

## 魚類急性毒性試験

### 1. 供試物質の概要

名 称	日 本 名	6-tert-ブチル-2,4-キシレノール		
	英 名	6-tert-Butyl-2,4-xyleneol		
	一般名・商品名			
構造式	分子式・示性式			
	分 子 量		178.27	
	水への溶解度			
	蒸 気 圧			
入手先	東京化成工業株式会社	製造年月日	年 月 日	
	TEL ( )	ロット番号	FAW01	
純 度	99% 不純物:			
その他の物性等				

### 2. 供試魚の概要

種名及び系統名	ヒメダカ		
由 来	機関育種		
飼育方法	馴致結果: 死亡 0% 餌の種類: テトラミン 量: 適量/回 給餌頻度: 1回/日		
平均体長	2.13 ± 0.14 cm (n=70)	平均体重	0.097 ± 0.021 g (n=70)

### 3. 試験条件

試験温度	23.0 ± 0.7 °C		
希釈水	供給源	脱塩素水道水	
	水 質	pH: 7.7 Ca/Mg比: 1.86 Na/K比: 6.18 硬度: 45.9 アルカリ度: 40.0 その他: 水質測定年月日: 1993年 2月 16日	

試験溶液	状態	無色透明	
	保管方法	冷蔵庫（冷暗所）	
	調製方法	溶解補助剤を使用 助剤名：DMSO：H <sub>2</sub> O＝40＝4：1	
飼育方法	半止水式		
	半止水式の場合	換水方法：全量交換 頻度：1回／1日	
	流水式の場合		
光源	蛍光灯 照光周期：16L8D		

#### 4. 試験結果

- (1) 魚類急性毒性試験結果（→様式3-1～3-3）
- (2) 試験終了時における濃度－死亡率曲線のグラフ（→図3-3）

#### 5. その他、特記事項

(様式3-1)

魚類急性毒性試験結果 (予備試験)

供試物質名 : 6-tert-ブチル-2,4-キシレンール

試験実施期間 : 1992年 9月29日 ~ 1992年10月 3日 ( 4日間)

試験実施機関 : 福岡県保健環境研究所

濃度公比 : 10

区分	溶液量 L	物質濃度 mg/L	助剤濃度 mg/L	試験開始時			24時間			48時間			72時間			96時間		
				供試魚数	pH	DO mg/L	生存数	pH	DO mg/L	生存数	pH	DO mg/L	生存数	pH	DO mg/L	生存数	pH	DO mg/L
対照	1	0	0	5	7.7	8.6	5	7.2	5.7	5	7.3	6.2	5	7.3	6.3	5	7.4	6.8
助剤対照	1	0	1000	5	7.7	8.7	5	7.2	6.1	5	7.4	6.6	5	7.3	6.3	5	7.3	6.9
1	1	0.1	0.9	5	7.7	8.7	5	7.2	5.8	5	7.4	6.0	5	7.3	6.7	5	7.4	7.1
2	1	1.0	9.0	5	7.7	8.7	5	7.1	5.6	5	7.4	6.0	5	7.2	6.5	5	7.3	7.1
3	1	10	90	5	7.6	8.6	0	7.2	7.6									
4	1	100	900	5	7.6	8.0	0	7.6	8.0									
5	1	1000	1000	5	7.6	8.2	0	7.6	8.2									
観察事項、pH変動の理由							1000mg/L白濁、10分後全個体死亡 100mg/Lやや白濁 20分後全個体死亡 10mg/L9時間後横転沈下											

\* 供試物質濃度を測定した場合、その値を( )の中に入れて物質濃度欄に記入すること。

\*\* pH, DOは上段に換水前、下段に換水後の測定値を記入すること。

試験開始後96時間で大部分の魚が生存した最高濃度	1.0 mg/L
試験開始後48時間で大部分の魚が死亡した最低濃度	10 mg/L

【本試験の設定濃度及び設定根拠】

公比	設定濃度区 (mg/L)					設定根拠
	1	2	3	4	5	
1.8	1.0	1.8	3.2	5.6	10	予備試験結果より

(様式3-2) 魚類急性毒性試験結果 (本試験①)

供試物質名 : 6-tert-ブチル-2,4-キシレノール  
 試験実施期間 : 1992年10月 5日 ~ 1992年10月 9日 ( 4日間)  
 試験実施機関 : 福岡県保健環境研究所  
 濃度公比 : 1.8

区分	溶液量 L	物質濃度 mg/L	助剤濃度 mg/L	試験開始時			24時間			48時間			72時間			96時間		
				供試魚数	pH	DO mg/L	生存数	pH	DO mg/L	生存数	pH	DO mg/L	生存数	pH	DO mg/L	生存数	pH	DO mg/L
対照	2	0	0	10	7.7	8.7	10	7.3 7.8	6.4 8.6	10	7.3 7.7	6.7 8.6	10	7.4 7.8	6.5 8.5	10	7.3	6.1
助剤対照	2	0	990	10	7.7	8.7	10	7.3 7.7	6.9 8.6	10	7.4 7.6	7.2 8.7	10	7.4 7.8	7.1 8.5	10	7.4	6.9
1	2	1.0	99	10	7.7	8.7	10	7.3 7.7	6.8 8.6	10	7.4 7.6	7.1 8.6	10	7.4 7.8	6.9 8.5	10	7.3	6.8
2	2	1.8	178	10	7.7	8.7	10	7.3 7.7	7.0 8.6	9	7.4 7.6	7.2 8.7	9	7.4 7.8	7.0 8.5	9	7.3	7.0
3	2	3.2	317	10	7.6	8.7	8	7.3 7.7	7.3 8.7	8	7.4 7.6	7.5 8.6	8	7.4 7.8	7.0 8.5	8	7.4	7.0
4	2	5.6	554	10	7.7	8.7	6	7.3 7.7	6.4 8.6	5	7.4 7.6	7.4 8.7	4	7.4 7.8	7.0 8.5	3	7.4	7.2
5	2	10	990	10	7.7	8.7	2	7.3 7.7	6.5 8.7	0	7.3	8.0						
観察事項、pH変動の理由							10.5.6mg/L, 6時間後横転水面浮上											

\* 供試物質濃度を測定した場合、その値を( )の中に入れて物質濃度欄に記入すること。

\*\* pH, DOは上段に換水前、下段に換水後の測定値を記入すること。

(様式3-3)

## 魚類急性毒性試験結果 (本試験②)

供試物質名 : 6-tert-ブチル-2,4-キシレンール

試験実施機関 : 福岡県保健環境研究所

## 【魚類に対する影響】

区分	物質濃度 mg/L	助剤濃度 mg/L	各観察時における 累積死亡率			
			24時間	48時間	72時間	96時間
対照	0	0	0	0	0	0
助剤対照	0	990	0	0	0	0
1	1.0	99	0	0	0	0
2	1.8	178	0	10	10	10
3	3.2	317	20	20	20	20
4	5.6	554	40	50	60	70
5	10	990	80	100	100	100
死亡率100% の最低濃度	mg/L (mmol/L)		( )	10 (0.0561)	10 (0.0561)	10 (0.0561)
死亡率0% の最高濃度	mg/L (mmol/L)		1.8 (0.0101)	1.0 (0.00561)	1.0 (0.00561)	1.0 (0.00561)
LC <sub>50</sub>	mg/L (mmol/L)		6.021 (0.0342)	5.858 (0.0261)	4.983 (0.0247)	4.434 (0.0234)
95%信頼限界			6.021 ≤ LC <sub>50</sub> ≤ 10.51	3.782 ≤ LC <sub>50</sub> ≤ 5.495	3.482 ≤ LC <sub>50</sub> ≤ 29.21	3.246 ≤ LC <sub>50</sub> ≤ 9.338
算出方法			プロビット法 ver.3	プロビット法 ver.3	プロビット法 ver.3	プロビット法 ver.3
その他の観察された影響及び それらが認められた濃度	5.6mg/L : 生存個体横転水面浮上					

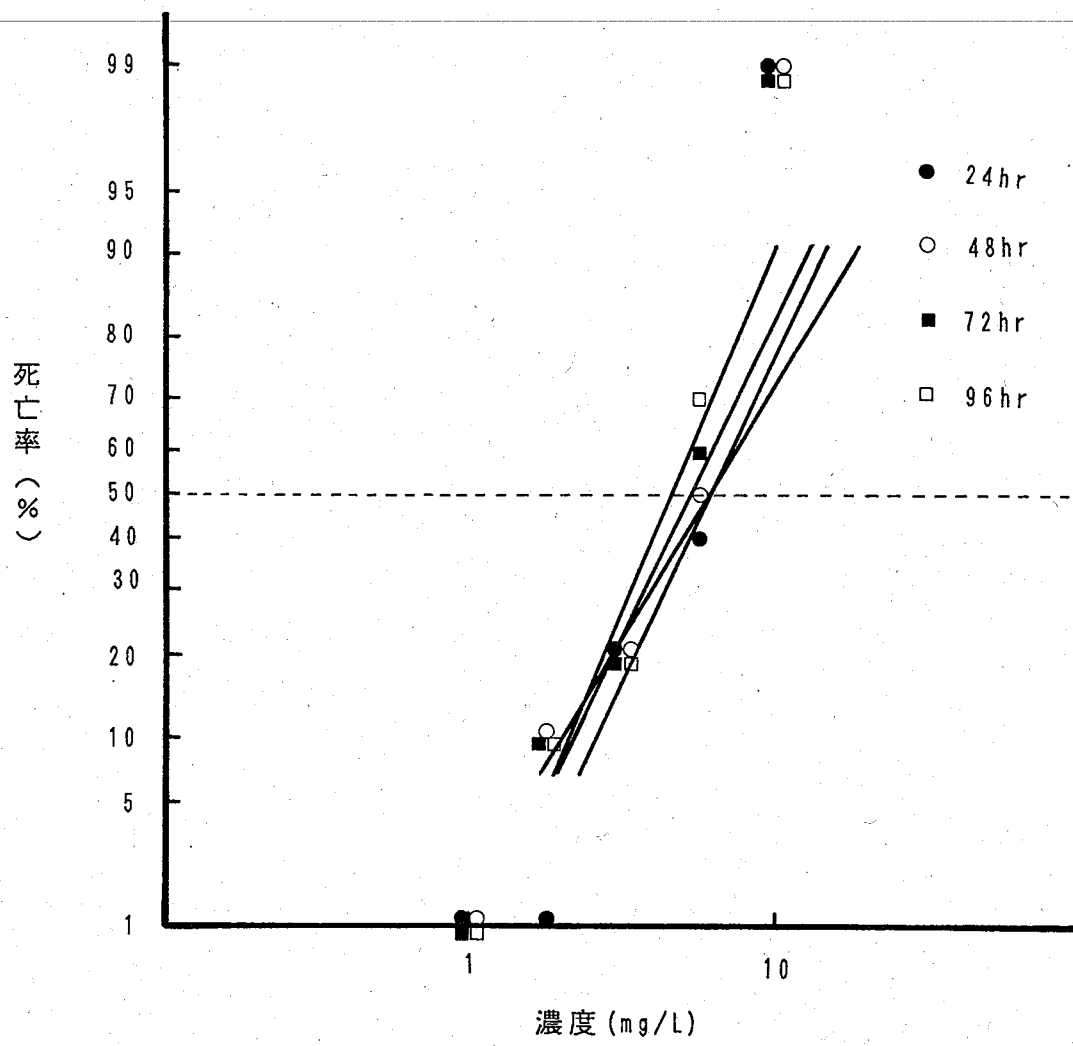
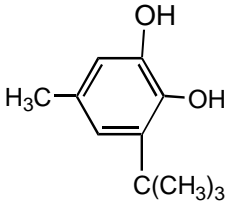


図3-3 ヒメダカ急性毒性試験における  
6-tert-ブチル-2,4-キシレノール  
の濃度と死亡率の関係



**SIDS INITIAL ASSESSMENT PROFILE**

<b>CAS No.</b>	1879-09-0
<b>Chemical Name</b>	2,4-Xylenol, 6-t-butyl-
<b>Structural Formula</b>	
<b>CONCLUSIONS AND RECOMMENDATIONS</b>	
<p>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.</p> <p>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.</p>	
<b>SHORT SUMMARY WHICH SUPPORTS THE REASONS FOR THE CONCLUSIONS AND RECOMMENDATIONS</b>	
<p>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".</p> <p>For the environment, various NOEC and LC<sub>50</sub> values were gained from test results; LC<sub>50</sub> = 4.4 mg/l (acute fish); EC<sub>50</sub> = 5.6 mg/l (acute daphnia); EC<sub>50</sub> = 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 <i>Daphnia magna</i> (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.</p> <p>The chemical showed no genotoxic effects in bacteria and in a chromosomal aberration test <i>in vitro</i>.</p> <p>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.</p> <p>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.</p>	
<b>NATURE OF FURTHER WORK RECOMMENDED</b>	



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 polyploidy 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 exogenous 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-Butyl-2,4-xyleneol 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<sub>1</sub> 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 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. 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-xyleneol 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-xyleneol are summarized in Table 2. No other ecotoxicological data are available.

Various NOEC and LC<sub>50</sub> values were gained from above tests; 96h LC<sub>50</sub> = 4.4 mg/l (acute fish); 24h EC<sub>50</sub> = 5.6 mg/l (acute daphnia); 72h EC<sub>50</sub> = 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-xyleneol 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-xyleneol to aquatic organisms.

Species	Endpoint <sup>*1</sup>	Conc. (mg/L)	Reference
<i>Selenastrum capricornutum</i> (algae)	Biomass: EC <sub>50</sub> (72h) NOEC	3.6 mg/L 1.7 mg/L	EA, Japan. (1994)
<i>Daphnia magna</i> (water flea)	Imm: EC <sub>50</sub> (24h)	5.6 mg/L	
	Imm: EC <sub>50</sub> (21d)	2.5 mg/L	
	Rep: EC <sub>50</sub> (21d)	0.60 mg/L	
	NOEC(21d)	0.32 mg/L	
<i>Oryzias latipes</i> (fish, Medaka)	Mor: LC <sub>50</sub> (24h)	6.0 mg/L	
	Mor: LC <sub>50</sub> (72h)	5.0 mg/L	
	Mor:LC <sub>50</sub> (96h)	4.4 mg/L	

Notes: <sup>\*1</sup> Mor; mortality, Rep; reproduction, Imm; immobilisation

## 4.2 Initial Assessment for the Environment

6-tert-Butyl-2,4-xyleneol 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<sub>50</sub> values were gained from test results; 96h LC<sub>50</sub> = 4.4 mg/l (acute fish); 24h EC<sub>50</sub> = 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-xyleneol 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.

