Initial Cell Number: 10,000 cells/mL
h) Water Temperature: 23±2ºC
i) Light Condition: 4,000 - 5,000 lux, continuously
j) Shaking: 100 rpm

- Methods of Analysis: Test concentrations were measured at the start and the 72nd hour. Start of exposure: extraction of the sample (100 mL)
End of test: proper quantity extraction of the sample was carried out from the examination tank (3/ concentration division) of each concentration division, and equivalent mixture was carried out and it considered as the liquid for analysis of 100mL(s). It measured after centrifugal separation to remove the algae. It measured by HPLC It computed from the peak area ratio.

- Statistical Method:
a) Data Analysis: Simple regression or Doudroff method for EC50, Dunnett method for NOEC
b) Method of Calculating Mean Measured Concentrations (i.e. arithmetic mean, geometric mean, etc.): Time-weighted Mean

Remark : NOEC was determined based on growth inhibition.

Result : - Measured Concentrations : The tested concentrations were measured at the start and the 72nd hour. All of them, the

deviation from the nominal were less than ± 20%.

Nominal Conc.	Measured Conc., mg/L		Percent of nominal		
	----------		Mean		
mg/L	0 Hour Fresh	72 Hour Old	mg/L	0 Hour Fresh	72 Hour Old
Control	<0.002	<0.002	---	---	---
Solv. Cont.	<0.002	<0.002	---	---	---
0.10	0.107	0.100	0.103	107	100
0.22	0.237	0.229	0.233	108	104
0.46	0.509	0.482	0.495	111	105
1.0	1.18	1.10	1.14	118	110
2.2	2.51	2.36	2.43	114	107
4.6	5.18	4.97	5.07	113	108
10	11.2	10.6	10.9	112	106

Fresh: freshly prepared test solution
Old: test solution after 72 hours exposure
Mean: Time-weighted Mean

- Water chemistry (pH) and temperature in test: pH was measured for control and each concentration at the start and end of test. At the start and end of test, the pH was 7.8 - 7.9 and 8.0 - 10.5, respectively. temperature: 24 ± 0 degree C

-Effect Data:Area Method
EbC50 (0-72hr) =0.76 mg/L (95% C. I.: 0.65 - 0.90 mg/L) (nc)
NOEC (0-72hr) = 0.22 mg/L (nc)

Rate Method
ErC50 (24-48hr) = 1.1 mg/L (95% C. I.: 1.1 - 1.3 mg/L) (nc)
NOEC (24-48hr) = 0.46 mg/L ErC50 (24-72hr) = 1.6 mg/L (nc)
NOEC (24-72hr) = 1.0 mg/L (nc)
nc: based on nominal concentration

- Percent Growth Inhibition of Selenastrum capricornutum

Nominal Conc.	Area under the growth curves (Average)	
	Area	Inhibition (%)*1
mg/L	A (0-72hr)	IA (0-72hr)
Control	22,203,600	---
Solv. Cont.	22,727,200	-2.36
0.10	23,612,000	-6.34
0.22	23,082,000	-3.96
0.46	17,620,400	20.64
1.0	6,357,600	71.37
2.2	1,339,600	93.97
4.6	937,200	91.62
10	915,200	97.70

Nominal Conc.	Growth rates and percent inhibition (Average)			
	----------		----------	
	Rate	Inhibition(%)	Rate	Inhibition(%)
mg/L	u(24-48hr)	Im(24-48hr)	u(24-72hr)	Im(24-72hr)

Control	0.074725	---	0.052284	---
Solv. Con.	0.069865	6.50	0.048669	6.92
0.10	0.067417	9.78	0.046266	5.77
0.22	0.071305	4.58	0.049507	5.31
0.46	0.070560	5.57	0.050257	3.88
1.0	0.046356	37.96	0.049966	4.44
2.2	0.010696	85.69	0.009576	81.68
4.6	0.006867	95.78	0.004383	91.62
10	0.002190	95.88	0.001201	97.7

- Growth Curves: Log phase during the test period

- Calculation of toxic value: It was the nominal concentrations. The reason is that all deviation from the nominal were less than ± 20%.

The test period (ex. 24-48hr), which was suitable, was used for the calculations.

Reliability : (1) valid without restriction
Flag : Critical study for SIDS endpoint
03.12.2003

(28)

Species : Selenastrum capricornutum (Algae)
Endpoint : other
Exposure period : 72 hour(s)
Unit : mg/l
NOEC : = .1
EC10 : = .14
EC50 : = .4
Limit test :
Analytical monitoring : yes
Method : OECD Guide-line 201 "Algae, Growth Inhibition Test"
Year : 1998
GLP : yes
Test substance : as prescribed by 1.1 - 1.4

Remark : The result shown is as below.

2,4,6-TRIBROMOPHENOL Cell growth (0-72h) :

concentration (mg/l) nominal	actual(0)	Area (A) mean	Inhibition (%)
Acetone-blank		1466.54	
0.10	0.76	1445.02	1.5
0.18	n.m.(1)	1224.53	16.5
0.32	n.m.(1)	896.69	38.9
0.56	0.56	468.58	68.0
1.0	n.m.(1)	226.36	84.6
2.2	2.67	187.32	87.2

(0)Average of concentration measured at the start and after 72 h.
(1)Concentrations not measured.

The actual value for the batch of nominal concentration 0.10 mg/l may possibly be 0.076. Attached analytical report describe that analysis for the batch "no value given due to analytical problems". And 48 days after a extra batch without algea was analysed to give 92 % and 62 % recovery at 0 and 72 hours of sampling time.
The value 0.76 is used in all tables in the report, and cannot be assume

simple typographical error.
Furthermore, Assuming 0.76 is typographical error and extra sample without algea can represent actual situation, 0.076 fulfill the criteria to use nomimal concentration while actual concentrations are not given to all the concentration level and recalculation using measured concentration is impossible. One misconduct might be technical error but coincidental two can disgrace the reliability.

Result : Selenastrum capricornutum algae were exposed to 2,4,6-Tribromophenol (FR-613) concentrations ranging from nominal 0.10 to 2.2 mg/l,increasing with a factor of 1.8, with acetone used as presolvent. The initial cell density was 10E4 cell/ml. The total test period was 72 hours. The test included a blank control (only in range finding study) and an acetone control (0.1 ml/l).
Samples for analyses were taken at 0.10, 0.56 and 2.2 mg/l at the start of the test and after 72 hours. Analyses of these samples showed that the actual concentration was in agreement with nominal at 0.56mg/l, while the recovery was ca.120% at 2.2 mg/l. Analysis of 0.10 mg/l batch failed, then analysis of samples taken from the solution without algae was supplemented to show that the actual exposure concentration remained nearly 80% relative to the initial concentration. 2,4,6-TRIBROMOPHENOL(FR-613) inhibited cell growth of the fresh water algae species Selenastrum capriconutum significantly at 0.18 mg/l and higher.
The EC50 for cell growth inhibition was 0.40 mg/l.
The EC10 for cell growth inhibition was 0.14 mg/l.
The NOEC of 2,4,6- Tribromophenol for algal growth was 0.1 mg/l, but 2,4,6- Tribromophenol was not algicidal at concentrations up to and including 2.2 mg/l.

Reliability : (4) not assignable
04.03.2005

(17)

4.4 TOXICITY TO MICROORGANISMS E.G. BACTERIA

Type : aquatic
Species : Tetrahymena pyriformis (Protozoa)
Exposure period : 60 hour(s)
Unit : mg/l
EC50 : = 2.95
Method :
Year : 1985
GLP : no data
Test substance : other TS

Method : -Test Conditions:
a) Nominal Concentrations: Each replicate was a 5-step graded concentration series using freshly prepared stock solutions.
b) Stock Solutions Preparations and Stability: Stock solutions of the individual test compounds were prepared in dimethylsulfoxide (DMSO) at a number of concentrations: 5,000, 10,000, 25,000, 50,000 mg/L.
c) Vehicle/Solvent and Concentrations: In all cases the amount of stock solution added to the cultures was less than 0.75% dimethylsulfoxide (DMSO).
d) Number of Replicates: duplicate

- Statistical Method:
a) Data Analysis: Biological response was determined using

probit analysis. The 60-h IGC50 value (50% inhibitory growth concentration) and 95% confidence fiducial limits were determined prior to transformation mmol/L for comparative purposes.

Reliability : (2) valid with restrictions
Flag : Critical study for SIDS endpoint
11.07.2003 (62)

4.5.1 CHRONIC TOXICITY TO FISH

4.5.2 CHRONIC TOXICITY TO AQUATIC INVERTEBRATES

Species	:	Daphnia magna (Crustacea)
Endpoint	:	reproduction rate
Exposure period	:	21 day(s)
Unit	:	mg/l
NOEC	:	= .1
LOEC	:	>= .1
EC50	:	>= .1
Analytical monitoring	:	yes
Method	:	other: OECD Guide-line 211
Year	:	2000
GLP	:	yes
Test substance	:	other TS: Wako Pure Chemical Industries, Ltd., Lot. No.; JPH9500, Purity = 99.7 %

Method :

-Test Organisms:
a) Age: < 24 hours old
b) Supplier/Source: Test organisms were obtained from National Institute for Environmental Studies (JAPAN) and had been reproduced in the testing laboratory for one year.
c) Any pretreatment: Parental daphnids were acclimated for at least 14 days on test conditions before testing, any groups showing high mortality were not used for testing.

- Test Conditions:
a) Dilution Water Source: Dechlorinated tap water (Tsukuba city, Ibaraki, Japan).
b) Dilution Water Chemistry: pH: = 7.7-7.9
Total hardness (as CaCO3): = 82-86 mg/L
c) Exposure Vessel Type: 80 mL test solution in 100 mL glass beaker
d) Nominal Concentrations: control, solvent control, 0.010, 0.022, 0.046 and 0.10 mg/L
Dose setting reason: The 48-h EC50 for Daphnia magna was 2.2mg/L. However, the concentration which did not affect Daphnia magna was set at 1.0 mg/L as maximum concentration. Therefore, test substance maximum concentration was set at 0.10 mg/L (solvent : 1.0 mg/L).
e) Vehicle/Solvent and Concentrations: Dimethyl sulphoxide and polyoxyethylene sorbitan fatty were used for solvent. 1.0 mg/L solvent was contained in each concentration.
f) Number of Replicates: 10
g) Individuals per Replicates: 10 daphnids per replicates (1 daphnid per beaker)
h) Renewal Rate of Test Water: 3 times per week
i) Water Temperature: 20±1ºC
j) Light Condition: 16:8 hours, light-darkness, =< 1,200

lux
k) Feeding: 0.15 mg carbon/day/individual (Chlorella vulgaris: Green Algae)

- Methods of Analysis: The test concentrations were measured for both renewal and old test solution at the startof test and 2nd, 7th 9th, 14th and 16th day.

- Statistical Method:
a) Data Analysis: Dunnett method for NOEC
b) Method of Calculating Mean Measured Concentrations (i.e.arithmetic mean, geometric mean, etc.): Time-weighted Mean

Remark : NOEC was determined based on the cumulative number of alive juveniles produced per adult alive for 21 days.

Result : - Effect: reproduction- Measured Concentrations of test solutions.

Nominal Conc. mg/L	Measured Conc., mg/L 0day Fresh	2days Old	TWM mg/L	Percent of nominal 0day Fresh	2days Old
Control	<0.002	<0.002	---	---	---
Solv. Cont	<0.002	<0.002	---	---	---
0.010	0.00992	0.00944	0.00968	99	94
0.022	0.0219	0.0221	0.0220*	100	100
0.046	0.0458	0.0441	0.0449	100	96
0.10	0.0973	0.0984	0.0979*	97	98

Nominal Conc. mg/L	Measured Conc., mg/L 7days Fresh	9days Old	TWM mg/L	Percent of nominal 7days Fresh	9days Old
Control	<0.002	<0.002	---	---	---
Solv. Cont.	<0.002	<0.002	---	---	---
0.010	0.00942	0.00961	0.00952*	94	96
0.022	0.0218	0.0218	0.0218*	99	99
0.046	0.0446	0.0445	0.0446	97	97
0.10	0.0957	0.0946	0.0951	96	95

Nominal Conc. mg/L	Measured Conc., mg/L 14days Fresh	16days Old	TWM mg/L	Percent of nominal 14days Fresh	16days Old
Control	<0.002	<0.002	---	---	---
Solv. Cont.	<0.002	<0.002	---	---	---
0.010	0.00984	0.00849	0.00915	98	85
0.022	0.0220	0.0197	0.0208	100	90
0.046	0.0452	0.0421	0.0438	98	92
0.10	0.0962	0.0868	0.0914	96	87

Fresh: Start of renewal period
Old: End of renewal period
TWM: Time-weighted mean of measured concentration during 21days

*: Arithmetic mean
- The time-weighted mean value on measured concentrations of the test solution of 2,4,6-Tribromophenol at each period in the 21-day reproduction test on Daphnia magna under the semi-static test conditions

Nominal Conc. mg/L	The time-weighted mean value on measured concentration (mg/L) 0-7days	0-14days	0-21days	percentage of nominal 0-7days	0-14days	0-21days
0.010	0.00968	0.00960	0.00945	97	96	95
0.022	0.0220	0.0219	0.0215	100	100	98
0.046	0.0449	0.0447	0.0444	98	97	97
0.10	0.0979	0.0965	0.0948	98	97	95

-Water chemistry (pH and DO) and temperature in test: Water chemistry and temperature were measured for control and each concentration at the start of test and before and after renewal of the test solutions.
pH: 7.7 - 8.4
DO: 8.2 - 9.8 mg/L
Water Temperature: 19.3 - 20.8 degree C
-Total hardness: 82 - 85 mg/L
-Effect Data:
LC50 (21day) >=0.10 mg/L (nc)
EC50 (21day) >= 0.10 mg/L (nc)
NOEC (21day) = 0.10 mg/L (nc)
LOEC (21day) >= 0.10 mg/L (nc)
nc: nominal concentration

- Cumulative Number of Dead Parental Daphnids: No test organism was killed at control solvent control and all concentrations.

Nominal Conc. (mg/L)	Cumulative Number of Dead Parental Daphnids (days) 1	2	3	4	5	6	7	8	9	10
Control	0	0	0	0	0	0	0	0	0	0
Solv. Cont.	0	0	0	0	0	0	0	0	0	0
0.010	0	0	0	0	0	0	0	0	0	0
0.022	0	0	0	0	0	0	0	0	0	0
0.046	0	0	0	0	0	0	0	0	0	0
0.10	0	0	0	0	0	0	0	0	0	0

Nominal Conc. (mg/L)	Cumulative Number of Dead Parental Daphnids (days) 11	12	13	14	15	16	17	18	19	20	21
Control	0	0	0	0	0	0	0	0	0	0	0
Solv. Cont.	0	0	0	0	0	0	0	0	0	0	0
0.010	0	0	0	0	0	0	0	0	0	0	0
0.022	0	0	0	0	0	0	0	0	0	0	0
0.046	0	0	0	0	0	0	0	0	0	0	0
0.10	0	0	0	0	0	0	0	0	0	0	0

-Effect Data(reproduction):Juveniles were first product on the 8th day control, solvent control and all concentrations.

Nominal Conc. mg/L	Mean Cumulative Numbers of Juveniles Produced per Adult (days) 0 - 7	8	9	10	11	12	13	14
Control	0 - 0	5.6	6.4	6.4	15.6	16.7	16.7	33.1
Solv. Cont.	0 - 0	7.3	8.0	8.0	18.9	20.7	34.7	36.6
0.010	0 - 0	7.4	9.1	9.1	19.0	22.3	22.3	38.4
0.022	0 - 0	6.8	6.8	6.8	18.0	18.0	18.0	39.2
0.046	0 - 0	8.6	8.6	8.6	22.6	22.6	22.6	44.1
0.10	0 - 0	4.7	6.8	6.8	17.7	20.0	20.0	35.0

Nominal Conc. mg/L	Mean Cumulative Numbers of Juveniles Produced per Adult (days) 15	16	17	18	19	20	21
Control	35.5	35.5	59.1	61.5	61.5	94.4	97.3
Solv. Cont.	36.6	36.6	66.2	69.1	69.1	105.1	108.3
0.010	42.8	42.8	65.0	70.4	70.4	96.0	102.7
0.022	39.2	39.2	65.9	65.9	65.9	97.8	97.8
0.046	44.1	44.1	71.7	71.7	71.7	101.2	101.2
0.10	39.7	39.7	63.4	68.7	68.7	95.0	101.9

-Cumulative numbers of juveniles produced per adult alive for 21days

Vessel No.	Solv 2) Cont.	0.010 Cont. (0.00945)	0.022 (0.0215)	0.046 (0.0444)	0.10 (0.0948)
1	90	106	99	96	110	96
2	114	108	95	95	103	99
3	83	105	90	90	87	113
4	93	117	102	102	98	101
5	99	107	101	101	106	91
6	101	105	101	101	95	101
7	104	118	104	104	103	101
8	94	109	95	95	110	100
9	96	102	101	101	98	102
10	99	106	93	93	102	106
Mean	97.3	108.3	102.7	97.8	101.2	101.9
S. D.	8.4	5.2	7.5	4.6	7.0	6.4
Inhibiton rate(%)	---	-11.3	-5.5	-0.5	-4.0	-4.7
Significant difference 3)	---	NS	NS	NS	NS	NS

1): Time-weighted mean measured concentration
2): Solvent control; Inhibition rate was calculated versus control.
3): Indicates a significant difference from the control by

Dunnet type multiple comparisons procedure, one-sided test.
*: significant (p<0.05)
**: significant (p<0.01)
NS: No significant (p>=0.01)

- Calculation of toxicity values: The calculation of toxicity values was the mean measured concentrations. The reason is that all deviation from the nominal were less than ± 20%.

Reliability : (1) valid without restriction
Flag : Critical study for SIDS endpoint
03.12.2003

(30)

4.6.1 TOXICITY TO SEDIMENT DWELLING ORGANISMS

4.6.2 TOXICITY TO TERRESTRIAL PLANTS

4.6.3 TOXICITY TO SOIL DWELLING ORGANISMS

4.6.4 TOX. TO OTHER NON MAMM. TERR. SPECIES

4.7 BIOLOGICAL EFFECTS MONITORING

4.8 BIOTRANSFORMATION AND KINETICS

4.9 ADDITIONAL REMARKS

5.0 TOXICOKINETICS, METABOLISM AND DISTRIBUTION

5.1.1 ACUTE ORAL TOXICITY

Type : LD50
Value : = 1486 ml/kg bw
Species : rat
Strain : Crj: CD(SD)
Sex : male/female
Number of animals : 10
Vehicle : other: Corn oil
Doses :
Method : OECD Guide-line 401 "Acute Oral Toxicity"
Year : 1999
GLP : yes
Test substance : other TS: 99.8%

Result : LD50 value is 1486 (1215-1792) mg/kg bw for both sexes (95 % confidence limit).

Deaths of both sexes occurred in the 1300 mg/kg and more groups. Hypoactivity was observed in all groups and salivation appeared in most of animals. Furtheremore, in 1300 mg/kg or higher groups of both sexes, chlonic convulsions, tremors, adoption of a prone and/or lateral position were observed before the animals died.

The body weight of survived animals increased on day 7 and 14 after administration. No macroscopic abnormalities were observed by autopsy for either of the dead animals and the survived animals.

Numbers of dead animals by doses
[Males]

Dose (mg/kg)	Number of animals	Number of deaths day 1	Number of deaths day 2-14	Mortality
1000	5	0	0	0 / 5
1300	5	2	0	2 / 5
1690	5	4	0	4 / 5
2197	5	4	0	4 / 5
2856	5	5	-----	5 / 5

[Females]

Dose (mg/kg)	Number of animals	Number of deaths day 1	Number of deaths day 2-14	Mortality
1000	5	0	0	0 / 5
1300	5	2	0	2 / 5
1690	5	4	0	4 / 5
2197	5	4	0	4 / 5
2856	5	5	-----	5 / 5

LD50 value was determined by Probit method based on the results of mortality on day 14.

Test condition : Doses:
LD50 was previously reported more than 2000 mg/kg and no death was reported at 1000 mg/kg/day in 28 days repeated oral dose toxicity test. The doses of this test were set at 0, 1000, 1300, 1690, 2197, and 2856 mg/kg bw.

Animals:
5 males of 175 to 202 g body weight and 5 females of 130 to 156 g body weight were selected.

Test substance: 200, 260, 338, 439.4 and 571.2 mg of the test substance (99.8 wt % purity) were suspended in corn oil.
0.5 mL/100 g bw suspended solution was administrated via oral gavage.

Test period : 14 days.
Observation: every 1 hr till 6 hrs after administration.
After 6 hrs, twice/day. Appearances and activities of surviving animals were observed. Dead animals and survived animals were dessected just after died and after 14 days test respectively. Macroscopical and pathological findings were recorded.

Test substance : Lot No.: 70909 (MANAC, Hiroshima, JAPAN)
Reliability : (1) valid without restriction
Flag : Critical study for SIDS endpoint
04.12.2003 (54)

Type : LD50
Value : > 5000 mg/kg bw
Species : rat
Strain :
Sex : male/female
Number of animals : 10
Vehicle :
Doses :
Method : OECD Guide-line 401 "Acute Oral Toxicity"
Year : 1985
GLP : yes
Test substance : other TS: 99%

Result : The acute oral toxicity of 2,4,6-tribromophenol was investigated in a group of five male and five female CD rats at a dose of 5000 mg/kg. This dose level, which was the maximum practical dose, was selected on the basis of results obtained in a preliminary range finding test.
Animals were observed over aperiod of 14 days and then subjected to necropsy. No clinical signs of reaction to treatment were seen. No mortality occurred. All animals made expected body weight gains over the study period. No abnormalities were detected in any of the animals at the necropsy.
There was no information about vehicle.

Reliability : (2) valid with restrictions
Flag : Critical study for SIDS endpoint
03.12.2003 (22)

5.1.2 ACUTE INHALATION TOXICITY

Type	:	
Value	:	> 50 mg/l
Species	:	rat
Strain	:	
Sex	:	male/female
Number of animals	:	10
Vehicle	:	
Doses	:	
Exposure time	:	4 hour(s)
Method	:	other
Year	:	1974
GLP	:	no data
Test substance	:	other TS: Lot No. 812-141
Result	:	Acute toxicity was evaluated in Spartan albino rats (5 rats/sex), receiving whole-body exposure to micronized tribromophenol at a concentration of 50 mg/l, for 4 hours, in a dynamic air flow chamber. During the exposure period, rats exhibited decreased motor activity, eye squint, slight dyspnea, erythema and ocular porphyrin discharge. At 24 hrs, rats exhibited diarrhea, ocularporphyrin discharge, and slight dyspnea. During the 14-day observation period following exposure, rats exhibited diarrhea, ocular porphyrin discharge, clear nasal discharge, and slight dyspnea. The treatment had no adverse effects with respect to mortality rate or body weight gain. A necropsy of all rats following the 14 day observation period did notreveal any compound related findings. In accordance with the results obtained, the acute inhalation toxicity of TBP would be greater than 50 mg/L. (No additional details available.)
Reliability	:	(2) valid with restrictions
Flag	:	Critical study for SIDS endpoint

03.12.2003 (38)

5.1.3 ACUTE DERMAL TOXICITY

Type	:	LD50
Value	:	> 2000 mg/kg bw
Species	:	rat
Strain	:	Crj: CD(SD)
Sex	:	male/female
Number of animals	:	10
Vehicle	:	
Doses	:	
Method	:	OECD Guide-line 402 "Acute dermal Toxicity"
Year	:	1997
GLP	:	yes
Test substance	:	other TS: 99%
Result	:	There were no deaths. No signs of systemic toxicity were noted during the study. No signs of irritation were noted during the study. All animals showed an expected gain in body weight during the study. No abnormalities were noted at the necropsy.

Test condition	:	A study was performed to assess the acute dermal toxicity of the test material in the Sprague-Dawley CD strain rat. A group of ten animals (five males and five females) was given a single 24-hours, semi-occluded dermal application to intact skin at a dose level of 2000 mg/kg body weigth. The animals were observed for 14 days after the day of treatment and were then killed for gross pathological examination.
Reliability	:	(1) valid without restriction
Flag	:	Critical study for SIDS endpoint

11.07.2003 (20)

Type	:	
Value	:	> 8000 mg/kg bw
Species	:	rabbit
Strain	:	New Zealand white
Sex	:	male/female
Number of animals	:	4
Vehicle	:	
Doses	:	
Method	:	
Year	:	1974
GLP	:	no data
Test substance	:	no data

Result	:	There were no deaths. No signs of systemic toxicity were noted during the study. No signs of irritation were noted during the study. All animals showed an expected gain in body weight during the study. No abnormalities were noted at the necropsy.
Test condition	:	A study was performed to assess the acute dermal toxicity of the test material in male and female albino rabbits. Two male and 2 female New Zealand White rabbits were used in this test. The hair was removed from the back of each rabbit with an electric clipper. The skin of 1 male and 1 female rabbit was abraded with a scalpel blade. TBP was applied once only to the back of each rabbit at a dosage level of 8000 mg/kg. The animals were observed for 14 days after the day of treatment and were then killed for gross pathological examination.
Reliability	:	(2) valid with restrictions
Flag	:	Critical study for SIDS endpoint

10.07.2003 (34)

5.1.4 ACUTE TOXICITY, OTHER ROUTES

5.2.1 SKIN IRRITATION

Species	:	rabbit
Concentration	:	
Exposure	:	
Exposure time	:	
Number of animals	:	6
Vehicle	:	
PDII	:	
Result	:	not irritating
Classification	:	not irritating
Method	:	OECD Guide-line 404 "Acute Dermal Irritation/Corrosion"

Year : 1985
GLP : yes
Test substance : other TS: 99%

Result : One rabbit had a very slight erythema 5 and 24 hours after dosing.
Under the conditions of this study, Tribromophenol is assessed asbeing a non-irritant material to the rabbit skin.

Animal No. and sex	Type of response	Score at time after dosing 5 hrs	24 hrs	48 hrs	72 hrs
1 male	E/O a)	0,0	0,0	0,0	0,0
2 male	E/O a)	1,0	1,0	0,0	0,0
3 male	E/O a)	0,0	0,0	0,0	0,0
1 female	E/O a)	0,0	0,0	0,0	0,0
2 female	E/O a)	0,0	0,0	0,0	0,0
3 female	E/O a)	0,0	0,0	0,0	0,0

a) E/O: Erythema/Oedema (respectively)

Test condition : The potential of Tribromophenol to cause skin irritation was tested in a single dose (500 mg) of Tribromophenol which was applied for a period of four hours to the skin of the rabbit under occluded conditions. Assessment of the skin irritation responses was made 1, 24, 48, and 72 hours after application of the test material. No vehicle was used.
Reaction of the test sites were scored according to the criteria of Draize (1959).
Reliability : (1) valid without restriction
Flag : Critical study for SIDS endpoint
04.12.2003 (25)

Species : rabbit
Concentration : 500 other:mg
Exposure :
Exposure time :
Number of animals : 6
Vehicle :
PDII : .3
Result : not irritating
Classification :
Method :
Year : 1974
GLP : no data
Test substance : no data

Result : Based on the computed primary irritation score of 0.3, TBP would not be considered a primary skin irritant nor would this material present a corrosive hazard to the skin when employed in the manner described in the test condition.

Observation	Examination Interval (No. reacting/No. dosed) Intact sites 24 hrs	72 hrs	Abraded sites 24 hrs	72 hrs
Erythma and Eschar				

		No erythema 1/3 3/3 1/3 2/3 Very slight erythema 2/3 --- 2/3 1/3 --- Edema 3/3 3/3 3/3 3/3 ---
Test condition	:	Three male and three female New Zealand White rabbits were used in this test. The hair was removed from the back of each rabbit with an electric clipper. The skin of 3 of the rabbits was abraded with a scalpel blade. 500 mg of TBP was applied to the back of each rabbit. The area of application was then wrapped with a gauze bandages and occluded with Saran Wrap. No vehicle was used. Twenty four hours later the bandages were removed and the area was washed with tap water and examined for skin irritation in accordance with the regulation of the Federal Hazardous Substance Act. These examinations were repeated at 72 hours.
Reliability	:	(2) valid with restrictions
Flag	:	Critical study for SIDS endpoint

04.12.2003 (37)

5.2.2 EYE IRRITATION

Species	:	rabbit
Concentration	:	
Dose	:	100 other: mg
Exposure time	:	
Comment	:	
Number of animals	:	3
Vehicle	:	
Result	:	moderately irritating
Classification	:	irritating
Method	:	OECD Guide-line 405 "Acute Eye Irritation/Corrosion"
Year	:	1997
GLP	:	yes
Test substance	:	other TS: 99%

Result : A single application of the test material to the non-irrigated eye of the three rabbits produced diffuse corneal opacity, iridial inflammation and moderate conjuctival irritation. Treated eyes appeared normal at the 7 or 14-day observation. The test material produced a maximum group mean score of 27.0 and was classified as a moderate irritant (class 5 on 1 to 8 scale) to the rabbit eye according to a modified Kay and Calandra classification system.

Rabbit No. and sex	Time afte treatment	Corneal Opacity	Iridial Inflammation	Cojunctival Redness	Cojunctival Chemosis
1 male	24 hrs	1	1	2	2
1 male	48 hrs	1	1	2	2
1 male	72 hrs	1	0	2	2
total(mean)		3(1.0)	2(0.7)	6(2.0)	6(2.0+)
2 male	24 hrs	1	1	2	2
2 male	48 hrs	1	1	2	2
2 male	72 hrs	1	0	2	1
total(mean)		3(1.0)	2(0.7)	6(2.0)	5(1.7)

3 male	24 hrs	1	1	2	2	
3 male	48 hrs	1	1	2	2	
3 male	72 hrs	1	1	2	1	
total(mean)		3(1.0)	1(1.0+)	6(2.0)	5(1.7)	

+: posotive criterion

Test condition : Three male New Zealand White Rabbits were used for this study. One rabbit was initially treated. The test material (100 mg) was placed into the conjunctival sac of the right eye, formed by gently pulling the lower lid away from the eye ball. The upper and lower eyelids were held together for about one second immediately after application, to prevent loss of the test material, and then released. The left eye remained untreated and used for control purposes. Immediately after administration of the test material, an assessment of the initial pain reaction was made. After consideration of the ocular responses produced in the first treated animal, two additional animals were treated. No vehicle was used. Assessment of ocular damage/irritation was made approximately 1 hr and 24, 48 and 72 hours following treatment, according to the numerical evaluation method of Draize J. H. (1977). Additional observations were made on days 7 and 14 to assess the reversibility of the ocular effects.

Test substance : Lot No.: 950225
Strage conditions: <25 degree C, shielded from light

Reliability : (1) valid without restriction

Flag : Critical study for SIDS endpoint

04.12.2003 (21)

Species : rabbit
Concentration :
Dose : 100 other: mg
Exposure time :
Comment :
Number of animals : 6
Vehicle :
Result : irritating
Classification : irritating
Method :
Year : 1974
GLP : no data
Test substance : other TS

Result : Examination at 72 hours revealed that there was slight corneal damage in five of the six rabbits tested. Average total score was 6.7: Cornea score 0.1, iris score 0 and conjunctive score 6.6. Based on the results obtained, TBP would be considered an eye irritant.

Observation	Examination Interval (No. positive/No. dosed) Intact sites 24 hrs	48 hrs	Abraded sites 72 hrs	7 days
Cornea				
-Cornea normal	6/6	5/6	5/6	6/6
-Dulling normal corneal luster	---	1/6	1/6	---

Iris				
-Iris normal	6/6	6/6	6/6	6/6
Conjunctive				
-Redness normal	2/6	---	---	5/6
very slight	---	---	1/6	---
slight	3/6	1/6	2/6	1/6
moderate	1/6	5/6	3/6	---
marked	---	---	---	---
-Chemosis normal	4/6	---	---	4/6
very slight	2/6	4/6	5/6	1/6
slight	---	2/6	---	1/6
moderate	---	---	1/6	---
marked	---	---	---	---
-Discharge normal	6/6	2/6	3/6	5/6
very slight	---	---	---	---
slight	---	2/6	2/6	---
moderate	---	1/6	---	---
marked	---	1/6	1/6	1/6
Other-Injury to the epithelim	0/6	0/6	5/6	0/6

Test condition : Three male and three female New Zealand White Rabbits were used in this test. Prior to compound administration, the eyes of each rabbit were examined with ultraviolet light after instillation of one drop of a 2.0 % sodium fluoresccin solution. This procedure is employed routinely so that those rabbits with normal eyes are used in Eye Irritation Studies. 100 mg of the test material was instilled into the conjunctival sac of the right eye of each rabbit. No vehicle was used.
Examination were made for ocular irritation at 24, 48, and 72 hours and at 7 days. At 72 hour examination, sodium fluoresccin and ultraviolet light were used again to aid in revealing possible corneal injury.

Reliability : (2) valid with restrictions
Flag : Critical study for SIDS endpoint
04.12.2003

(35)

5.3 SENSITIZATION

Type : Guinea pig maximization test
Species : guinea pig
Number of animals : 30
Vehicle : other: Arachis oil
Result : sensitizing
Classification : sensitizing
Method : OECD Guide-line 406 "Skin Sensitization"
Year : 1997
GLP : yes
Test substance : other TS: 99%

Result : -75% w/w in Arachis Oil BP
Positive skin responses (very slight to well-difined erythema - grades 1 or 2 and incidents of very slight to slight oedema) were noted at the challenge sites of twelve test group animals at the 24-hour observation and in ten test group animals ath the 48-hour observation. Desquamation

was noted at the challenge site of two test group animals at the 48-hour observation.
No skin reactions were noted at the challenge sites of control group animals at 24 and 48-hour observations.

-50% w/w in Arachis Oil BP
Positive skin responses (very slight to moderate to severe erythema - grades 1 or 3 and incidents of very slight to slight oedema) were noted at the challenge sites of fifteen test group animals at the 24-hour observation and in thirteen test group animals ath the 48-hour observation.
other skin reactions noted in test group animals were small superfical scattered scabs and desquamation.
No skin reactions were noted at the challenge sites of control group animals at 24 and 48-hour observations.

Test condition : A study was performed to assess the contact sensitization potential of the test material in the albino guinea pig. Twenty test and ten control animals were used for the mainstudy. Based on results of sighting tests, the concentration of the test material for the induction and challenge phases were selected as follows: Intradermal induction 10% w/v in arachis oil BP, Topical induction 50 % w/w in arachis oil b.p, Topical challenge 75 % and 50 % w/w in arachis oil bp.

Test substance : Lot No.: 950225
Strage conditions: <25 degree C, shielded from light

Conclusion : The test material Produces 75% (15/20) sensitization rate and was classified as a strong sensitiser to guinea pig skin.

Reliability : (1) valid without restriction

Flag : Critical study for SIDS endpoint

04.12.2003 (23)

Type :
Species : guinea pig
Number of animals : 12
Vehicle :
Result : sensitizing
Classification : sensitizing
Method :
Year : 1975
GLP : no data
Test substance : no data

Result : All of the guinea pigs used in this study appeared essentially normal at all time. All animals exhibited normal body weight gains during the study period.
Four of the eight guinea pigs responded to the challenge dose, exhibiting a flare response slightly greater than that obtained in the sensitizing doses. The other four guinea pigs exhibited essentially negative response (flare) to the challenge dose.
No significant effect was noted in the wheal response obtained in the sensitizing doses. Based on the results obtained, the test compound would be considered a possible sensitizing agent.

Test condition : Twelve male albino guinea pigs were used for this study. Observations were made daily for dermal and pharmaco toxic signs. Each control and test substance group were injected intradermally into a prepared area on the back and flanks of

the respective guinea pigs.
The control or test compounds were injected every other day, three times each week, until a total of ten sensitizing doses had been given. The volume for the first sensitizing dose was 0.05 mL and thereafter for the remaining nine doses a volume of 0.10 mL was used. The injection sites were read and scored for diameter and intensity of erythema (flare) and height of edema(wheal) at 24 and 48 hours after following each injection.
Two weeks following the administration of the tenth sensitizing dose, a challenge dose, at a volume of 0.05 mL was given by intradermal injection of respective control (positive: 2,4-Dinitro-1-Chlorobenzene, vehicle: 0.9% Sodium Chloride Solution) or test compounds.
Reaction to the challenge dose were read and scored at 24 and 48 hours as in the case of the sensitizing injections.
In the event that the score for a challenge dose was greater than the average score of the ten sensitizing doses, the control or test compound was considered to have produced dermal sensitization in the guinea pig.

Reliability : (2) valid with restrictions
Flag : Critical study for SIDS endpoint
04.12.2003 (32)

5.4 REPEATED DOSE TOXICITY

Type :
Species : rat
Sex : male/female
Strain : Crj: CD(SD)
Route of admin. : gavage
Exposure period : Male: 48 days starting from 14 days before mating.
Female: 41 to 45 days from 14 days before mating to day 3 of lactation.
48 days for the females not succeeded in mating.
Frequency of treatm. : Once daily
Post exposure period : 1 day
Doses : 0 (vehicle: corn oil), 100, 300, 1000 mg/kg/day
Control group : yes, concurrent vehicle
NOAEL : = 100 mg/kg
Method : OECD combined study TG422
Year : 1999
GLP : yes
Test substance : other TS: 99.8 %

Result : No mortality was observed for all groups up to the highest doses, 1000 mg/kg/day for the test period. Abnormal findings by dose and by sex are shown below.

[Males]
1) Appearance and activity
300 mg/kg/day or more : Salivation was observed.*
* Numbers of animals with salivation were increasing by increased dose.
This salivation, therefore, was considered as an adverse effect caused by the administration of this chemical.
100 mg/kg/day: No abnormality was observed.

2) Weight and food consumption
1000 mg/kg/day: Significant suppression of body weight gain

and significant decrease of food consumption were observed.

300 and 100 mg/kg/day: No significant changes were observed.

3) Hematology and coagulation parameters
100 to 1000 mg/kg/day: No adverse effects were observed.

4) Blood chemistry.
1000 mg/kg/day: Significant increases in total protein, albumin, A/G, and ALP were observed. BUN tended to increase. Significant decreases in total bilirubin and potassium were observed.
300 mg/kg/day or more: Significant increase in creatinine was observed. This increase suggested the toxicity of this chemical to liver and kidneys.
100 mg/kg/day: No significant adverse effects were observed.

[Blood chemical examination of male rats]
(1)

Dose (mg/kg/day)	No. of animals	T.protein (g/dL)	Albumin (g/dL)	A/G ---
0	12	5.87+/-0.22	3.36+/-0.13	1.34+/-0.06
100	12	5.84+/-0.14	3.33+/-0.09	1.33+/-0.09
300	12	5.95+/-0.26	3.39+/-0.19	1.33+/-0.10
1,000	12	6.45+/-0.51**	3.88+/-0.29**	1.51+/-0.08**

(2)

Dose (mg/kg/day)	No. of animals	Creatinine (mg/dL)	T.bilirubin (mg/dL)	ALP (U/L)
0	12	0.27+/-0.03	0.05+/-0.01	354+/-74
100	12	0.30+/-0.04	0.05+/-0.01	440+/-162
300	12	0.33+/-0.07*	0.04+/-0.01	342+/-102
1,000	12	0.47+/-0.26**	0.02+/-0.01**	514+/-155*

(3)

Dose (mg/kg/day)	No. of animals	Potassium (mmol/L)	Chloride (mmol/L)
0	12	4.46+/-0.29	106.6+/-1.2
100	12	4.40+/-0.25	107.6+/-1.1
300	12	4.38+/-0.30	107.8+/-1.5
1,000	12	4.03+/-0.25**	119.0+/-3.6**

Values are shown as Mean +/- S.D.
* Significantly different from control : P < 0.05
** Significantly different from control : P < 0.01

5) Organ weight
1000 mg/kg/day: Significant absolute and relative weight increases of liver and significant relative weight increase of kidneys were observed. Significant absolute weight decrease of thymus was observed. In addition, relative weight increases of brain, adrenals and testes were observed. However these were not considered as adverse effects because no histopathological abnormalities were

found. 300 and 100 mg/kg/day: No significant changes were observed.

(1) Absolute organ weight

Dose (mg/kg)	No. of animals	Body wt. (g)	Absolute organ weight Thymus (mg)	Liver (g)
0	12	492+/-34	299+/-81	13.99+/-1.72
100	12	478+/-31	269+/-52	13.18+/-1.31
300	12	478+/-36	269+/-66	14.20+/-1.99
1,000	12	422+/-25	201+/-57**	16.23+/-2.32*

(2) Relative organ weight

Dose (mg/kg)	No. of animals	Relative organ weight Brain (g%)	Liver (g%)	Kidneys(g%)
0	12	0.460+/-0.042	2.834+/-0.218	0.678+/-0.054
100	12	0.465+/-0.033	2.751+/-0.152	0.661+/-0.053
300	12	0.473+/-0.041	2.964+/-0.285	0.679+/-0.083
1000	12	0.522+/-0.032**	3.837+/-0.447**	0.824+/-0.101**

(3) Relative organ weight

Dose (mg/kg)	No. of animals	Relative organ weight Adrenals(mg%)	Testes (g%)
0	12	12.257+/-1.299	0.721+/-0.062
100	12	11.807+/-1.277	0.733+/-0.067
300	12	13.494+/-1.966	0.729+/-0.080
1,000	12	15.304+/-1.697**	0.794+/-0.046*

Values are shown as Mean +/- S.D.
* Significantly different from control : P < 0.05
** Significantly different from control : P < 0.01

6) Necropsy and pathological findings
1000 mg/kg/day: By gross necropsy, enlargement of liver was observed. Histopathologically the incidence of hepatocyte hypertrophy was increased whereas that of fatty change was decreased. In addition, renal papillary necrosis, dilatation of tubules, lymphocytes infiltration, basophillic tubular epithelium and hyaline casts were observed in kidney.
300 and 100 mg/kg/day: No significant findings were observed.

(1) Pathological findings 1

Dose (mg/kg)	No. of animals examined	Liver fatty change	Kidney hypertrophy, hepatocyte	basophilic tubes
0	11	6	0	8
100	12	5	0	9
300	12	3	0	9
1,000	12	0**	12**	12

(2)Pathological findings 2

Dose (mg/kg)	No. of animals examined.	Kidney cast, hyaline	dilatation, tubules	eosinophilic body
0	11	1	0	5
100	12	1	0	11*
300	12	0	0	9
1,000	12	8**	7	7

(3) Pathological findings 3

Dose	No. of animals examined	Kidney(mg/kg) papillary necrosis	cellulat infiltration, lymphocyte.
0	11	0	1
100	12	0	1
300	12	0	0
1,000	12	5	6

*: Significant difference from control group P <0.05
**: Significant difference from control group P <0.01

[Females]

1) Appearance and activity
300 mg/kg/day or more : Salivation was observed.
** Numbers of animals with salivation were increasing by increased dose. This salivation, therefore, was considered as an adverse effect caused by the administration of this chemical.
100 mg/kg/day: No abnormality was observed.

2) Weight and food consumption
1000 mg/kg/day: Significant decrease of body weight was observed after 7th day of gestation and significant decreased body weight gain was observed during gestation period. Averaged daily food consumption was decreased during 0 to 4 day of lactation.
300 and 100 mg/kg/day: No significant changes were observed.

3) Organ weight
1000 mg/kg/day: Significant absolute and relative weight increases of liver and significant relative weight increase of kidneys were observed. In addition, relative weight increases of brain, adrenals were observed. However these were not considered as adverse effects because no histopathological abnormalities were found.
300 and 100 mg/kg/day: No significant changes were observed.

(1) Absolute organ weight

Dose (mg/kg)	No. of animals	Body wt (g)	Absolute organ weight Thymus (mg)	Liver (g)
0	11	332+/-16	157+/-46	13.70+/-0.80
100	12	317+/-27	134+/-48	13.48+/-2.07
300	12	333+/-22	168+/-75	14.39+/-1.76
1,000	11	307+/-15	137+/-32	15.74+/-1.28**

(2)Relative organ weight 1

Dose (mg/kg)	No. of animals	Relative organ weight Brain (g%)	Liver (g%)
0	11	0.613+/-0.034	4.138+/-0.287
100	12	0.657+/-0.067	4.230+/-0.396
300	12	0.602+/-0.038	4.312+/-0.393
1,000	11	0.665+/-0.025*	5.117+/-0.265**

(3) Relative organ weight 2

Dose (mg/kg)	No. of animals	Relative organ weight Kidneys (g%)	Adrenals (mg%)
0	11	0.649+/-0.072	23.171+/-1.572
100	12	0.694+/-0.078	25.991+/-3.418
300	12	0.666+/-0.047	25.988+/-4.091
1,000	11	0.772+/-0.094**	27.315+/-3.415**

Values are shown as Mean +/- S.D.
* Significantly different from control : P < 0.05
** Significantly different from control : P < 0.01

4) Necropsy and pathological findings
1000 mg/kg/day: By gross necropsy, enlargement of liver was observed. However no histopathological abnormalities were observed. Comparing to males, the toxicity of this chemical looked weaker to females.
300 and 100 mg/kg/day: No significant changes were observed.

Test condition : (Doses):
As acute oral LD 50 was previously reported as 2000 mg/kg bw., a preliminary test of 14 days was conducted with the doses of 0 (vehicle; corn oil), 100, 300 and 1000 mg/kg/day. Based on the results of the preliminary test, the highest dose was set at 1000 mg/kg/day where clear adverse effects would appear. A vehicle (corn oil) treated group served as the control.

(Test duration):
Males: Total 48 days; before mating 14 days, mating period 14 days and after mating 20 days.
Females : Total 41 to 45 days, before mating 14 days, mating period 14 days(at the longest), gestation period and lactation 3 days. As to females not succeeded in mating, total 48 days just same as males.

Test substance : Lot No.: 70909 (MANAC, Hiroshima, JAPAN)
Reliability : (1) valid without restriction
Flag : Critical study for SIDS endpoint
04.12.2003 (54)

Type :
Species : rat
Sex : male/female
Strain :
Route of admin. : inhalation
Exposure period : 6 hours/day
Frequency of treatm. : 5 days/week, 3 weeks

Post exposure period	:	none
Doses	:	Dust at 0.00, 0.10 and 0.92 mg/l (analytical determination).
Control group	:	yes
NOAEL	:	< .1 mg/l
LOAEL	:	= .1 mg/l
Method	:	other: not reported
Year	:	
GLP	:	no data
Test substance	:	other TS:2,4,6-tribromophenol.
Method	:	A subacute dust inhalation toxicity study was conducted. Two groups of 10 albino rats each were exposed to either a low (T-I) concentration or a high (T-II) of dust of 2,4,6-Tribromophenol for 6 hours per day, 5 days per week, for 3 weeks. An additional 10 rats served as untreated control animals for comparison and received no dust exposure. Target, gravimetric and analytical dust concentrations were all 0.00 for the control, 0.15 and 0.10 for T-I, respectively, and 1.00, 0.98 and 0.92 for T-II, respectively. At the end of the 21 day period, all surviving animals were sacrificed and subjected to gross necropsy.
Remark	:	Sponsor: Michigan Chemical Corp.
Result	:	There were no deaths among the T-I rats. One T-II male and one T-II female died after 10 and 11 exposures, respectively. Untoward reactions noted in both groups included hypoactivity, salivation, lacrimation and red nasal discharge. One T-II animal exhibited hyperpnea on day 11. Body weight gains for male animals in T-I compared favorably with those of the control males. However, T-I females and both the males and females in T-II exhibited lower weight gains than did their respective control groups. There were no significant differences between test and control animals with respect to hematologic, clinical chemistry or urinalysis values obtained at respect to hematologic, clinical chemistry or urinalysis values obtained at either interval or investigation. Gross and histopathologic changes involving the liver and kidneys were noted among the T-II rats.
Source	:	U.S. EPA Challenge Program: 201-14177A (2002)
Reliability	:	(3) invalid

04.12.2003 (43)

Type	:	
Species	:	rabbit
Sex	:	male/female
Strain	:	New Zealand white
Route of admin.	:	dermal
Exposure period	:	28 days
Frequency of treatm.	:	5 days/week, 4 weeks
Post exposure period	:	2 days
Doses	:	0, 100, 300, and 1000 mg/kg
Control group	:	yes, concurrent vehicle
NOAEL	:	= 300 mg/kg bw
Method	:	other: not reported
Year	:	
GLP	:	no data
Test substance	:	other TS: 2,4,6- Tribromophenol, Lot No. 3106.
Method	:	A 28 day subacute dermal toxicity study was conducted with 2,4,6-Tribromophenol, Lot No. 3106. Four groups of 4 male and 4 female New Zealand white rabbits were administered

Tribromophenol at doses of 0, 100, 300 or 1000 mg/kg. Skin sites on 2 males and 2 females in each group were abraded. The test material was ground to a fine powder and suspended (1% w/v) in aqueous methylcellulose prior to application. Doses were applied dermally to the clipped, unoccluded skin sites 5 days/week for 4 weeks.

Remark : Sponsor: Michigan Chemical Corp.

Result : One rabbit in the 1000 mg/kg group died after receiving 15 dermal applications; the cause of death could not be determined from the tissues examined. 2,4,6-Tribromophenol was slightly irritating to the skin upon repeated exposure. No pharmacotoxic symptoms were observed at any time during the study. No treatment related effects were noted on body weight, hematology, clinical blood chemistry or urinalysis. Treatment-related lesions were noted on the test skin sites of all animals. All of the other gross and microscopic lesions were compatible with those of naturally occurring diseases or related to the method of sacrifice. There were no statistically significant inter-group differences in organ weight or ratio data.

Source : U.S. EPA Challenge Program: 201-14177A (2002)

Reliability : (3) invalid

04.12.2003

(42)

5.5 GENETIC TOXICITY 'IN VITRO'

Type : Bacterial reverse mutation assay

System of testing : Salmonella typhimurium TA100, TA1535, TA98, TA1537 and Escherichia coli WP2 urvA

Test concentration :

Cycotoxic concentr. :

Metabolic activation : with and without

Result : negative

Method : Guidelines for screening mutagenicity testing of chemicals, JAPAN

Year : 1999

GLP : yes

Test substance : other TS: 99.8 %

Result : The numbers of the reverse mutation colonies were within 2 times of negative control as shown below.

<<Table 1-1 test results without S9 mix. S. typhimurium>>

Test Substance Concentration (ug/plate)	Number of revertants (number of colonies/plate) Base-Pair substitution type TA100	TA1535	Frameshift type TA98	TA1537
0				
(1)	131 +/- 4.2	14 +/- 4.7	22 +/- 2.6	10 +/-5.8
(2)	149 +/- 9.8	14 +/- 2.1	18 +/- 0.6	11 +/-4.6
15.6				
(1)	122 +/- 14.8	8 +/- 1.0	19 +/- 6.1	NT
(2)	147 +/- 39.2	10 +/- 5.7	24 +/- 8.0	NT
31.3				
(1)	141 +/- 21.6	11 +/- 1.5	20 +/- 8.1	6 +/-2.5

(2) 134 +/- 14.0 12 +/- 1.7 22 +/- 1.5 5 +/-1.5

62.5
(1) 132 +/- 21.9 11 +/- 1.5 22 +/- 4.2 5 +/-1.0
(2) 135 +/- 13.2 13 +/- 1.2 18 +/- 2.1 6 +/-2.6

125.0
(1) 138 +/- 6.8 14 +/- 3.8 18 +/- 4.2 7 +/-4.6
(2) 122 +/- 14.2 11 +/- 0.6 16 +/- 5.5 7 +/-1.0

250.0
(1) 109 +/- 8.1 12 +/- 2.1 15 +/- 2.1 3 +/-0.6
(2) 105 +/- 9.3 8 +/- 1.0 11 +/- 6.0 3 +/-0.6

500.0
(1) 32* +/- 4.6 3* +/- 0.6 9* +/- 1.2 0*+/-0.0
(2) 20* +/- 11.6 2* +/- 1.2 5* +/- 2.5 1+/-0.6

1000.0
(1) NT NT NT 0* +/-0.0
(2) NT NT NT 0* +/-0.0

Positive control without S9 mix

Name	AF-2	SA	AF2	9AA
Conc. (ug/plate)	0.01	0.5	0.1	80

No of revertants
(1) 503 +/- 21.3 548 +/- 33.0 548 +/- 25.7 377+/-25.6
(2) 522 +/- 31.2 559 +/- 8.6 606 +/- 12.9 479+/-95.1

<<Table 1-2 test results without S9 mix. E. Coli.>>

Test Substance Concentration (ug / plate)	Number of revertants (number of colonies/plate) Base-pair substitution type WP2 uvrA
0	
(1)	23 +/- 6.4
(2)	26 +/- 2.3
156.0	
(1)	23 +/- 3.2
(2)	26 +/- 4.2
313.0	
(1)	25 +/- 3.1
(2)	21 +/- 3.8
625.0	
(1)	22 +/- 2.9
(2)	20 +/- 3.2
1250.0	
(1)	14 +/- 5.1
(2)	14 +/- 4.6
2500.0	
(1)	0* +/- 0.0
(2)	0* +/- 0.0

5000.0
(1) 0* +/- 0.0
(2) 0* +/- 0.0

<< Table 2-1 test results with S9 mix. S. typhimurium>>

Test Substance Concentration (ug/plate)	Number of revertants (number of colonies/plate) Base-Pair substitution type TA100	TA1535	Frameshift type TA98	TA1537
0				
(1)	164 +/- 11.8	10 +/- 1.5	37 +/- 7.6	15 +/- 4.4
(2)	153 +/- 20.5	11 +/- 3.0	32 +/- 7.2	16 +/- 3.6
15.6				
(1)	164 +/- 11.2	8 +/- 1.0	NT	14 +/- 1.7
(2)	165 +/- 21.4	15 +/- 2.6	NT	16 +/- 5.9
31.3				
(1)	159 +/- 11.1	11 +/- 6.2	33 +/- 6.7	14 +/- 4.0
(2)	173 +/- 8.0	12 +/- 3.1	35 +/- 1.5	12 +/- 3.6
62.5				
(1)	176 +/- 5.5	10 +/- 4.0	28 +/- 7.0	10 +/- 2.5
(2)	198 +/- 7.1	11 +/- 2.5	30 +/- 7.4	12 +/- 2.5
125.0				
(1)	166 +/- 5.1	10 +/- 1.5	40 +/- 9.9	11 +/- 2.6
(2)	185 +/- 6.6	10 +/- 2.6	29 +/- 5.9	11 +/- 0.6
250.0				
(1)	143 +/- 9.3	10 +/- 1.7	22 +/- 1.5	5 +/- 2.5
(2)	146 +/- 33.7	8 +/- 1.5	32 +/- 3.1	5 +/- 2.1
500.0				
(1)	60* +/- 10.1	3* +/- 0.0	10 +/- 2.1	2*+/-1.0
(2)	86* +/- 33.4	1* +/- 0.6	9 +/- 3.5	4* +/-1.5
1000.0				
(1)	NT	NT	0* +/- 0.0	NT
(2)	NT	NT	0* +/- 0.0	NT

Positive control without S9 mix Name	2AA	2AA	2AA	2AA
Conc. (ug/plate)	1	2	0.5	2
No of revertants				
(1)	1111 +/-115.4	437 +/- 77.5	545 +/- 27.8	372+/-19.5
(2)	932 +/- 20.4	372 +/- 15.5	444 +/- 48.8	429+/-62.2

<<Table 2-2 test results with S9 mix. E. Coli.>>

Test Substance Concentration (ug / plate)	Number of revertants (number of colonies/plate) Base-pair substitution type WP2 uvrA

0
(1) 31 +/- 8.5
(2) 31 +/- 1.2

156.0
(1) 38 +/- 9.7
(2) 36 +/- 7.2

313.0
(1) 38+/- 4.0
(2) 34+/- 3.5

625.0
(1) 28 +/- 2.9
(2) 25 +/- 2.1

1250.0
(1) 23 +/- 5.5
(2) 21 +/- 8.1

2500.0
(1) 0* +/- 0.0
(2) 0* +/- 0.0

5000.0
(1) 0* +/- 0.0
(2) 0* +/- 0.0

Note:Values are shown as Mean +/- S.D
* : Growth inhibition was observed.
AF-2: 2-(2-Furyl)-3-(5-nitro-2-furyl)acrylamide
SA: Sodium Azaide, 9AA: 9-Aminoacridine
2AA: 2-Aminoanthracene
NT : Not tested.

Test condition **:** [- S9 mix] -0, 15.6, 31.3, 62.5, 125, 250, 500 ug/plate for S. typhi. TA100, 1535, and 98
-0, 31.3, 62.5, 125, 250, 500, 1000 ug/plate for S. typhi. TA1537
-0, 156, 313, 625, 1250, 2500, 5000 ug/plate for E.coli. WP2 uvrA

[+ S9 mix] -0, 15.6, 31.3, 62.5, 125, 250, 500 ug/plate for S. typhi. TA100, 1535, and 1537
-0, 31.3, 62.5, 125, 250, 500, 1000 ug/plate for S. typhi. TA98
-0, 156, 313, 625, 1250, 2500, 5000 ug/plate for E.coli. WP2 uvrA
Procedures: Pre-incubation method (incubation 37 degree C, for 20 minutes)
Solvent: DMSO
Positive control:
-S9 mix. : AF-2 (0.01 ug/plate for TA100 and WP2 urvA, 0.1 ug/plate for TA98), Sodium Azaide (0.5 ug/plate for TA1535), 9-Aminoacridine (80 ug/plate for TA1537)
+S9 mix : 2-Aminoanthracene (10 ug/plate for WP2 uvrA, 2 ug/plate for TA1535 and TA1537, 1 ug/plate for TA100, 0.5 ug/plate for TA98)

Incubation condition: 37 degree C, 48 hours

Plates/test : 3
Number of replicates : 2

[Preliminary test to find the cytotoxic concentration]
(without S9 mix)
500 ug/plate and greater for TA100, TA1535, and TA98
1500 ug/plate and greater for TA 1537
5000 ug/plate for WP2 urvA
(with S9 mix)
500 ug/plate and greater for TA100, TA1535, and TA1537
1500 ug/plate and greater fot TA 98
5000 ug/plate for WP2 urvA

[Main test concentration]
[without S9 mix]
0, 15.6, 31.3, 62.5, 125, 250, 500 ug/plate for S. typhimurium TA100, TA1535, and TA98
0, 156, 313, 625, 1250, 2500, 5000 ug/plate for E.coli. WP2 urvA
[with S9 mix]
0, 15.6, 31.3, 62.5, 125, 250, 500 ug/plate for S. typhimurium TA100, TA1535, and TA1537
0, 15.6, 31.3, 62.5, 125, 250, 500, 1000 ug/plate for S. typhimurium TA 98
0, 156, 313, 625, 1250, 2500, 5000 ug/plate for E. coli. WP2 urvA

Test substance : Lot No.: 70909 (MANAC, Hiroshima, JAPAN)
Reliability : (1) valid without restriction
Flag : Critical study for SIDS endpoint
04.12.2003 (54)

Type : Ames test
System of testing : Salmonella typhimurium strains TA1535,TA1537,TA1538,TA98,TA100
Test concentration : 5 to 500 ug/plate
Cycotoxic concentr. : No details available.
Metabolic activation : with and without
Result : negative
Method : OECD Guide-line 471
Year : 1996
GLP : yes
Test substance : other TS: Purity 99.9%

Result : Salmonella typhimurium strains TA1535, TA1537, TA1538, TA98 and TA100 were treated with the test material using the Ames plate incorporation method at up to six dose levels, in triplicate, both with and without the addition of a rat liver homogenate metabolising system (10 % liver S9 in standard co-factors). The dose range was determined in a preliminary toxicity assay and was 5 to 1500 ug/plate in the first experiment. The experiment was repeated on a separate day using a dose range of 5 to 500 ug/plate, fresh culture of the bacterial strains and fresh test material formulations. An extra dose level was included in experiment1 to allow for the toxicity of the test material.The vehicle (dimethyl sulphoxide) control plates produced counts of revertant colonies within the normal range. All of the positive control chemicals used in the test induced marked increases in the frequency of revertant colonies, both with and without the metabolising system. No significant increase in the frequency of revertant colonies was recorded for any of the bacterial strains with any dose of the test material, either with or without metabolic activation. The test material was considered to be NON-MUTAGENIC under the conditions of this test.

Reliability : (2) valid with restrictions
Flag : Critical study for SIDS endpoint
04.12.2003 (18)

Type : Ames test
System of testing : preincubation modification of the Salmonella/microsome test
Test concentration :
Cycotoxic concentr. :
Metabolic activation : with and without
Result : negative
Method :
Year : 1987
GLP :
Test substance :

Result : The results and data from the testing of 255 chems. for mutagenicity in Salmonella are presented. All chem. were tested under code using a preincubation modification of the Salmonella/microsome test in the absence of exogenous metabolic activation and in the presence of liver S-9 from Aroclor-induced male Sprague-Dawley rats and Syrian hamsters.
Reliability : (4) not assignable
04.12.2003 (27)

Type : Chromosomal aberration test
System of testing : Chinese hamster CHL/IU cells
Test concentration : See Test Condition
Cycotoxic concentr. : See Test Condition
Metabolic activation : with and without
Result : positive
Method : OECD Guide-line 473
Year : 1999
GLP : yes
Test substance : other TS: Purity 99.8 %

Result : Cells with structural chromosomal aberrations including gaps were apparently increased at the highest doses in the short-term treatment, with and without metabolic activation (frequencies: 23.5 % at 0.1 mg/mL and 10.5 % at 0.050 mg/mL, respectively). Polyploidy was not induced.

<<Chromosome analysis of CHL/IU continuously treated with 2,4,6-tribromophenol (TBP) without S9 mix.>>
[Time of exposures: 24 hrs]
Number of cells analysed: 200 cells except for 0.20 mg/mL

Dose ug/mL	No. of structural aberrations gap	ctb	cte	csb	cse	mul	total	others
Solvent (DMSO) 0	0	0	0	2	0	0	2	0
Test Substance 0.025	0	1	0	0	0	0	1	0
0.050	0	0	1	2	1	0	4	0
0.10	0	2	0	3	0	0	5	1
0.20#	Not analysed							

MC									
0.00005	3	27	115	1	0	0	146	0	

Dose ug/mL	No. of cells with aberration TGA(%)	TG(%)	Polyploid (%)	Concurrent cytotoxicity (%)	Mitotic index (%)
Solvent (DMSO)					
0	1(0.5)	1(0.5)	0.13	100.0	----
Test Substance					
0.025	1(0.5)	1(0.5)	0.13	93.5	----
0.050	4(2.0)	4(2.0)	0.00	69.5	----
0.10	4(2.0)	4(2.0)	0.00**	43.5	7.0
0.20 #	----	---	---	29.5	0.0***
MC					
0.00005	94*(47.0)	92*(46.0)	0.00	-----	----

[Time of exposures: 48 hrs]
Number of cells analyzed: 200 cells except for 0.20 mg/mL

Dose ug/mL	No. of structural aberrations gap	ctb	cte	csb	cse	mul	total	others
Solvent (DMSO)								
0	0	0	0	4	0	0	4	0
Test Substance								
0.013	0	0	0	0	0	0	0	0
0.025	0	0	1	0	0	0	1	0
0.050	1	0	0	0	0	0	1	0
0.10 #	Not analysed							
0.20 #	Not analysed							
MC								
0.00005	5	51	180	11	1	50	298	7

Dose ug/mL	No. of cells with aberration TGA(%)	TG(%)	Polyploid (%)	Concurrent cytotoxicity (%)	Mitotic index (%)
Solvent (DMSO)					
0	1(0.5)	1(0.5)	0.00	100	----
Test Substance					
0.013	0(0.0)	0(0.0)	0.25	98.5	----
0.025	1(0.5)	1(0.5)	0.13	92.5	----
0.050	1(0.5)	1(0.5)	0.13	49.5	4.0
0.10#			----	14.0	----
0.20 #			----	6.0	----

MC
0.00005 134*(67.0) 133*(66.5) 0.88 ---- ----

Note:
1) #: Chromosome analysis was not performed because there was small number of metaphases due to cytotoxicity.
2) * : Significantly different from solvent control at p < 0.01 by Fisher's exact probability test.
3) Others: Such as attenuation and premature chromosome condensation, were excluded from the no. of structural aberrations.
4) Polyploid: Eight hundred cells were analysed in each group.
5) Concurrent cytotoxicity: Cell confluency, representing cytotoxicity, was measured with a Monocellater TM.
6) Mitotic index: Number of metaphases per 500 cells was scored in each dish in order to select the highest dose enable to analyse chromosomes.
7) ** : Seven hundred and forty cells were analysed.
8) *** : Eight hundred and ten cells were analysed from two dishes.

Abbreviations:
gap: chromatid gap and chromosome gap
ctb: chromatic break
cte: chromatid exchange
csb: chromosome break
cse: chromosome exchange (dicentric and ring)
mul: multiple aberrations (More than nine aberrations in a cell were scored as 10)
TGA: total number of cells with aberrations
TG: total number of cells with aberrations except gap
DMSO: dimethylsulfoxide (solvent)
MC: mitomycin C (positive control)

<<Chromosome analysis of CHL/IU, 6hr short treatment with 2,4,6-tribromophenol(TBP) without S9 mix.>>
Time of exposure : 6 - (18) hrs
Number of cells analyzed: 200 cells except for 0.1 mg/mL and 0.2 mg/mL

Dose ug/mL	No. of structural aberrations							
	gap	ctb	cte	csb	cse	mul	total	others
Solvent (DMSO)								
0	0	0	1	0	0	0	1	0
Test Substance								
0.013	0	1	4	1	0	0	6	0
0.025	0	0	1	1	0	0	2	1
0.050	1	16	30	4	0	0	51	0
0.10 #	Not analysed							
0.20 #	Not analysed							
CPA								
0.005	0	0	0	1	0	0	1	0

Dose ug/mL	No. of cells with aberration TGA(%)	TG(%)	Polyploid (%)	Concurrent cytotoxicity (%)	Mitotic index (%)
Solvent (DMSO)					
0	1(0.5)	1(0.5)	0.13	100.0	----
Test Substance					
0.013	1(0.5)	1(0.5)	0.13	94.0	----
0.025	2(1.0)	2(1.0)	0.13	88.0	----
0.050	21*(10.5)	20*(10.0)	0.63	47.0	5.1
0.10#				19.0	----
0.20#				1.5	----
CPA					
0.005	1(0.5)	1(0.5)	0.13	----	----

<<Chromosome analysis of CHL/IU, 6 hr short treatment with 2,4,6-tribromophenol(TBP) with S9 mix.>>
Time of exposure : 6 - (18) hrs
Number of cells analyzed: 200 cells except for 0.2 mg/mL

Dose ug/mL	No. of structural aberrations gap	ctb	cte	csb	cse	mul	total	others
Solvent (DMSO)								
0	0	0	0	0	0	0	0	0
Test Substance								
0.025	1	0	0	1	0	0	2	0
0.050	0	0	2	1	0	0	3	0
0.10 #	1	19	84	11	0	20	135	2
0.20 #	Not analysed							
CPA								
0.005	0	6	19	4	0	0	29	1

Dose ug/mL	No. of cells with aberration TGA(%)	TG(%)	Polyploid (%)	Concurrent cytotoxicity (%)	Mitotic index (%)
Solvent (DMSO)					
0	0(0.0)	0(0.0)	0.13	100.0	----
Test Substance					
0.025	1(0.5)	1(0.5)	0.00	91.5	----
0.050	2(1.0)	2(1.0)	0.38	78.5	----
0.10	47*(23.0)	46*(23.0)	0.13	40.5	11.7
0.20#	-----	-----	----	24.5	Tox
CPA					
0.005	25*(12.5)	25*(12.5)	0.00	----	----

Note:
1) #: Chromosome analysis was not performed because there was small number of metaphases due to cytotoxicity.
2) * : Significantly different from solvent control at p < 0.01 by Fisher's exact probability test.
3) Others: Such as attenuation and premature chromosome condensation, were excluded from the no. of structural aberrations.
4) Polyploid: Eight hundred cells were analysed in each group.
5) Concurrent cytotoxicity: Cell confluency, representing cytotoxicity, was measured with a Monocellater TM.
6) Mitotic index : Number of metaphases per 500 cells was scored in each dish in order to select the highest dose enable to analyse chromosomes.

Abbreviations:
gap: chromatid gap and chromosome gap
ctb: chromatic break
cte: chromatid exchange
csb: chromosome break
cse: chromosome exchange (dicentric and ring)
mul: multiple aberrations (More than nine aberrations in a cell were scored as 10)
TGA: total number of cells with aberrations
TG: total number of cells with aberrations except gap
DMSO: dimethylsulfoxide (solvent)
CPA: cyclophosphamide
Tox: cytotoxicity

Test condition : Solvent : DMSO
Positive control: -S9 mix: Mitomycin C (MC), +S9 mix.: Cyclophosphamide (CPA)
S9 Rat liver, induced with phenobarbital and 5,6-benzoflavone.
Plates/test: 2

Doses:
-S9 mix (24 hr continuous treatment): 0, 0.025, 0.050, 0.10 mg/mL
-S9 mix (48 hr continuous treatment): 0, 0.013, 0.025, 0.050 mg/mL
-S9 mix (short-term treatment): 0, 0.013, 0.025, 0.050 mg/mL
+S9 mix (short-term treatment): 0, 0.025, 0.050, 0.10 mg/mL

Cytogenetic effects:
-S9 mix (24 hr continuous treatment): 0.20 mg/mL
-S9 mix (48 hr continuous treatment): 0.10 mg/mL
-S9 mix (short-term treatment): 0.10 mg/mL
+S9 mix (short-term treatment): 0.20 mg/mL

Test substance : Lot No.: 70909 (MANAC, Hiroshima, JAPAN)
Reliability : (1) valid without restriction
Flag : Critical study for SIDS endpoint
04.12.2003

(54)

5.6 GENETIC TOXICITY 'IN VIVO'

Type : Micronucleus assay
Species : mouse
Sex : male/female
Strain : NMRI

Route of admin.	:	i.p.
Exposure period	:	
Doses	:	0 (vehicle: corn oil), 75, 150, 300 mg/kg bw.
Result	:	negative
Method	:	OECD Guide-line 474 "Genetic Toxicology: Micronucleus Test"
Year	:	2002
GLP	:	yes
Test substance	:	other TS: Purity 99.79%

Result :

It is concluded that TBP is not mutagenic in the micronucleus test under the experimental conditions described in this report.

Summary of the report:
TBP was tested in the Micronucleus Test in mice, to evaluate its genotoxic effect on erythrocytes in bone marrow. Four groups, each comprising 5 males and 5 females, received a single intraperitoneal injection. This route of administration was chosen to maximize the chance of the test article reaching the target tissue.

The doses 0 (vehicle: corn oil), 75, 150 and 300 mg/kg bw. were chosen based on a dose range finding study. Two groups were dosed with 300 mg/kg body weight, one group was dosed with 150 mg/kg and one group was dosed with 75 mg/kg body weight. Appropriate positive and negative control groups were included.

After dosing, all animals of the dose level of 300 mg/kg body weight were lethargic, showed ataxia and tremors. Within 17 hours all animals had recovered from the treatment.

The animals of the groups treated with 150 and 75 mg/kg body weight and the animals of the negative and positive control groups showed no abnormalities.

A vehicle treated group served as negative control, a group treated with a single intraperitoneal injection of cyclophosphamide (CP) at 50 mg/kg body weight served as positive control.

Bone marrow of the group treated with TBP was sampled 24 or 48 hours after dosing. Bone marrow from the negative control group was harvested at 24 hours after dosing only and bone marrow from the positive control group was harvested at 48 hours after dosing only.

Cyclophosphamide, the positive control substance, induced a statistically significant increase in the number of micronucleated polychromatic erythrocytes in both sexes.

No increase in the frequency of micronucleated polychromatic erythrocytes was observed in the polychromatic erythrocytes of the bone marrow of animals treated with TBP.

The groups that were treated with TBP showed no decrease in the ratio of polychromatic to normochromatic erythrocytes compared to the vehicle controls, which reflects a lack of toxic effects of this compound on the erythropoiesis. The groups that were treated with CP showed a decrease in the

ratio of polychromatic erythrocytes compared to the vehicle controls. It is concluded that TBP is not mutagenic in the micronucleus test under the experimental conditions described in this report.

Test condition : The number of cells analyzed per animal: 2000 polychromatic erythrocytes

Reliability : (1) valid without restriction

Flag : Critical study for SIDS endpoint

04.12.2003 (24)

5.7 CARCINOGENICITY

Remark : Not known to be a carcinogen.
Not classified by IARC, Not included in NTP 10th Report on Carcinogens.

Reliability : (2) valid with restrictions

19.06.2003

5.8.1 TOXICITY TO FERTILITY

Type : One generation study
Species : rat
Sex : male/female
Strain : Crj: CD(SD)
Route of admin. : gavage
Exposure period : males: 14 days before mating.
females: from 14 days before mating to day 3 of lactation.
Frequency of treatm. : once daily
Premating exposure period
Male : 14 days
Female : 14 days
Duration of test : Male : 48 days starting from 14 days before mating.
Female: 41 to 45 days from 14 days before mating to day 3 of lactation.
48 days for the females not succeeded in mating.
No. of generation studies :
Doses : 0 (vehicle: corn oil), 100, 300, 1000 mg/kg/day
Control group : yes, concurrent vehicle
NOAEL parental : = 1000 mg/kg bw
NOAEL F1 offspring : = 3000 ml/kg bw
Method : other: OECD TG422, combined repeated dose and reproduction/developmental toxicity screening test
Year : 1999
GLP : yes
Test substance : other TS: Purity 99.8 %

Result : No adverse effects were observed in estrus cycle, copulation, fertility results and duration of gestation period as well as finding for delivery, number of corpora lutea, implants, total pups and live pups born and implantation and delivery indices in any treatment groups. With regard to the effects on neonates, viability on day 4 lactation and body weights on day 0 and 4 of lactation in 1000 mg/kg/day group were lowered in both sexes. In conclusion, NOAELs for reproductive/developmental toxicity are considered to be 1000 mg/kg/day for parents, and 300

mg/kg/day for the F1 generation.

[Maternal toxicity]

1) Appearance and activity
300 mg/kg/day or more : Salivation was observed.
** Numbers of animals with salivation were increasing by increased dose. This salivation, therefore, was considered as an adverse effect caused by the administration of this chemical.
100 mg/kg/day: No abnormality was observed.

2) Weight and food consumption
1000 mg/kg/day: Significant decrease of body weight was observed after 7th day of gestation and significant decreased body weight gain was observed during gestation period. Averaged daily food consumption was decreased during 0 to 4 day of lactation.
300 and 100 mg/kg/day: No significant changes were observed.

3) Organ weight
1000 mg/kg/day: Significant absolute and relative weight increases of liver and significant relative weight increase of kidneys were observed. In addition, relative weight increases of brain, adrenals were observed. However these were not considered as adverse effects because no histopathological abnormalities were found.
300 and 100 mg/kg/day: No significant changes were observed.

(1) Absolute organ weight

Dose (mg/kg)	No. of animals	Body wt (g)	Absolute organ weight Thymus (mg)	Liver (g)
0	11	332+/-16	157+/-46	13.70+/-0.80
100	12	317+/-27	134+/-48	13.48+/-2.07
300	12	333+/-22	168+/-75	14.39+/-1.76
1,000	11	307+/-15	137+/-32	15.74+/-1.28**

(2)Relative organ weight 1

Dose (mg/kg)	No. of animals	Relative organ weight Brain (g%)	Liver (g%)
0	11	0.613+/-0.034	4.138+/-0.287
100	12	0.657+/-0.067	4.230+/-0.396
300	12	0.602+/-0.038	4.312+/-0.393
1,000	11	0.665+/-0.025*	5.117+/-0.265**

(3) Relative organ weight 2

Dose (mg/kg)	No. of animals	Relative organ weight Kidneys (g%)	Adrenals (mg%)
0	11	0.649+/-0.072	23.171+/-1.572
100	12	0.694+/-0.078	25.991+/-3.418
300	12	0.666+/-0.047	25.988+/-4.091
1,000	11	0.772+/-0.094**	27.315+/-3.415**

Values are shown as Mean +/- S.D.
* Significantly different from control : P < 0.05
** Significantly different from control : P < 0.01

4) Necropsy and pathological findings
1000 mg/kg/day: By gross necropsy, enlargement of liver was observed. However no histopathological abnormalities were observed. Comparing to males, the toxicity of this chemical looked weaker to females.
300 and 100 mg/kg/day: No significant changes were observed.

<<<Reproduction performance>>>

Dose (mg/kg)	No. of pairs mated	No. of pairs copulated	No. of pregnant females
0	12	11	11
100	12	12	12
300	12	12	12
1000	12	12	12

Dose (mg/kg)	Copulation index (%) a)	Fertility index (%) b)	Estrus cycle (day) c)
0	91.7	100.0	4.2 +/- 0.3
100	100.0	100.0	4.3 +/- 0.3
300	100.0	100.0	4.3 +/- 0.5
1000	100.0	100.0	4.2 +/- 0.3

Note:
a): (No. of animals with successful copulation/no. of animals mated) x 100
b): (No. of pregnant animals/ no. of animals with successful copulation) x 100
c): Values are mean +/- S.D.

<<<Findings of delivery in dams and observation on their pups>>>

Dose (mg/kg)	No. of dams observed.	No. of dams delivered live pups	Duration of gestation #
0	11	11	22.5 +/- 0.5
100	12	12	22.5 +/- 0.5
300	12	12	22.5 +/- 0.7
1000	12	12	22.0 +/- 0.0 *

: Mean +/- S.D.
* : Significant difference from control group; P < 0.05

Dose (mg/kg)	No. of total corpora lutea	No. of total implants	No. of total pups born
0	209(19.0+/-3.9)	175(15.9+/-2.0)	161(14.6+/-2.0)
100	231(19.3+/-3.7)	204(17.0+/-2.3)	188(15.7+/-1.9)
300	209(17.4+/-1.8)	195(16.3+/-19)	175(14.8+/-3.2)
1000	200(16.7+/-2.0)	189(15.8+/-1.4)	174(14.5+/-1.9)

( ): Mean +/- S.D.

Dose (mg/kg)	No. of total live pups born	No. of total live male pups born	No. of total live female pups born
0	161(14.6+/-2.0)	87(7.3+/-1.4) f)	74(6.7+/-1.9) f)
100	187(15.6+/-1.9)	97(8.1+/-2.3) f)	90(7.5+/-1.8) f)
300	175(14.5+/-2.6)	89(7.4+/-2.5)	85(7.1+/-1.0) f) g)
1000	174(14.5+/-1.9)	79(6.6+/-2.1) f)	95(7.9+/-1.2) f)

( ): Mean +/- S.D.
Note: f) : Includes live pups died before observation.
g) : Includes a pup retained on day 1 after birth.

Dose (mg/kg)	Sex ratio (male/female)	No. of live pups on day 4 (male)	No. of live pups on day 4(female)
0	1.29+/-0.54	83(7.3+/-1.2)	72(6.5+/-1.9)
100	1.17+/-0.50	87(7.3+/-2.8)	84(7.0+/-2.2)
300	1.07+/-0.42	86(7.2+/-2.3)	80(6.7+/-1.2)
1000	0.88+/-0.42	42(3.5+/-2.4)**	49(4.1+/-2.9)*

( ): Mean +/- S.D.

Dose (mg/kg)	N0. of dead pups born	No. of dead pups born: Stillbirth	No. of dead pups born: cannibalism
0	0(0.0 +/- 0.0)	0(0.0 +/- 0.0)	0(0.0 +/- 0.0)
100	1(0.1 +/- 0.3)	0(0.0 +/- 0.0)	1(0.1 +/- 0.0)
300	1(0.1 +/- 0.3)	1(0.1 +/- 0.3)	1(0.0 +/- 0.0)
1000	0(0.0 +/- 0.0)	0(0.0 +/- 0.0)	0(0.0 +/- 0.0)

( ) : Mean +/- S.D.

Dose (mg/kg)	Gestation index (%) a)	Implantation index (%) b)	Delivery index (%) c)
0	100	83.5 +/- 11.7	92.1 +/- 5.8
100	100	90.1 +/- 13.2	92.5 +/- 6.6
300	100	93.3 +/- 6.9	89.3 +/- 9.4
1000	100	94.9 +/- 5.9	91.9 +/- 7.0

a): (No. of females with live pups / no. of pregnant females) x 100
b): (No. of implants / no. of corpora lutea) x 100: Mean +/-S.D.
c): (No. of pups born / no. of implants) x 100: Mean +/-S.D.

Dose (mg/kg)	Live birth index (%) d)	Viability index on day 4 e) Males (%)	Females(%)
0	100.0 +/- 0.0	96.2 +/- 8.6	97.6 +/- 5.4
100	99.5 +/- 1.8	88.6 +/- 23.7	92.7 +/- 15.5

300	99.5 +/- 1.7	97.4 +/- 6.3	94.0 +/- 9.6
1000	100.0 +/- 0.0	53.3 +/- 34.2 **	50.4 +/- 35.1 **

d): (No. of live pups born / no. of pups born) x 100. Mean+/- S.D.
e): (No. of live pups on day 4 after birth / no. of live pups born) x 100. Mean +/- S.D.
** : Significant difference from control group ; P <0.01

Test substance : Lot No.: 70909 (MANAC, Hiroshima, JAPAN)
Conclusion : NOAEL for parents: 1000 mg/kg/day
NOAEL for the F1 generation: 300 mg/kg/day
Reliability : (1) valid without restriction
Flag : Critical study for SIDS endpoint
04.12.2003

(54)

5.8.2 DEVELOPMENTAL TOXICITY/TERATOGENICITY

Species : rat
Sex : male/female
Strain : Crj: CD(SD)
Route of admin. : gavage
Exposure period : males: 14 days before mating.
females: from 14 days before mating to day 3 of lactation.
Frequency of treatm. : once daily
Duration of test : Male : 48 days starting from 14 days before mating.
Female: 41 to 45 days from 14 days before mating to day 3 of lactation.
48 days for the females not succeeded in mating.
Doses : 0 (vehicle: corn oil), 100, 300, 1000 mg/kg/day
Control group : yes, concurrent vehicle
Method : other: OECD TG422, combined repeated dose and reproduction/developmental toxicity screening test
Year : 1999
GLP : yes
Test substance : other TS: Purity 99.8 %

Result : No adverse effects were observed in estrus cycle, copulation, fertility results and duration of gestation period as well as finding for delivery, number of corpora lutea, implants, total pups and live pups born and implantation and delivery indices in any treatment groups. With regard to the effects on neonates, viability on day 4 lactation and body weights on day 0 and 4 of lactation in 1000 mg/kg/day group were lowered in both sexes. In conclusion, NOAELs for reproductive/developmental toxicity are considered to be 1000 mg/kg/day for parents, and 300 mg/kg/day for the F1 generation.

[Maternal toxicity]

1) Appearance and activity
300 mg/kg/day or more : Salivation was observed.
** Numbers of animals with salivation were increasing by increased dose. This salivation, therefore, was considered as an adverse effect caused by the administration of this chemical.
100 mg/kg/day: No abnormality was observed.

2) Weight and food consumption

1000 mg/kg/day: Significant decrease of body weight was observed after 7th day of gestation and significant decreased body weight gain was observed during gestation period. Averaged daily food consumption was decreased during 0 to 4 day of lactation.
300 and 100 mg/kg/day: No significant changes were observed.

3) Organ weight
1000 mg/kg/day: Significant absolute and relative weight increases of liver and significant relative weight increase of kidneys were observed. In addition, relative weight increases of brain, adrenals were observed. However these were not considered as adverse effects because no histopathological abnormalities were found.
300 and 100 mg/kg/day: No significant changes were observed.

(1) Absolute organ weight

Dose (mg/kg)	No. of animals	Body wt (g)	Absolute organ weight Thymus (mg)	Liver (g)
0	11	332+/-16	157+/-46	13.70+/-0.80
100	12	317+/-27	134+/-48	13.48+/-2.07
300	12	333+/-22	168+/-75	14.39+/-1.76
1,000	11	307+/-15	137+/-32	15.74+/-1.28**

(2)Relative organ weight 1

Dose (mg/kg)	No. of animals	Relative organ weight Brain (g%)	Liver (g%)
0	11	0.613+/-0.034	4.138+/-0.287
100	12	0.657+/-0.067	4.230+/-0.396
300	12	0.602+/-0.038	4.312+/-0.393
1,000	11	0.665+/-0.025*	5.117+/-0.265**

(3) Relative organ weight 2

Dose (mg/kg)	No. of animals	Relative organ weight Kidneys (g%)	Adrenals (mg%)
0	11	0.649+/-0.072	23.171+/-1.572
100	12	0.694+/-0.078	25.991+/-3.418
300	12	0.666+/-0.047	25.988+/-4.091
1,000	11	0.772+/-0.094**	27.315+/-3.415**

Values are shown as Mean +/- S.D.
* Significantly different from control : P < 0.05
** Significantly different from control : P < 0.01

4) Necropsy and pathological findings
1000 mg/kg/day: By gross necropsy, enlargement of liver was observed. However no histopathological abnormalities were observed. Comparing to males, the toxicity of this chemical looked weaker to females.
300 and 100 mg/kg/day: No significant changes were observed.

<<<Reproduction performance>>>

Dose (mg/kg)	No. of pairs mated	No. of pairs copulated	No. of pregnant females
0	12	11	11
100	12	12	12
300	12	12	12
1000	12	12	12

Dose (mg/kg)	Copulation index (%) a)	Fertility index (%) b)	Estrus cycle (day) c)
0	91.7	100.0	4.2 +/- 0.3
100	100.0	100.0	4.3 +/- 0.3
300	100.0	100.0	4.3 +/- 0.5
1000	100.0	100.0	4.2 +/- 0.3

Note:
a): (No. of animals with successful copulation/no. of animals mated) x 100
b): (No. of pregnant animals/ no. of animals with successful copulation) x 100
c): Values are mean +/- S.D.

<<<Findings of delivery in dams and observation on their pups>>>

Dose (mg/kg)	No. of dams observed.	No. of dams delivered live pups	Duration of gestation #
0	11	11	22.5 +/- 0.5
100	12	12	22.5 +/- 0.5
300	12	12	22.5 +/- 0.7
1000	12	12	22.0 +/- 0.0 *

: Mean +/- S.D.
* : Significant difference from control group; P < 0.05

Dose (mg/kg)	No. of total corpora lutea	No. of total implants	No. of total pups born
0	209(19.0+/-3.9)	175(15.9+/-2.0)	161(14.6+/-2.0)
100	231(19.3+/-3.7)	204(17.0+/-2.3)	188(15.7+/-1.9)
300	209(17.4+/-1.8)	195(16.3+/-19)	175(14.8+/-3.2)
1000	200(16.7+/-2.0)	189(15.8+/-1.4)	174(14.5+/-1.9)

( ): Mean +/- S.D.

Dose (mg/kg)	No. of total live pups born	No. of total live male pups born	No. of total live female pups born
0	161(14.6+/-2.0)	87(7.3+/-1.4) f)	74(6.7+/-1.9) f)
100	187(15.6+/-1.9)	97(8.1+/-2.3) f)	90(7.5+/-1.8) f)
300	175(14.5+/-2.6)	89(7.4+/-2.5)	85(7.1+/-1.0) f) g)
1000	174(14.5+/-1.9)	79(6.6+/-2.1) f)	95(7.9+/-1.2) f)

( ): Mean +/- S.D.
Note: f) : Includes live pups died before observation.
g) : Includes a pup retained on day 1 after birth.

Dose (mg/kg)	Sex ratio (male/female)	No. of live pups on day 4 (male)	No. of live pups on day 4(female)
0	1.29+/-0.54	83(7.3+/-1.2)	72(6.5+/-1.9)
100	1.17+/-0.50	87(7.3+/-2.8)	84(7.0+/-2.2)
300	1.07+/-0.42	86(7.2+/-2.3)	80(6.7+/-1.2)
1000	0.88+/-0.42	42(3.5+/-2.4)**	49(4.1+/-2.9)*

( ): Mean +/- S.D.

Dose (mg/kg)	N0. of dead pups born	No. of dead pups born: Stillbirth	No. of dead pups born: cannibalism
0	0(0.0 +/- 0.0)	0(0.0 +/- 0.0)	0(0.0 +/- 0.0)
100	1(0.1 +/- 0.3)	0(0.0 +/- 0.0)	1(0.1 +/- 0.0)
300	1(0.1 +/- 0.3)	1(0.1 +/- 0.3)	1(0.0 +/- 0.0)
1000	0(0.0 +/- 0.0)	0(0.0 +/- 0.0)	0(0.0 +/- 0.0)

( ) : Mean +/- S.D.

Dose (mg/kg)	Gestation index (%) a)	Implantation index (%) b)	Delivery index (%) c)
0	100	83.5 +/- 11.7	92.1 +/- 5.8
100	100	90.1 +/- 13.2	92.5 +/- 6.6
300	100	93.3 +/- 6.9	89.3 +/- 9.4
1000	100	94.9 +/- 5.9	91.9 +/- 7.0

a): (No. of females with live pups / no. of pregnant females) x 100
b): (No. of implants / no. of corpora lutea) x 100: Mean +/-S.D.
c): (No. of pups born / no. of implants) x 100: Mean +/-S.D.

Dose (mg/kg)	Live birth index (%) d)	Viability index on day 4 e) Males (%)	Females(%)
0	100.0 +/- 0.0	96.2 +/- 8.6	97.6 +/- 5.4
100	99.5 +/- 1.8	88.6 +/- 23.7	92.7 +/- 15.5
300	99.5 +/- 1.7	97.4 +/- 6.3	94.0 +/- 9.6
1000	100.0 +/- 0.0	53.3 +/- 34.2 **	50.4 +/- 35.1 **

d): (No. of live pups born / no. of pups born) x 100. Mean+/- S.D.
e): (No. of live pups on day 4 after birth / no. of live pups born) x 100. Mean +/- S.D.
** : Significant difference from control group ; P <0.01

Test substance : Lot No.: 70909 (MANAC, Hiroshima, JAPAN)
Conclusion : NOAEL for parents: 1000 mg/kg/day
NOAEL for the F1 generation: 300 mg/kg/day
Reliability : (1) valid without restriction
Flag : Critical study for SIDS endpoint
04.12.2003

(54)

Species : rat

Sex	:	female
Strain	:	Wistar
Route of admin.	:	inhalation
Exposure period	:	Day 1-21 of gestation
Frequency of treatm.	:	24hr/day
Duration of test	:	through day 60 post-partum
Doses	:	0.03, 0.1, 0.3, 1.0 mg/m3
Control group	:	yes
NOAEL maternal tox.	:	= .1 mg/m³
other: LOAEL Maternal Tox.	:	= .3 mg/m³
other: NOAEL Embryotox. and Fetotox.	:	= .03 mg/m³
other: LOAEL Embryotox. and Fetotox.	:	= .1 mg/m³
Method	:	
Year	:	
GLP	:	no data
Test substance	:	other TS

Method :

Animals:
Wistar rats were obtained from the Rappolovo animal facility (St. Petersburg, Russia). Three females 180-200 g were caged with one male for mating. The day of finding spermatozoa in vaginal smears was designated as day 1 of pregnancy.

Statistical analysis:
Statistical analysis was performed using SAS package version 6.12. For analysis of continuous outcome variable the author used one-way ANOVA (PROC GLM). Dunnet's two-tailed t test was used to identify the concentrations differing from control values.
Differences were considered statistically significant if $p<0.05$.
For analysis of parental and postnatal mortality, and incidence of visceral and sceletal variants, Wilcoxon rank-sum test (PROC NPAR1WAY) was applied (litter was considered a statistical unit). Each concentration was compared to control, and Boferroni adjustment was used to keep experimentwise $p<0.05$.

Result :

Maternal Toxicity:
There were no maternal deaths during the study and also no effects of TBP exposure on mean body weight or rectal temperature in pregnant dams. Significant decreases in orientation reactions were noted at concentrations of 1.0 mg/m3 ($p<0.05$) in the open field test. Nonsignificant trends ($P>0.05$) toward decreased horizontal movement and emotionality in the open field and increased electrical impulse skin pain threshold (SPT) were also observed.
No significant exposure-related differences were seen in the nonspecific immunological status (phagocytosis and blood anti-microbial activity) of pregnant rats.
In pregnant dams exposed to TBP at the maximal concentration of 1.0 mg/m3, significant increases were observed in the level of alkaline phosphatase in blood serum (29.0 - control groups, 65.0 Milli Equivalents (ME)- experimental group, $p<0.01$), total amino nitrogen in urine, excretion of total phenols in urine, and level of progesterone in blood plasma

(61.3 plus or minus 7.1 - control group, 93.5 plus or minus 7.3 mg/L - experimental group, p<0.01). These parameters were not affected by any of the lower concentrations of TBP. The corticosterone level in blood plasma was not significantly changed at any of the concentration of TBP; a dose-related effect of TBP on plasma levels of this hormone was not observed. There were also no significant changes in estradiol blood levels in any of the experimental groups.

Embryotoxic and Fetotoxic Effects:
TBP proved to have an embryotoxic effect. As compared to the control group, a significant increase in total embryolethality [(corpora lutea - live pups/corpora lutea) X 100], as well as in preimplantation and postimplantation loss, has been shown. A concentration dependent effect of total embryolethality which could be expressed by the linear regression equation was observed. The smallest concentration found to be embryolethal (i.e. producing statistically significant increase in preimlantation and total embryolethality) was 0.1 mg/m3.
The weight and length of fetuses collected via cesarean section on the 21st day of gestation and placenta weight decreased with increasing TBP concentration from 0.1 to 1.0 mg/m3. Body length decreases over this concentration range were, however, not statistically significant. At a concentration of 1 mg/m3, fetal body weight, and at concentrations of 0.1 and 1.0 mg/m3, placental weight were significantly decreased compared to those for controls.
A nonsignificant dose-dependent increase in lipid peroxidation in placenta was observed at TBP concentrations of 0.3 and 1.0 mg/m3, (45% and 68% above control, respectively, p>0.05).
No visible external variations or increases in subcutaneous dermal hematomas were found in fetuses prenatally exposed to TBP. Dissection of embryos according to the method of Wilson (1965) did not reveal any severe developmental malformations. The number of hematomas in different parts of the fetal head was not significantly higher in the 1.0 mg/m3 group (0.31 vs. 0.02 in controls, p<0.05). We did not find any dose-response for any visceral anomalies.

Skeletal Effects:
No skeletal anomalies were revealed. The lengths of femur, humerus, ulna and radius bones were decreased in the treated groups in comparison with control group in the range of concentrations from 0.1 to 1.0 mg/m3, but these differences were found statistically nonsignificant. The number of metacarpal and metatarsal bones and the number of sternum ossification centers were also decreased in groups exposed to TBP at concentrations of 0.1 mg/m3 and higher. This decrease was significant for the numbers of centers of sternum ossification in the 0.1 (3.85 plus or minus 0.42 vs. 6.05 plus or minus in control, p<0.05), 0.3 (4.98 plus or minus 0.27, p<0.05) and 1.0 mg (4.95 plus or minus 0.27, p<0.05) groups. The mean number of metacarpal and metatarsal bones was significantly decreased in fetuses prenatally exposed to TBP at a concentration of 0.1 mg/m3 : 2.54 plus or minus 0.26 vs. 3.31 plus or minus 0.11 in control group (metacarpals) and 3.4 plus or minus 0.1 vs. 3.98 plus or minus 0.03 in control groups (metatarsals).
The surface area of the parietal bone was significantly decreased at a concentration of 0.1 mg/m3 (3.77 plus or

minus 0.75 vs. 6.25 plus or minus 0.2 mm2 in control, p<0.05).
No signs of fetal skeletal growth retardation were found at the lowest concentration studied (0.03 mg/m3).

Postnatal Developmental and Neurobehavioral Effects:
Body weights of fetuses from the maximal concentration (1.0 mg/m3) group were significantly decreased on PND 1 (4.29 plus or minus 0.4 g vs. 5.27 plus or minus 0.16 g in control, p<0.05).
There was a significant increase in the number of dead pups found on PND 5 in the 1.0 mg/m3 group (17.75% - Control, 76% - experimental, p<0.05) and pup deaths continued such that between PND5 and PND 21 the mean pup death was 40% compared to 4.18% in the control group (p>0.05). Pup death in the other experimental groups was not significantly different from the control group.
For pup physical development, both ear unfolding and lower incisor eruption were significantly delayed in the 0.3 mg/m3 experimental group. There were, however, no significant treatment related effects on the appearance of downy hair, upper incisor eruption or eye opening.
Emotionality of 30-day-old male pups was significantly decreased in subjects exposed to concentrations of 0.3 mg/m3. The grooming behavior of male progeny was significantly less than control in all experimental groups.
Orientation reactions and emotionality indices in 30-day-old female pups declined with increasing prenatal exposure to TBP. Grooming behavior in subjects exposed to concentration of 0.3 mg/m3 and emotionality in subjects exposed to concentration of 1mg/m3 were decreased significantly.
At 60 days of age emotional reactions were significantly decreased in female subjects from the 0.03; 0.3 and 1.0 mg/m3 groups. A nonsignificant trend (p>0.05) toward decreased grooming behavior in female pups of the same age was observed.
SPT was significantly increased in both male and female subjects from the 1 mg/m3 group on PND 60 (2.87 plus or minus 0.07 vs. 2.43 plus or minus 0.12 in controls for males and 2.63 plus or minus 0.14 vs. 1.98 plus or minus 0.16 in controls for females; p<0.01). Taken together, these data suggest that TBP has a disruptive effect on both maternal and offspring CNS.
Analysis of organ weights in 2-month old offspring did not reveal any significant changes in relative weights for liver, kidneys or heart in either males or females. At the maximal concentration studied, a decrease in relative testis weight was found. Significant increases in the glands (0.1 and 0.3 mg/m3) in female progeny were also observed. Increases in relative ovarian weights were seen in all experimental groups, but this effect was statistically significant only in subjects exposed to a concentration of 0.1 mg/m3.
Abstract:
Pregnant Wistar rats were exposed to 2,4,6-Tribromophenol (TBP) by whole body inhalation (0, 0.03, 0.1, 0.3, 1.0 mg/m3, 24 hr/day, 7 days/week from day 1 to 21 of gestation). Significant decreases in orientation reaction were noted at concentration of 1.0 mg/m3 (p<0.05) in the openfield test. Non significant trends towards decreases horizontal movements and emotionality in the open field and increased lectrical impulse skin pain threshold (SPT) were

observed. No significant exposure-related differences in the nonspecific immunological status (phagocytosis and blood anti-microbe activity) of pregnant rats were seen after the exposure.

Preimplantation and postimplantation embryo losses were significantly increased in a dose -dependent manner and were seen in all treated groups except the lowest concentration (0.03 mg/m3) group. Signs of retarded fetal skeletal development and increased frequencies of visceral abnormalities were found at concentration of 0.1 and 1.0 mg/m3. Significant effects were found for lower incisor eruption and ear unfolding at a concentration of 0.3 mg/m3.

The grooming behavior of 30-day old male progeny was significantly less than control in all experimental groups. Grooming behavior in female subjects exposed to a concentration of 0.3 mg/m3 and emotionality in subjects exposed to a concentration of 1.0 mg/m3 were decreased significantly. At 60 days of age emotional reaction were significantly decreased in female subjects from 0.03, 0.3 and 1.0 mg/m3 groups. SPT was significantly increased in 1.0 mg/m3 group for both male and female pups. Thus,evidence of CNS depression influence of TBP both in maternal and off spring groups was found.

The NOEL for developmental neurotoxicity is thus <0.03 mg/m3 The NOEL for maternal neurotoxicity is 0.3 mg/m3.

These results suggest that exposure to TBP for 24 hr/day throughout gestation may cause developmental neurotoxicity, embryotoxicity, and fetotoxicity, but not immunotoxicity.

Test substance : TBP: Research grade, manufacturer: NPO (Iodobrom, Saci, Russia)
Reliability : (2) valid with restrictions
Flag : Critical study for SIDS endpoint
11.07.2003 (48)

Species : rat
Sex : female
Strain : other
Route of admin. : gavage
Exposure period : Days 6 through 15 of gestation
Frequency of treatm. : Daily
Duration of test : To day 20 of gestation
Doses : 10, 30, 100, 300, 1000 and 3000 mg/kg/day
Control group : yes
NOAEL maternal tox. : = 1000 mg/kg bw
NOAEL teratogen. : = 300 mg/kg bw
Method : other
Year : 1978
GLP : no data
Test substance : other TS: Tribromoohenol, FM246, lot #3287

Method : Reproductive toxicity was evaluated in 6 groups of 5 pregnant Charles River CD female rats receiving 2,4,6-Tribromophenol via oral gavage at dose level of 10,30, 100, 300, 1000 and 3000 mg/kg/day on gestation days 6 through 15. A control group received the vehicle, corn oil, at 10 mg/kg/day.
During gestation the females were observed for clinical

signs of effect, mortality and body weight changes. These rats were sacrificed on gestation day 20 and uterine contents examined for viable and non viable fetuses, early and late resportion and total implantations.

Result : No effects were noted on maternal behavior or appearance of the group that received 1000 mg/kg/day or less. Total mortality was observed at 3000 mg/kg/day dose. There were no effects due to the administration of this chemical on maternal body weights, food consumption, number of corpora lutea, viable ornonviable fetuses, resorptions, or implantantions at dose levels of 300 mg/kg/day or less. There were slight decreases in body weight gains between gestation day 6 and 12, an increase in post-implantation losses, and a slight decrease in the number of viable fetuses in the 1000 mg/kg/day group which may be attributed to treatment.
The maximum suggested dosage level for a teratology study is 1000 mg/kg/day.

Reliability : (2) valid with restrictions
04.12.2003 (36)

5.8.3 TOXICITY TO REPRODUCTION, OTHER STUDIES

5.9 SPECIFIC INVESTIGATIONS

5.10 EXPOSURE EXPERIENCE

5.11 ADDITIONAL REMARKS

Type : other: Pharmacokinetic test

Remark : The absorption, distribution and elimination of 2,4,6-Tribromophenol were examined in 5 groups of male or female Eolzman's albino rats (2 or 3 per group) orally administered doses from 4.04 to 5.34 mg/kg. The post dosing monitoring period lasted from 8 to 96 hours, followed by sacrifice and tissue sampling.

Urine and feces were collected daily. Blood was collected at 1, 2, 4, 8, 17, 24 and 48 hours after dosing from each of four rats by drawing blood (0.2 to 0.4 g) from a tail incision. Ten tissues (heart, lungs, muscle, fat, gonads, uterus, spleen, kidneys, liver, brain) were excised.

The proportion of the administered 14C remaining in each of the 11 tissues after 48 hours did not exceed 0.005%, only kidney, liver and lungs retained detectable residues. The retention half-life of 14C in the blood was 2.03 hours, and ranged from 1.45 to 2.3 hours for the other tissues. After 48 hours the total excretion of radiocarbon in the urine ranged from 50.3 to 91.2% of the dose. During the same period, between 3.90 and 13.74% of the administered 14C was eliminated in the feces.

Conclusion : A single oral dose of 2,4,6-tribromophenol(TBP) was rapidly absorbed in rats. The bulk of radioactivity (77.0%) was

readily excreted via the urine and 2 to 14% was eliminated feces, within 48 hours. Male rats excreted TBP slightly more rapidly than females. The only tissues retaining detectable residues 48 hours after dosing were kidney, liver and lungs. Blood concentrations of TBP peaked 1 hour after dosing at 4.57 ppm and then plunged to 0.002 ppm by 24 hours. The pharmacokinetics of this compound in rats appears to follow a one-compartment open model system. The chemical israpidly distrbuted in the body and the rate of elimination in urine is proportional to the concentration of the chemical in the blood. The rate constant for elimination (Ke) is 0.3 and the half-life (T1/2)in the blood is is 2.03 hours. Based on the results of this study, TBP should neither be persistent nor accumulative in mammalian system.

Reliability : (2) valid with restrictions
Flag : Critical study for SIDS endpoint
11.07.2003 (33)

Type : Metabolism

Remark : Rapidly absorbed from the gastro-intestinal tract.
Reliability : (2) valid with restrictions
Flag : Critical study for SIDS endpoint
04.08.2003 (7)

Type : other

Remark : Certain halogenated dibenzo-p-dioxins and dibenzofurans (HDDs and HDFs) are recognized as having potential public health and environmental significance because of their potential to produce toxic effects at very low doses. As a result, the United States Environmental Protection Agency (USEPA) promulgated regulations under Section 4 and 8 of the TSCA for chems. that may be contaminated with chlorinated or brominated dibenzo-p-dioxins and dibenzofurans. The regulations require anal. testing of certains chems. for HDD and HDF contamination, submission of health and safety studies on HDDs and HDFs, and submission of worker allegations of significant adverse reactions to the HDDs and HDFs.The data and information submitted to the USEPA will be used for exposure and risk assessments.

Reliability : (2) valid with restrictions
Flag : Critical study for SIDS endpoint
04.08.2003 (59)

(1) Broderius, S.J., M.D. Kahl, and M.D. Hoglund, (1995), Use of Joint Toxic Response to Define the Primary Mode of Toxic Action for Diverse Industrial Organic Chemicals., Environ.Toxicol.Chem.14(9):1591-1605

(2) Budavari, S. (ed.): The Merck Index - An Encyclopedia of Chemicals, Drugs, and Biologicals. Whitehouse Station, NJ, Merck and Co., Inc., No. 9687(2001)

(3) Chemicals in the Environment; Environmental Health and Safety Division, Environmental Health Department, Environment Agency of Japan (1998) p.568 in Japanease.

(4) Chen, Y. P., Lincoln, D. E., Woodin, S. A., Lovell, C, R.,(1991), Purification and properties of a unique flavin-containing chloroperoxidase from the capitellid polychaete, Notomastus lobatus. J. Biol. Chem.; 266, 23909-23915

(5) CITI, Japan (1981) Report No. 20492, Chemical Inspection and Testing Institute, unpublished data

(6) CITI, Japan (1999) Report No. 80492K, Chemical Inspection and Testing Institute, unpublished data

(7) Clayton et al: Patty's Industrial Hygienes and Toxiology 3rd. ed., 1981, 2A, 2615-2616

(8) CRC Handbook of chemistry and physics, Ed. D.R.Lide, 72nd edition 1991-2,p. 3-385, No. 11023.

(9) CRC Handbook of chemistry and physics, Ed. David R. Lide 72nd edition,1991-2, p. 3-385, No.11023.

(10) Danish EPA, Bromited flame retardant; Toxicity and ecotoxicity, Evironmental project No. 568 2000 Miljoprojekt (2000)

(11) Degradation of halogenated phenols in anoxic natural marine sediments. Marine pollution bulletin, 1991, Vol. 22 No. 5 p. 227-233.

(12) Devillers, J., Bintein, S. and Domine, D. Comparison of BCF models based on log P.; Chemosphere; (1996), 33:1047-65

(13) DSBG/Bromine compounds Ltd MSDS January 2002, Revision 4.

(14) DSBG/Bromine compounds Ltd, 96-hour Acute Toxicity Study in carp with 2,4,6-Tribromophenol (FR-613), (STATIC), August 14 (1998).

(15) DSBG/Bromine compounds Ltd, Acute toxicity study in Daphnia magna with 2,4,6-Tribromophenol (FR-613), (static), August 4 (1998).

(16) DSBG/Bromine compounds Ltd, Determination of water Solubility of 2,4,6- Tribromophenol (FR-613),(1998).

(17) DSBG/Bromine compounds Ltd, Fresh Water Algal Growth Inhibition Test with 2,4,6 -Tribromophenol (FR-613), August 4 (1998).

(18) DSBG/Bromine compounds Ltd, Reverse Mutation Assay "Ames Test" Using Salmonella Typhimurium, November 26 (1996).

(19) DSBG/Bromine compounds Ltd, Unpublished Report (1997)

(20) DSBG/Bromine compounds Ltd, unpublished study, Acute Dermal Toxicity (limittest) in Rat, February 14 (1997).

(21) DSBG/Bromine compounds Ltd, unpublished study, Acute Eye Irritation Test in the Rabbit, February (1997).

(22) DSBG/Bromine compounds Ltd, unpublished study, Acute Oral Toxicity in the Rat, November 11 (1985).

(23) DSBG/Bromine compounds Ltd, unpublished study, Magnusson & Kligman Maximisation Study in the Guinea Pig, February 14 (1997).

(24) DSBG/Bromine compounds Ltd, unpublished study, Micronucleus Test in Bone Marrow Cells of the Mouse with Tribromophenol, (2002)

(25) DSBG/Bromine compounds Ltd, unpublished study, Primary Skin Irritation Study in Rabbits, June 3 (1985).

(26) Ed. Sweetman J A; Simmons M S. The production of bromophenols resulting from chlorination of waters containing bromide ion and phenol. Water Res. (1980). Vol.14No. 3, p. 287-290.

(27) Environ. Mutagen. Salmonella mutagenicity tests: Results from the testing of 255 chemicals, 1987, 9 (Suppl. 9), 1-109

(28) Environmental Agency of Japan,(2000),Ecotoxicity testing report(unpublished),Test Number;10031, Growth inhibition Test to Algae(Selenastrum capricornutum); Japan Food Research Laboratories.

(29) Environmental Agency of Japan,(2000),Ecotoxicity testing report(unpublished),Test Number;10032, Acute Toxicity to Daphnid (Daphnia magna); Japan Food Research Laboratories.

(30) Environmental Agency of Japan,(2000),Ecotoxicity testing report(unpublished),Test Number;10033, , Reproduction Test to Daphnia Magna; Japan Food Research Laboratories.

(31) Environmental Agency of Japan,(2000),Ecotoxicity testing report(unpublished),Test Number;10034, Acute Toxicity to Himedaka (Orizas lapties); Japan Food Research Laboratories.

(32) Great Lakes Chemical Corp., Dermal sensitization study in the Albino Guinea pig by International Research and Development Corporation for Michigan Chemical Corporation, (1975) (EPA/OTS; Doc #86-90000308)

(33) Great Lakes Chemical Corp., unpublished report, Pharmacokinetic Study of 2,4,6-Tribromophenol in Rats., Velsicol Chemical Corp., (1977) (EPA/OTS; Doc# 86-900000322)

(34) Great Lakes Chemical Corp., unpublished report, Acute dermal toxicity in Male and Female Albino Rabbits by International Research and Development Corporation for Michigan Chemical Corporation, (1974) (EPA/OTS; Doc #86-90000306.)

(35) Great Lakes Chemical Corp., unpublished report, Eye irritation study in Albino Rabbits by International Research and Development Corporation for Michigan Chemical Corporation, (1974), (EPA/OTS; Doc #86-90000304)

(36) Great Lakes Chemical Corp., unpublished report, Pilot Teratology study Rats by International Research and Development Corporation for Versicol Chemical Corporation, (1978)(EPA/OTS; Doc #86-90000316)

(37) Great Lakes Chemical Corp., unpublished report, Primary skin irritation study in Albino Rabbits by International Research and Development Corporation for Michigan Chemical Corporation, (1974), (EPA/OTS; Doc #86-90000303)

(38) Great Lakes Chemical Corp.,unpublished report, Acute inhalation toxicity in the Albino rat by International Research and Development Corporation for Michigan Chemical Corporation, (1974) (EPA/OTS; Doc #86-90000305.)

(39) Hansch C et al; Exploring QSAR. Hydrophobic, Electronic, and Steric Constants. ACS Prof Ref Book. Heller SR, consult. ed., Washington, DC: Amer Chem Soc p. 16 (1995)

(40) Higa, T., Fujiyama, T., Scheuer, P.J. (1980), Halogenated phenol and indole constituents of acorn worms. Comp. Biochem. Physiol., 65B, 525-530

(41) HPV Challenge Program, 201-14177A (2002)

(42) Industrial Bio-Test Laboratories, Inc, #8530-09439A, Oct. 27, 1977.

(43) Industrial Bio-Test Laboratories, Inc, #8562-09438.

(44) JISHA (2002), Japan Industrial Safety and Health Association, unpublished data

(45) King GM; Environ Microbiol 54: 3079-3085 (1988)

(46) Kopperman, H.L., R.M. Carlson, and R. Caple, (1974), Aqueous Chlorination and Ozonation Studies. I. Structure-Toxicity Correlations of Phenolic Compounds to Daphnia magna, Chem.-Biol.Interact. 9(4):245-251

(47) Lyman WJ et al; Handbook of Chemical Property Estimation Methods. Washington, DC: Amer Chem Soc (1990),pp. 7-4, 7-5

(48) Lyubimov, Alexander V; Babin, Vadim V; Kartashov Alex, I, Developmental neurotoxicity of 2,4,6-Tribromophenol in Wistar rats, Neurotoxicology, 19(2), 303-312, 1998

(49) MANAC Inc. Unpublished report

(50) Manac Inc., (2003) Water Quality Report, unpublished data

(51) Mar. Ecol. Prog. Ser (1997),Biogenic bromophenols as negative recruiment cues. 157, p.303-306.

(52) Marine Pollution Bulletin, (1991), Identification and occurrence of brominated and nitrated phenols in estuarine sediments. Vol. 22, No. 12 pp.603-607.

(53) Meylan, W.M. and P.H. Howard. Computer estimation of the atmospheric gas-phase reaction rate of organic compounds with hydroxyl radicals and ozone. Chemosphere (1993), 26, 2293-2299

(54) MHW Japan, 1999: Ministry of Health and Welfare, Toxicity Testing Reports of Environmental Chemicals 7, 387-421

(55) Nacalai Tesque, MSDS (MSDS No.34514) July (2001)

(56) NIOSH, National Occupational Exposure Survey (NOES) (1983)

(57) Oeberg T., Warman K. and Bergstroem J.,(1987) Brominated aromatics from combustion; Chemosphere 16: 2451-65

(58) Phipps, G.L., G.W. Holcombe, and J.T. Fiandt, (1981), Acute Toxicity of Phenol and Substituted Phenols to the Fathead Minnow., Bull.Environ.Contam.Toxicol. 26(5):585-593

(59) Polyhalogenated dibenzo-p-dioxins/dibenzofurans testing and reporting requirements under the toxic substances control act (TSCA). Chemosphere (1989), 19(1-6), 849-52.

(60) Saitama-prefecture White Paper on the Environment (1997) in Japanese

(61) Saitama-prefecture White Paper on the Environment (1998) in Japanese

(62) Schultz, T.W., and G.W. Riggin, (1985), Predictive Correlations for the Toxicity of Alkyl- and Halogen-Substituted Phenols, Toxicol.Lett. 25:47-54

(63) Sithole B.B. and Williams DT (1986) Halogenated phenols in water at forty canadian potable water treatment facilities; J Assoc Off Anal Chem 69: 807-10

(64) Sithole B.B., Williams D.T., Lastoria C. And Robertson J.L., (1986) Determination of Halogenated Phenols in raw and potable water by selected ion gas chromatography-mass spectrometry; J Assoc Off Anal Chem 69: 466-73

(65) Spehar R.L.; Carlson R.W., Lemke A.E., Mount D.I., Pickering G.H. and Snarski V.M.; Effects of pollution on freshwater fish.; J. Water Pollut. Control Fed.; (1980), 52:1703-74

(66) Steward, C Charles; Dixon Terry C; Chen, Yung Pin; Lovell; Charles R. Enrichment and isolation of a reductively debrominating bacterium from the burrow of a bromometabolite-producing marine hemichordate. Can.J.Microbiol. (1995), 41(7), 637-42.

(67) Stoner Laboratories, Inc, Project#780240, Donald E. Nye, July 11, 1978.

(68) The Condensed Chemical Dictionary, Ninth Edition, Van Nostrand Reinhold,p.126, 1977.

(69) The Dictionary of substances and their effects, M .L Richardson; S. Gangolli, 1994, Vol 7 p. 522. (Refered by Worne, H. E, Tijdschrift Van Let BECEWA Liege)

(70) The Dictionary of Substances and their Effects.Ed. M. L Richardson ,S. Gangolli.Vol.7, p.522, 1994.

(71) The Sigma Aldrich Library of chemical Safety Data,edition I,1985, Robert.E.Lenga, p.1728.

(72) Tolosa I., Bayona J.M. and Albaiges J., (1991) Identification and Occurrence of Brominated and Nitrated Phenols in estuarine sediments; Marine Pollut Bull 22: 603-7

(73) Velsicol Chemical Corp., Project#428148, report#4, June 22, 1978.

(74) Wako Pure Chemical Industries, Ltd., MSDS(No. JW200437) June (2002)

(75) Watanabe I., Takahashi K. and Tatsukawa R., (1985) Brominated phenols and anisoles in river and marine sediments in Japan; Bull Environ Contam Toxicol 35: 272-78

(76) Water Sci. Technol. The source of bromophenols in some species of Australian ocean fish, 1995, 31(11 , off-Flavorous in the Aquatic Environment 1994), 113-20.

(77) Whitfield F.B., Helidoniotis F. Svoronos D., Shaw K.J. and Ford G.L., (1995) The source of bromophenols in some species of australian ocean fish; Wat. Sci. Tech. 31: 113-120

(78) Whitfield F.B., Helidoniotis F., Shaw K.J. and Svoronos D., (1997), Distribution of bromophenols in Australian wild harvested and cultivated prawns (shrimp). Journal of Agricultural & Food Chemistry; 45(11):4398-405

(79) Whitfield F.B., Helidoniotis F., Shaw K.J. and Svoronos D., (1998), Distribution of bromophenols in Australian wild harvested and cultivated prawns (shrimp). Journal of Agricultural & Food Chemistry; 46(9):3750-7

(80) Whitfield F.B., Shaw K.J. and Walker D.I., (1992) The source of 2,6-dibromophenol: cause of an iodoform taint in australian prawns; Wat. Sci. Tech. 25: 131-138

(81) Yalkowsky SH, Dannenfelser RM; Aquasol Database of Aqueous Solubility. Version 5. College of Pharmacy, University of Arizona-Tucson, AZ. PC version