FOREWORD INTRODUCTION

6-tert-Butyl-2,4-xylenol

CAS N°: 1879-09-0

SIDS Initial Assessment Report

For

SIAM 4

Tokyo, Japan, 20-22 May 1996

1. Chemical Name: 6-tert-Butyl-2,4-xylenol

2. CAS Number: 1879-09-0

3. Sponsor Country: Japan
National SIDS Contact Point in Sponsor Country:
Mr. Yasuhisa Kawamura, Ministry of Foreign Affairs, Japan

4. Shared Partnership with:

5. Roles/Responsibilities of the Partners:

- Name of industry sponsor /consortium
- Process used

6. Sponsorship History

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

As a high priority chemical for initial assessment, 6-tert-butyl-2,4-xylenol was selected in the framework of the OECD HPV Chemicals Programme.
SIDS Dossier and Testing Plan were reviewed at a SIDS Review Meeting in 1993, where the following SIDS Testing Plan was agreed:

No testing ( )
Testing(X)

Physical-Chemical Properties
- Vapour pressure
- Partition coefficient
- Water solubility

Environmental fate/Biodegradation
- Photodegradation
- Stability in water

Ecotoxicity
- Acute toxicity to fish
- Acute toxicity to daphnids
- Toxicity to algae
- Chronic toxicity to daphnids

Toxicity
Repeated dose toxicity
Reproductive/developmental toxicity
Gene mutation
Chromosomal aberration in vitro

7. Review Process Prior to the SIAM: The original report was already circulated in August 1995, and the report was revised according to the comments from member countries.
At SIAM-4, The conclusion was approved with comments.
Comments at SIAM-4: Rearrangement of the documents.

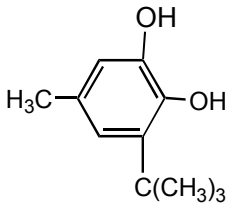
8. Quality check process:

9. Date of Submission: 30 April 1996

10. Date of last Update:

11. Comments:

SIDS INITIAL ASSESSMENT PROFILE

CAS No.	1879-09-0
Chemical Name	2,4-Xylenol, 6-t-butyl-
Structural Formula	

CONCLUSIONS AND RECOMMENDATIONS

A potential hazard to man due to a low no-effect-level in repeated dose animal studies is identified, but exposure is considered to be low.

Unless further information on exposure in other member countries presents evidence to the contrary, it is currently considered of low potential risk and low priority for further work.

SHORT SUMMARY WHICH SUPPORTS THE REASONS FOR THE CONCLUSIONS AND RECOMMENDATIONS

6-tert-Butyl-2,4-xylenol is not produced in Japan, and there are no imported volumes. However, this chemical is registered in TSCA and EINECS. This chemical is stable in acidic, neutral and alkaline solutions, and is considered as “not readily biodegradable”.

For the environment, various NOEC and LC_{50} values were gained from test results; LC_{50} = 4.4 mg/l (acute fish); EC_{50} = 5.6 mg/l (acute daphnia); EC50 = 3.6 mg/l (algae), NOEC = 1.7 mg/l (algae); NOEC = 0.32 mg/l (long-term daphnia reproduction). Therefore, the chemical is considered to be moderately toxic to fish and daphnids and algae. The lowest chronic toxicity result, 21 d-NOEC (reproduction) of *Daphnia magna* (0.32 mg/l), was adopted for the calculation of the PNEC, applying an assessment factor of 100. Thus the PNEC of 6-tert-butyl-2,4-xylenol is 0.0032 mg/l. Since the chemical is not produced in member countries, PEC/PNEC ratio could not be calculated. Therefore, it is considered to be currently of low potential risk for the environment.

The chemical showed no genotoxic effects in bacteria and in a chromosomal aberration test *in vitro*.

In a combined repeat dose and reproductive/developmental toxicity screening test, there were no clinical observations attributed to the administration of the test substance in parental animals. However, increases of liver and kidney weights were observed at the middle and highest dose level (30 and 150 mg/kg/day). In addition, histopathological examination showed swelling of liver cells and degeneration and protein cast of the proximal renal tubules in the groups. From the view point of reproductive/developmental end-points, only a few females at the highest dose lost their litters during lactation period. Other effects (e.g. mating, fertility and estrous cycle) were not observed. Therefore, the NOEL was 6 mg/kg/day for repeated dose toxicity and 30 mg/kg/day for reproductive toxicity.

For human health, daily intake of the chemical could not be estimated, because of the lack of exposure scenarios. However, the health risk is presumably low due to its exposure situation.

NATURE OF FURTHER WORK RECOMMENDED

FULL SIDS SUMMARY

6-tert-Butyl-2, 4-xylenol

CAS NO: 1879-09-0		SPECIES	PROTOCOL	RESULTS
PHYSICAL-CHEMICAL				
2.1	Melting Point			21 – 22 °C
2.2	Boiling Point			247.8 – 248.3 °C
2.3	Density			No data available
2.4	Vapour Pressure		OECD TG 104	1.7 Pa at 25 °C
2.5	Partition Coefficient (Log Pow)		OECD TG 107	4.08 at 25 °C
2.6 A.	Water Solubility		OECD TG 105	150 mg/l at 25 °C
B.	pH			No data available.
	pKa			No data available
2.12	Oxidation: Reduction Potential			No data available.
ENVIRONMENTAL FATE AND PATHWAY				
3.1.1	Photodegradation		Calculation	Half-life: 2.16 years (direct photolysis in water)
3.1.2	Stability in Water		OECD TG 111	Stable at pH 4.0, 7.0 and 9.0
3.2	Monitoring Data			No data available
3.3	Transport and Distribution		Calculated (Fugacity Level III)	100% released to water, In Air 0.72% In Water 40.70% In Soil 30.70% In Sediment 27.88%
3.5	Biodegradation		OECD TG 301C	Not readily biodegradable: 3-5% (BOD) in 28 days, 0-4% (GC) in 28 days
3.6	Bioaccumulation			No data available
ECOTOXICOLOGY				
4.1	Acute/Prolonged Toxicity to Fish	*Oryzias latipes*	OECD TG 203	LC_{50} (24hr): 6.0 mg/L LC_{50} (96hr): 4.4 mg/L
4.2	Acute Toxicity to Aquatic Invertebrates (*Daphnia*)	*Daphnia magna*	OECD TG 202	EC_{50} (24hr): 5.6 mg/l
4.3	Toxicity to Aquatic Plants e.g. Algae	*Selenastrum capricornutum*	OECD TG 201	EC_{50} (72hr): 3.6 mg/l NOEC: 1.7 mg/l
4.5.2	Chronic Toxicity to Aquatic Invertebrates (*Daphnia*)	*Daphnia magna*	OECD TG 202	EC_{50} (21d, Immobility): 2.5 mg/l EC_{50} (21d, Reproduction): 0.60 mg/l NOEC (21d, Repro): 0.32 mg/l
4.6.1	Toxicity to Soil Dwelling Organisms			No data available.
4.6.2	Toxicity to Terrestrial Plants			No data available.

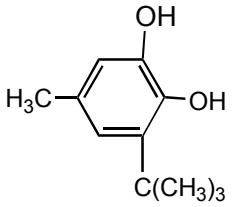
CAS NO: 1879-09-0		SPECIES	PROTOCOL	RESULTS
(4.6.3)	Toxicity to Other Non- Mammalian Terrestrial Species (Including Birds)			No data available
TOXICOLOGY				
5.1.1	Acute Oral Toxicity	Rat		LDLo: 1,400 mg/kg
5.1.2	Acute Inhalation Toxicity			No data available.
5.1.3	Acute Dermal Toxicity			No data available
5.4	Repeated Dose Toxicity	Rat	OECD TG 422	NOEL = 6 mg/kg/day
5.5	Genetic Toxicity In Vitro			
A.	Bacterial Test (Gene mutation)	*S. .typhimurium* *E. coli*	OECD Guidelines No.471 and 472 and Japanese	Negative in all bacterial strains tested with and without metabolic activation)
B.	Non-Bacterial In Vitro Test (Chromosomal aberrations)	CHL cells	OECD Guideline No.473 and Japanese Guideline	Negative (With metabolic activation) Negative (Without metabolic activation)
5.6	Genetic Toxicity In Vivo			No data available
5.8	Toxicity to Reproduction	Rat	OECD TG 422	NOEL Parental = 30 mg/kg/day NOEL F1 offspring = 30 mg/kg/day
5.9	Developmental Toxicity/ Teratogenicity			
5.11	Experience with Human Exposure			

SIDS Initial Assessment Report

1 IDENTITY

1.1 Identification of the Substance

CAS Number: 1879-09-0
IUPAC Name: Phenol, 2-(1,1-dimethylethyl)-4,6-dimethyl-
Molecular Formula: $C_{12}H_{18}O$
Structural Formula:



Synonyms: 6-tert-Butyl-2, 4-xylenol

1.2 Purity/Impurities/Additives

Degree of Purity: Unknown (Tests were performed using reagent grade: 98.5%)

Major Impurities: Unknown

Essential Additives: Unknown

1.3 Physico-Chemical properties

Melting Point:	21-22 °C
Boiling Point	247.8-248.3 °C
Vapour Pressure	1.7 Pa at 25 °C
Partion Coefficient LogKow	4.8
Water Solubility	150 mg/l at 25 °C

2 GENERAL INFORMATION ON EXPOSURE

6-tert-Butyl-2,4-xylenol is not produced in Japan, and there is no information about imported volumes. 6-tert-Butyl-2,4-xylenol is not readily biodegradable (OECD 301C: 3 % degradation after 28 days). 6-tert-Butyl-2,4-xylenol is not hydrolyzed at pH 4, 7 and 9. Direct photodegradation is not expected because 6-tert-butyl-2, 4-xylenol does not absorb UV light.

2.1 Environmental Exposure and Fate

2.1.1 Photodegradation

The half-life time of 2.16 years is estimated for the degradation of 6-tert-butyl-2, 4-xylenol in water by direct photodegradation. (Lyman et al., 1981).

2.1.2 Stability in Water

The chemical is stable in water at pH 4, 7 and 9 (OECD TG 111).

2.1.3 Biodegradation

If released into water, this substance is not readily biodegraded (MITI (I), corresponding to the OECD 301C: 3 - 5 % degradation during 28 days based on BOD and 0 - 4 % based on GC analysis).

2.1.4 Bioaccumulation

No data are available on bioaccumulation of 6-tert-butyl-2,4-xylenol.

2.1.5 Global exposure

The potential environmental distribution of 6-tert-butyl-2,4-xylenol obtained from a generic level III fugacity model is shown in Table 1. The results show that if 6-tert-Butyl-2,4-xylenol is released mainly to air or soil, it is likely to distribute into soil compartment. But, if 6-tert-butyl-2,4-xylenol is released mainly to water, it is likely to be transported to soil and sediment. Due to the low vapour pressure of 6-tert-butyl-2,4-xylenol, it is unlikely to distribute into air.

No information is available on local exposure.

Table 1: Environmental distribution 6-tert-butyl-2,4-xylenol using a generic level III fugacity model.

Compartment	Release: 100% to air	Release: 100% to water	Release: 100% to soil
Air	2.25%	0.72%	0.01%
Water	1.07%	40.70%	0.19%
Soil	95.95%	30.70%	99.67%
Sediment	0.73%	27.88%	0.13%

2.2 Human Exposure

2.2.1 Occupational Exposure

No information available

2.2.2 Consumer Exposure

No information available

2.2.3 Exposure via the Environment

No information available

3 HUMAN HEALTH HAZARDS

3.1 Effects on Human Health

3.1.1 Acute Toxicity

LDLo in acute oral toxicity study in rats was reported to be 1,400 mg/kg. LC_{50} and LD_{50} values for acute inhalation and dermal toxicity are not available.

3.1.2 Repeated Dose Toxicity

There is only one key study on repeated dose toxicity of 6-tert-butyl-2,4-xylenol. This chemical was studied for oral toxicity in rats according to the OECD combined repeated dose and reproductive/developmental toxicity test [OECD TG 422]. As the study was well controlled and conducted under GLP, this was appropriate to regard as a key study. Male and female SD rats were orally administered (gavage) at doses of 0, 6, 30 and 150 mg/kg/day.

There were no clinical observations attributable to the administration of test substance. However, two dead animals (one of them during the delivery) were observed in female rats given 150 mg/kg at the end of the gestation period. Although the body weight gain of females given 150 mg/kg was lower than that of the controls during the gestation period, body weight gain of males and food consumption of both sexes did not change. Hematological examination showed decreases in hematocrit, hemoglobin and red blood cells, increases in reticulocyte (slight trend of anemia) in males given 150 mg/kg. Blood clinical examination revealed increases in gamma-GTP in 30 and 150 mg/kg males. Increases or tendency to increases of liver and kidney weights were observed in males given 30 mg/kg or more and females given 150 mg/kg. Histopathological examination showed swelling of liver cells in the centrilobules in both males and females given 150 mg/kg, and showed degeneration and protein cast of the proximal renal tubules, PAS positive granules deposited at renal papilla in females given 150 mg/kg. The results described above led to a conclusion that effects of repeated dose toxicity study were considered to appear at 30 mg/kg/day or more in male rats and at 150 mg/kg/day in female rats (MHW, Japan, 1994). The NOEL for repeated dose toxicity in rats is considered to be 6 mg/kg/day in males and 150 mg/kg/day in female rats.

3.1.3 Mutagenicity

In vitro Studies

Bacterial test

Reverse gene mutation assay was conducted in line with Guidelines for Screening Mutagenicity Testing of Chemicals (Japan) and OECD Test Guidelines 471 and 472, using the pre-incubation method. This study was well controlled and regarded as a key study. The chemical showed negative results in *Salmonella typhimurium* TA100, TA1535, TA98, TA1537 and *Escherichia coli* WP2 *uvr*A at concentrations up to 0.5 mg/plate with or without Metabolic activation system (MHW, 1993).

Non-bacterial test

A chromosomal aberration test in line with Guidelines for Screening Mutagenicity Testing of Chemicals (Japan) and OECD Test Guideline 473 was conducted using cultured Chinese Hamster lung (CHL/IU) cells. This study was well controlled and regarded as a key study.

No structural chromosomal aberrations or polyproidy were recognized up to a maximum concentration of 3.5 mg/ml under conditions of both continuous treatment and short-term treatment with or without an exogeneous metabolic activation system (MHW, 1998).

In vivo Studies

No data are available on *in vivo* genotoxic effects.

3.1.4 Toxicity for Reproduction

6-tert-Butyl2,4-xylenol was studied for oral toxicity in rats according to the OECD combined repeated dose and reproductive/developmental toxicity test [OECD TG 422] at doses of 0, 6, 30 and 150 mg/kg/day.

Test substance showed no effects on mating, fertility and estrous cycle. In observation at delivery, three females given 150 mg/kg lost their litters during lactation period, and tendency to decrease of viability index of pups at Day 4 after birth was observed in 150 mg/kg group. The results described above led to a conclusion that effects of reproductive toxicity study were considered to appear at 150 mg/kg/day in rats (MHW, Japan, 1994). The NOEL for repeated dose toxicity in rats is considered to be 30 mg/kg/day in parental animals males and 30 mg/kg/day in F_1 offspring.

3.2 Initial Assessment for Human Health

The chemical showed no genotoxic effects in bacteria and in a chromosomal aberration test *in vitro*. In a combined repeat dose and reproductive/developmental toxicity screening test, there were no clinical observation attributed to the administration of the test substance in parental animals. However, increases of liver and kidney weights were observed at the midle and highest dose level (30 and 150 mg/kg/day). In addition, histpathological examination showed swelling of liver cells and degeneration and protein cast of the proximal renal tubules in the groups. From the view point of reproductive/developmental end-points, only a few females at the highest dose lost their litters during lactation period. Other effects (e.g. mating, fertility and estrous cycle) were not observed. Therefore, the NOEL was 6 mg/kg/day for repeated dose toxicity and 30 mg/kg/day for reproductive toxicity.

For human health, daily intake of the chemical could not be estimated, because of the lack of exposure scenarios. Therefore, the health risk is presumably low due to its exposure situation.

4 HAZARDS TO THE ENVIRONMENT

4.1 Aquatic Effects

6-tert-Butyl-2,4-xylenol has been tested in a limited number of aquatic species (*Selenastrum capricornutum*, *Daphnia magna* and *Oryzias latipes*), under OECD test guidelines [OECD TG 201, 202, 203]. Acute and chronic toxicity data to test organisms for 6-tert-butyl-2,4-xylenol are summarized in Table 2. No other ecotoxicological data are available.

Various NOEC and LC_{50} values were gained from above tests; 96h LC_{50} = 4.4 mg/l (acute fish); 24h EC_{50} = 5.6 mg/l (acute daphnia); 72h EC_{50} = 3.6 mg/l (acute algae); NOEC = 1.7 mg/L (algae), 21d NOEC = 0.32 mg/l (long-term daphnia reproduction). Therefore, the chemical is considered to

be moderately toxic to fish, daphnids and algae. As the lowest chronic toxicity result, the 21 d-NOEC (reproduction) of *Daphnia magna* (0.32 mg/l) was adopted. An assessment factor of 100 is applied. Thus PNEC of 6-tert-butyl-2, 4-xylenol is 0.0032 mg/l. Since the chemical is not produced in member countries, PEC/PNEC ratio could not be calculated. Therefore, it is considered to be currently of low potential risk for the environment.

Table 2. Acute and chronic toxicity data of 6-tert-butyl-2,4-xylenol to aquatic organisms.

Species	Endpoint[*1]	Conc. (mg/L)	Reference
Selenastrum capricornutum (algae)	Biomass: EC_{50} (72h) NOEC	3.6 mg/L 1.7 mg/L	**EA, Japan. (1994)**
Daphnia magna (water flea)	Imm: EC_{50}(24h) Imm: EC_{50}(21d) Rep: EC_{50}(21d) NOEC(21d)	5.6 mg/L 2.5 mg/L 0.60 mg/L 0.32 mg/L	
Oryzias latipes (fish, Medaka)	Mor: LC_{50}(24h) Mor: LC_{50}(72h) Mor:LC_{50}(96h)	6.0 mg/L 5.0 mg/L 4.4 mg/L	

Notes: [*1] Mor; mortality, Rep; reproduction, Imm; immobilisation

4.2 Initial Assessment for the Environment

6-tert-Butyl-2,4-xylenol is not produced in Japan, and there are no imported volumes. However, this chemical is registered in TSCA and EINECS. This chemical is stable in acidic, neutral and alkaline solutions, and is considered as “not readily biodegradable”.

For the environment, various NOEC and LC_{50} values were gained from test results; 96h LC_{50} = 4.4 mg/l (acute fish); 24h EC_{50} = 5.6 mg/l (acute daphnia); 72h NOEC = 1.7 mg/l (algae); 21d NOEC = 0.32 mg/l (long-term daphnia reproduction). Therefore, the chemical is considered to be moderately toxic to fish and daphnids and algae. As the lowest chronic toxicity result, the 21 d-NOEC (reproduction) of *Daphnia magna* (0.32 mg/l) was adopted. An assessment factor of 100 is applied. Thus the PNEC of 6-tert-butyl-2, 4-xylenol is 0.0032 mg/l. Since the chemical is not produced in member countries, PEC/PNEC ratio could not be calculated. Therefore, it is considered to be currently of low potential risk for the environment .

5 RECOMMENDATIONS

A potential hazard to man due to a low no-effect-level in repeated dose animal studies is identified, but exposure is considered to be low.

Unless further information on exposure in other member countries presents evidence to the contrary, it is currently considered of low potential risk and low priority for further work.

6 REFERENCES

EA, Japan (1994) "Investigation of the Ecotoxicological Effects of OECD High Production Volume Chemicals", Office of Health Studies, Environmental Health Department, Environment Agency, Japan (HPV/SIDS Test conducted by EA, Japan)

EA & MITI, Japan (1994) Unpublished Report on Exposure Estimation (HPV/SIDS Test conducted by EA and MITI, Japan)

ECDIN database (1994)

Lyman, W.J, W. F. Reehl and D. H. Rosenblatt (1981) "Handbook of Chemical Property Estimation Method", McGraw Hill Book Co.

MHW, Japan (1994a) Unpublished Report on Combined Repeat Dose and Reproductive/Developmental Toxicity Screening Test of 6-tert-butyl-2,4-xylenol. (HPV/SIDS Test conducted by MHW, Japan)

MHW, Japan (1994b) Unpublished Report on Mutagenicity Test of 6-tert-butyl-2,4-xylenol. (HPV/SIDS Test conducted by MHW, Japan)

MITI, Japan (1994a): Unpublished data

MITI, Japan (1994b) Unpublished Report (HPV/SIDS Test conducted by MITI, Japan. Test was performed in Chemicals Inspection and Testing Institute, Japan)

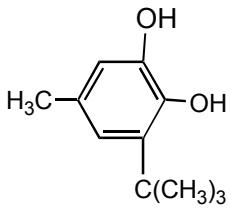
SIDS DOSSIER

Phenol, 2-(1,1-dimethylethyl)-4,6-dimethyl-

CAS No. 1879-09-0

Sponsor Country: Japan

S I D S P R O F I L E

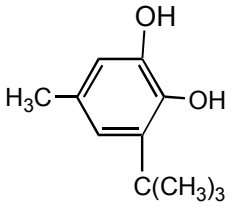
1.01 A.	**CAS No.**	1879-09-0
1.01 C.	**CHEMICAL NAME (OECD Name)**	Phenol, 2-(1,1-dimethylethyl)-4,6-dimethyl-
1.01 D.	**CAS DESCRIPTOR**	Not applicable
1.01 G.	**STRUCTURAL FORMULA**	
	OTHER CHEMICAL IDENTITY INFORMATION	
1.5	**QUANTITY**	Unknown
1.7	**USE PATTERN**	Unknown
1.9	**SOURCES AND LEVELS OF EXPOSURE**	Unknown
ISSUES FOR DISCUSSION (IDENTIFY, IF ANY)		

S I D S S U M M A R Y

6-tert-Butyl-2,4-xylenol

CAS NO: 1879-09-0		Information	OECD Study	GLP	Other Study	Estimation Method	Acceptable	SIDS Testing Required
STUDY		**Y/N**	**Y/N**	**Y/N**	**Y/N**	**Y/N**	**Y/N**	**Y/N**
PHYSICAL-CHEMICAL DATA								
2.1	Melting Point	Y	N	N	Y	N	Y	N
2.2	Boiling Point	Y	N	N	Y	N	Y	N
2.3	Density	N						N
2.4	Vapour Pressure	N						Y
2.5	Partition Coefficient	N						Y
2.6	Water Solubility	N						Y
	pH and pKa values	N						N
OTHER P/C STUDIES RECEIVED								
ENVIRONMENTAL FATE and PATHWAY								
3.1.1	Photodegradation	N						Y
3.1.2	Stability in water	N						Y
3.2	Monitoring data	N						N
3.3	Transport and Distribution	N						N
3.5	Biodegradation	N						Y
3.6	Bioaccumulation	N						N
OTHER ENV FATE STUDIES RECEIVED								
ECOTOXICITY								
4.1	Acute toxicity to Fish	N						Y
4.2	Acute toxicity to Daphnia	N						Y
4.3	Toxicity to Algae	N						Y
4.5.2	Chronic toxicity to Daphnia	N						Y
4.6.1	Toxicity to Soil dwelling organisms	N						N
4.6.2	Toxicity to Terrestrial plants	N						N
4.6.3	Toxicity to Birds	N						N
OTHER ECOTOXICITY STUDIES RECEIVED								
TOXICITY								
5.1.1	Acute Oral	Y	N	N	Y	N	Y	N
5.1.2	Acute Inhalation	N						N
5.1.3	Acute Dermal	N						N
5.4	Repeated Dose	N						Y
5.5	Genetic Toxicity *in vitro*							
	. Gene mutation	N						Y
	. Chromosomal aberration	N						Y
5.6	Genetic Toxicity *in vivo*	N						N
5.8	Reproduction Toxicity	N						Y
5.9	Development / Teratogenicity	N						Y
5.11	Human experience	N						N
OTHER TOXICITY STUDIES RECEIVED								

1.01 SUBSTANCE INFORMATION

A.	**CAS-Number**	1879-09-0
B.	**Name (IUPAC name)**	6-tert-Butyl-2,4-xylenol
C.	**Name (OECD name)**	Phenol, 2-(1,1-dimethylethyl)-4,6-dimethyl-
D.	**CAS Descriptor**	Not applicable
E.	**EINECS-Number**	217-533-1
F.	**Molecular Formula**	$C_{12}H_{18}O$
G.	**Structural Formula**	
H.	**Substance Group**	Not applicable
I.	**Substance Remark**	None
J.	**Molecular Weight**	178.30

1.02 OECD INFORMATION

A. Sponsor Country: Japan

B. Lead Organization:

Name of Lead Organization:
Ministry of Health and Welfare (MHW)
Ministry of International Trade and Industry (MITI)
Environment Agency (EA)

Contact person:
Mr. Yasuhisa Kawamura
Director
Second International Organization Bureau
Ministry of Foreign Affairs
Ministry of Labor (MOL)

Address:
2-2-1 Kasumigaseki, Chiyoda-ku
Tokyo 100, Japan
TEL 81-3-3581-0018
FAX 81-3-3503-3136

C. Name of responder

Name: Same as above contact person
Address:

1.1 GENERAL SUBSTANCE INFORMATION

A. Type of Substance

element **[ ]**; inorganic **[ ]**; natural substance **[ ]**;
organic **[X]**; organometallic **[ ]**; petroleum product **[ ]**

B. Physical State gaseous **[ ]**; liquid **[X]**; solid **[ ]**

C. Purity Unknown

1.2 SYNONYMS 6-tert-Butyl-2, 4-xylenol

1.3 IMPURITIES Unknown

1.4 ADDITIVES None

1.5 QUANTITY

Location	Production (tonnes)	Date
Japan	0 /year	1994

Reference: MITI, Japan (1994a)

1.6 LABELLING AND CLASSIFICATION

None

1.7 USE PATTERN

A. General

	Type of Use:	**Category:**
	(1) No use	
	(2) Industry	Antioxidant Rubber processing agent
Reference:	(1) MITI, Japan (1994a) (2) ECDIN database (1994)	

B. Uses in Consumer Products

Unknown

1.8 OCCUPATIONAL EXPOSURE LIMIT VALUE

Unknown

1.9 SOURCES OF EXPOSURE

(a)

Source:	Media of release: Water from a production site Quantities per media: 0 tonnes/year
Reference:	MITI, Japan (1994a)

1.10 ADDITIONAL REMARKS

A. Options for disposal Unknown

B. Other remarks None

2.1 MELTING POINT

Value:	21 - 22 °C
Decomposition:	Yes **[ ]** No **[X]** Ambiguous **[ ]**
Sublimation:	Yes **[ ]** No **[X]** Ambiguous **[ ]**
Method:	
GLP:	Yes **[ ]** No **[ ]** ? **[X]**
Reference:	Data attached to reagent (Tokyo Kasei)

2.2 BOILING POINT

Value:	247.8 - 248.3 °C
Pressure:	1013 hPa
Decomposition:	Yes **[ ]** No **[X]** Ambiguous **[ ]**
Method:	
GLP:	Yes **[ ]** No **[ ]** ? **[X]**
Reference:	Lange's Handbook of Chemistry (11th edition)

2.3 DENSITY (Relative density)

No data available

2.4 VAPOUR PRESSURE

Value:	1.7 Pa
Temperature:	25°C
Method:	calculated **[ ]**; measured **[X]** OECD Test Guideline 104 Dynamic method
GLP:	Yes **[X]** No **[ ]** ? **[ ]**
Reference:	MITI, Japan (1994b)

2.5 PARTITION COEFFICIENT $\log_{10}P_{ow}$

Log Pow:	4.08
Temperature:	25 °C
Method:	calculated **[ ]**; measured **[X]** OECD Test Guideline 107
GLP:	Yes **[X]** No **[ ]** ? **[ ]**
Reference:	MITI, Japan (1994b)

2.6 WATER SOLUBILITY

A. Solubility

Value:	150 mg/l
Temperature:	25 °C
Description:	Miscible **[ ]**; Of very high solubility **[ ]**; Of high solubility **[ ]**; Soluble **[ ]**; Slightly soluble **[X]**; Of low solubility **[ ]**; Of very low solubility **[ ]**; Not soluble **[ ]**
Method:	OECD Test Guideline 105
GLP:	Yes **[X]** No **[ ]** ? **[ ]**
Reference:	MITI, Japan (1994b)

B. pH Value, pKa Value

No data available

2.7 FLASH POINT

No data available

2.8 AUTO FLAMMABILITY

No data available

2.9 FLAMMABILITY

No data available

2.10 EXPLOSIVE PROPERTIES

No data available

2.11 OXIDIZING PROPERTIES

No data available

2.12 OXIDATION: REDUCTION POTENTIAL

No data available

2.13 ADDITIONAL DATA

A. Partition co-efficient between soil/sediment and water (Kd)

No data available

B. Other data

None

3.1 STABILITY

3.1.1 PHOTODEGRADATION

Type:	Air **[ ]**; Water **[X]**; Soil; Other **[ ]**	
Light source:	Sunlight **[X];** Xenon lamp **[ ];** Other **[ ]**	
Spectrum of substance:	epsilon = 6.24 at 300 nm	
Estimated parameter for calculation:		
	Quantum yield 0.01	
	Concentration	5×10^{-5} M
	Depth of water body	500 cm
	Conversion constant	6.023×10^{20}
Result:	Degradation rate	5.09×10^{-13} mol/l/s
	Half life	2.16 years
Reference:	W. J. Lyman, W. F. Reehl and D. H. Rosenblatt, "Handbook of Chemical Property Estimation Method", McGraw Hill Book Co., 1981.	

3.1.2 STABILITY IN WATER

Type:	Abiotic (hydrolysis) **[X]**; biotic (sediment) **[ ]**
Result:	Stable at pH 4, 7 and 9 at 25 °C
Method:	OECD Test guideline 111
GLP:	Yes **[X]** No **[ ]** ? **[ ]**
Test substance:	6-tert-Butyl-2,4-xylenol
Reference:	MITI, Japan (1994b)

3.1.3 STABILITY IN SOIL

No data available

3.2 MONITORING DATA (ENVIRONMENT)

No studies located

3.3 TRANSPORT AND DISTRIBUTION BETWEEN ENVIRONMENTAL COMPARTMENTS INCLUDING ESTIMATED ENVIRONMENTAL CONCENTRATIONS AND DISTRIBUTION PATHWAYS

3.3.1 TRANSPORT

No data available

3.3.2 THEORETICAL DISTRIBUTION (FUGACITY CALCULATION)

The potential environmental distribution of 6-tert-Butyl-2, 4-xylenol obtained from a generic level III fugacity model is shown in Table. The results show that if 6-tert-Butyl-2,4-xylenol is released mainly to air or soil, it is likely to distribute into soil compartment. But, if 6-tert-Butyl-2,4-xylenol is released mainly to water, it is likely to be transported to soil and sediment. Due to the low vapour pressure of 6-tert-Butyl-2, 4-xylenol, it is unlikely to distribute into air.

Environmental distribution 6-tert-Butyl-2, 4-xylenol using a generic level III fugacity model.

Compartment	Release: 100% to air	Release: 100% to water	Release: 100% to soil
Air	2.25%	0.72%	0.01%
Water	1.07%	40.70%	0.19%
Soil	95.95%	30.70%	99.67%
Sediment	0.73%	27.88%	0.13%

3.4 IDENTIFICATION OF MAIN MODE OF DEGRADABILITY IN ACTUAL USE

No data available

3.5 BIODEGRADATION

Type:	aerobic **[X]**; anaerobic **[ ]**
Inoculum:	adapted **[ ]**; non-adapted **[X]**;
Concentration of the chemical:	100 mg/l related to Test Substance **[X]**
Medium:	water**[ ];**water-sediment**[ ];**soil **[ ];**sewage treatment **[ ]** other **[**Japanese standard activated sludge**]**
Degradation:	Degree of degradation after 28 days 4, 3 and 5 % from BOD 0, 4 and 0 % from GC analysis
Results:	Readily biodeg. **[ ];** Inherently biodeg. **[ ]**; under test condition no biodegradation observed **[X]**
Method:	OECD Test Guideline 301 C
GLP:	Yes **[X]** No **[ ]** ? **[ ]**
Test substance:	6-tert-Butyl-2,4-xylenol
Reference:	MITI Japan (1992)

3.6 BOD_5,COD OR RATIO BOD_5/COD

Not applicable

3.7 BIOACCUMULATION

No data available

3.8 ADDITIONAL REMARKS

A. Sewage treatment None

B. Other information None

4.1 ACUTE/PROLONGED TOXICITY TO FISH

(a)

Type of test:	static **[ ]**; semi-static **[X]**; flow-through **[ ]**; other **[ ]** open-system **[X]**; closed-system **[ ]**
Species:	*Oryzias latipes*
Exposure period:	96 hr
Results:	LC_{50} (24h) =6.0 mg/l (95% confidence limits:6.0-11 mg/l) LC_{50} (48h) = 5.9 mg/l (95% confidence limits:3.8-5.5 mg/l) LC_{50} (72h) =5.0 mg/l (95% confidence limits:3.5-29 mg/l) LC_{50} (96h) = 4.4 mg/l (95% confidence limits:3.2-9.3 mg/l) NOEC = LOEC =
Analytical monitoring:	Yes **[ ]** No **[X]** ? **[ ]**
Method:	OECD Test Guideline 203 (1981)
GLP:	Yes **[ ]** No **[X]** ? **[ ]**
Test substance:	6-tert-Butyl-2,4-xylenol, purity = 99 %
Remarks:	A group of 10 fish were exposed to each of 5 nominal concentrations (1.0-10 mg/l). Stock solution was prepared with DMSO:HCO-40= 4:1(99-990 mg/l). Controls with and without this vehicle were taken for test.
Reference:	EA, Japan (1994)

4.2 ACUTE TOXICITY TO AQUATIC INVERTEBRATES

A. Daphnia

Type of test:	static **[X]**; semi-static **[ ]**; flow-through **[ ]**; other **[ ]**; open-system **[**X**]**; closed-system **[ ]**
Species:	*Daphnia magna*
Exposure period:	24 hr
Results:	EC_{50} (24h) = 5.6 mg/l (95% confidence limits:4.9-6.5 mg/l) EC_{50} (48h) = NOEC = LOEC =
Analytical monitoring:	Yes **[ ]** No **[X]** ? **[ ]**
Method:	OECD Test Guideline 202 (1984)
GLP:	Yes **[ ]** No **[X]** ? **[ ]**
Test substance:	6-tert-Butyl-2, 4-xylenol, purity = 99 %
Remarks:	20 daphnids (4 replicates; 5 organisms per replicate) were exposed to each of 5 nominal concentrations (1.0-10 mg/l). Stock solution was prepared with DMSO:HCO-40=9:1(100-1000 mg/l). Controls with and without this vehicle were taken for test.
Reference:	EA, Japan (1994)

B. Other aquatic organisms

No studies located

4.3 TOXICITY TO AQUATIC PLANTS e.g. Algae

Species:	*Selenastrum capricornutum* ATCC 22662

End-point:	Biomass **[X]**; Growth rate **[ ]**; Other **[ ]**
Exposure period:	72 hours
Results:	Biomass: EC_{50} (24h) =
	EC_{50} (72h) = 3.6 mg/l
	NOEC = 1.7 mg/l ($p < 0.05$)
	LOEC =
Analytical monitoring:	Yes **[ ]** No **[X]** ? **[ ]**
Method:	open-system **[ ]**; closed-system **[X]**
	OECD Test Guideline 201 (1984)
GLP:	Yes **[ ]** No **[X]** ? **[ ]**
Test substance:	6-tert-Butyl-2, 4-xylenol, purity = 99 %
Remarks:	The EC_{50} values for biomass were calculated based on 5 nominal concentrations (1.0-10 mg/l). Stock solution was prepared with DMSO(12.3 mg/l). Controls with and without this vehicle were taken for test. The vessel was sealed with a Parafilm and an aluminum film.
Reference:	EA, Japan (1994)

4.4 TOXICITY TO BACTERIA

No data available

4.5 CHRONIC TOXICITY TO AQUATIC ORGANISMS

4.5.1. CHRONIC TOXICITY TO FISH

No data available

4.5.2. CHRONIC TOXICITY TO AQUATIC INVERTEBRATES

Type of test:	static **[ ]**; semi-static **[**X**]**; flow-through **[ ]**; other **[ ]**;
	open-system **[X]**; closed-system **[ ]**
Species:	*Daphnia magna*
End-point:	Mortality **[ ]**; Reproduction rate **[X]**; Other **[X]**
Exposure period:	21 day
Results:	
Immobility:	EC_{50} (48 h) = 3.5 mg/l (95% confidence limits: 3.2-4.4 mg/l)
	EC_{50} (21 d) = 2.5 mg/l (95% confidence limits: 2.3-2.7 mg/l)
	NOEC =
	LOEC =
Reproduction:	EC_{50} (21d)=0.60 mg/l (95% confidence limits:0.59-0.60 mg/l)
	NOEC = 0.32 mg/l ($p < 0.05$)
	LOEC = 0.56 mg/l ($p < 0.05$)
Analytical monitoring:	Yes **[ ]** No **[X]** ? **[ ]**
Method:	OECD Test Guideline 202 (1984)
GLP:	Yes **[ ]** No **[X]** ? **[ ]**
Test substance:	6-tert-Butyl-2,4-xylenol, purity = 99 %
Remarks:	40 daphnids (4 replicates; 10 organisms per replicate) were exposed to each of 5 nominal concentrations (0.32-3.2 mg/l) Stock solution was prepared with DMSO:HCO-40 =9:1 (32-320 mg/l). Controls with and without this vehicle were taken for test.
Reference:	EA, Japan (1994)

4.6 TOXICITY TO TERRESTRIAL ORGANISMS

4.6.1 TOXICITY TO SOIL DWELLING ORGANISMS

No data available

4.6.2 TOXICITY TO TERRESTRIAL PLANTS

No data available

4.6.3 TOXICITY TO OTHER NON MAMMALIAN TERRESTRIAL SPECIES (INCLUDING AVIAN)

No data available

4.7 BIOLOGICAL EFFECTS MONITORING (INCLUDING BIOMAGNIFICATION)

No studies located

4.8 BIOTRANSFORMATION AND KINETICS IN ENVIRONMENTAL SPECIES

No data available

4.9 ADDITIONAL REMARKS

None

5.1 ACUTE TOXICITY

5.1.1 ACUTE ORAL TOXICITY

Type :	LD_0 **[ ]**; LD_{100} **[ ]**; LD_{50} **[ ]**; LDL_0 **[X]**; Other **[ ]**
Species/strain:	Rat
Value :	1,400 (mg/kg)
Method:	Unknown
GLP:	Yes **[ ]** No **[ ]** ? **[X]**
Test substance:	purity: Unknown
Remarks:	None
Reference:	J. Am. Pharm. Assoc., 38, 366 (1949)

5.1.2 ACUTE INHALATION TOXICITY

No data available

5.1.3 ACUTE DERMAL TOXICITY

No data available

5.1.4 ACUTE TOXICITY, OTHER ROUTES OF ADMINISTRATION

No data available

5.2 CORROSIVENESS/IRRITATION

5.2.1 SKIN IRRITATION/CORROSION

No data available

5.2.2 EYE IRRITATION/CORROSION

No data available

5.3 SKIN SENSITIZATION

No data available

5.4 REPEATED DOSE TOXICITY

Species/strain:	Rat (Crj:CD(SD))
Sex:	Female **[ ]**; Male **[ ]**; Male/Female **[X]**; No data **[ ]**
Route of Administration:	Oral gavage
Exposure period:	Males: 45 days including 14 days before mating Females: from 14 days before mating to day 3 of lactation
Frequency of treatment:	7 days/week
Post exposure observation period:	
Dose:	0, 6, 30 or 150 mg/kg (12 animals/group)
Control group:	Yes **[X]**; No **[ ]**; No data **[ ]**; Concurrent no treatment **[ ]**; Concurrent vehicle **[X]**; Historical **[ ]**
NOEL:	6 mg/kg/day
Results:	There were no clinical observations attributable to the

administration of test substance. However, two dead animals (one of them during the delivery) were observed in female rats given 150 mg/kg at the end of the gestation period. Although the body weight gain of females given 150 mg/kg was lower than that of control during the gestation period, body weight gain of males and food consumption of both sexes did not change. Hematological examination showed decreases in hematocrit, hemoglobin and red blood cell, increases in reticulocyte (slight trend of anemia) in males given 150 mg/kg. Blood clinical examination revealed increases in gamma-GTP in the 30 and 150 mg/kg males. Increases or tendency to increases of liver and kidney weights were observed in males given 30 mg/kg or more and females given 150 mg/kg. Histopathological examination showed swelling of liver cells in the centrilobules in both males and females given 150 mg/kg, and showed degeneration and protein cast of the proximal renal tubules, PAS positive granules deposited at renal papilla in females given 150 mg/kg.

Method: OECD Combined Repeat dose and reproductive/ Developmental Screening Toxicity Test (1992)

GLP: Yes **[X]** No **[ ]** ? **[ ]**

Test substance: Purity: 98.5 %

Reference: MHW, Japan (1994a)

5.5 GENETIC TOXICITY IN VITRO

A. BACTERIAL TEST

Type : Bacterial reverse mutation assay

System of testing:

Species/strain: S. typhimurium TA 98, TA 100, TA 1535, TA1537
E. coli WP2 uvrA

Concentration: 0, 6.25, 12.5, 25, 50, 100 and 200 µg/plate (-S9 mix)
0, 6.25, 12.5, 25, 50, 100, 200 and 400 µg/plate (+S9 mix)
0, 6.25, 12.5, 25, 50, 100 and 200 µg/plate (TA1537)

Metabolic activation: With **[ ]**; Without **[ ]**; With and Without **[X]**;No data**[ ]**

Results:

Cytotoxicity conc: With metabolic activation: 150-500 µg/plate
Without metabolic activation: 150-500 µg/plate

Precipitation conc:

Genotoxic effects:

S. typhimurium TA 100, TA1535, TA98, TA1537

	+	?	-
With metabolic activation:	**[ ]**	**[ ]**	**[X]**
Without metabolic activation:	**[ ]**	**[ ]**	**[X]**

E. coli WP2 uvrA

	+	?	-
With metabolic activation:	**[ ]**	**[ ]**	**[X]**
Without metabolic activation:	**[ ]**	**[ ]**	**[X]**

Method: Japanese Guideline for Screening Mutagenicity testing of chemicals

GLP: Yes **[X]** No **[ ]** ? **[ ]**

Teat substance: Reagent grade, purity: 98.5 %

Remarks: Procedure: Plate incorporation method
Plates/test: 3

Activation system: Liver S-9 fraction from Phenobarbital and 5,6-Benzoflavone pretreated male SD rats with NADPH-generating system
Media:Histidine selective
No. replicates: 2

Reference: MHW, Japan (1994b)

B. NON-BACTERIAL IN VITRO TEST

Type : Cytogenetics Assay
System of testing:
Species/strain: Chinese hamster lung (CHL/IU) cells
Concentration: -S9 (continuous treatment) 0, 0.008, 0.017, 0.033 mg/ml
-S9 (short-term treatment) 0, 0.008, 0.017, 0.033 mg/ml
+S9 (short-term treatment) 0, 0.014, 0.028, 0.056 mg/ml
Metabolic activation: With **[ ]**; Without **[ ]**; With and Without **[X]**;
No data **[ ]**
Results:
Cytotoxicity conc: With metabolic activation: 0.056 mg/ml
Without metabolic activation: 0.056 mg/ml
Precipitation conc:
Genotoxic effects:

	+	?	-
With metabolic activation:	**[ ]**	**[ ]**	**[X]**
Without metabolic activation:	**[ ]**	**[ ]**	**[X]**

Method: Japanese Guideline for Screening Mutagenicity Testing of Chemicals
GLP: Yes **[X]** No **[ ]** ? **[ ]**
Test substance: Reagent grade, purity 98.5 %
Remarks: Plates/test:2
Activation system: S-9 fraction from the liver of Phenobarbital and 5,6-Benzoflavone induced male SD derived rats with NADPH-generating system
Media: RPMI 1640 medium *plus* 10% foetal calf serum *plus* phytohaemagglutinin
No. replicates: 1
Reference: MHW, Japan (1994b)

5.6 GENETIC TOXICITY IN vivo

No data available

5.7 CARCINOGENICITY

No data available

5.8 TOXICITY TO REPRODUCTION

Type: Fertility **[ ]**; One generation study **[ ]**;
Two generation study **[ ]**; Other **[X]**
Species/strain: Rat Crj:CD(SD)
Sex: Female **[ ]**; Male **[ ]**; Male/Female **[X]**; No data **[ ]**
Route of Administration: Oral, gavage
Exposure period: Males: 45 days including 14 days before mating
Females: from 14 days before mating to day 3 of lactation.
Frequency of treatment: 7 days/week
Postexposure observation period:
Premating exposure period: male: 14 days, female: 14 days

Duration of the test;	
Doses:	0, 6, 30, 150 mg/kg (10 animals/sex/group)
Control group:	Yes **[X]**; No **[ ]**; No data **[ ]**; Concurrent no treatment **[ ]**; Concurrent vehicle **[X]**; Historical **[ ]**
NOEL Parental:	30 mg/kg/day
NOEL F1 Offspring:	30 mg/kg/day
NOEL F2 Offspring:	N/A
Results:	Test substance showed no effects on mating, fertility and estrous cycle. In observation at delivery, three females given 150 mg/kg lost their litters during lactation period, and tendency to decrease of viability index of pups at Day 4 after birth was observed in 150 mg/kg group.
Method:	OECD Combined Repeat dose and reproductive/ Developmental Screening Toxicity Test (1992)
GLP:	Yes **[X]** No **[ ]** ? **[ ]**
Test substance:	Reagent grade, purity 98.5 %
Remarks:	
Reference:	MHW, Japan (1994b)

5.9 DEVELOPMENTAL TOXICITY/ TERATOGENICITY

See 5.8

5.10 OTHER RELEVANT INFORMATION

A. Specific toxicities

No studies located

B. Toxicodynamics, toxicokinetics

No studies located

5.11 EXPERIENCE WITH HUMAN EXPOSURE

None

EA, Japan (1994) "Investigation of the Ecotoxicological Effects of OECD High Production Volume Chemicals", Office of Health Studies, Environmental Health Department, Environment Agency, Japan (HPV/SIDS Test conducted by EA, Japan)

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MITI, Japan (1994a): Unpublished data

MITI, Japan (1994b) Unpublished Report (HPV/SIDS Test conducted by MITI, Japan. Test was performed in Chemicals Inspection and Testing Institute, Japan)