11	CAS No.: 128-37-0	Substance: 2,6-Di-*tert*-butyl-4-methylphenol

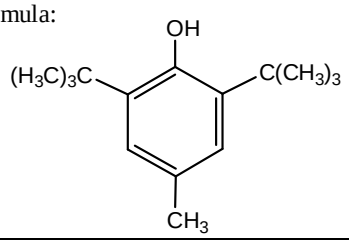
Chemical Substances Control Law Reference No.: 3-540 (Trialkyl (or alkenyl, C1-4) phenol) and 9-1805 (Reaction product from *p*-cresol and isobutylene)

PRTR Law Cabinet Order No.:

Molecular Formula: $C_{15}H_{24}O$

Molecular Weight: 220.35

Structural Formula:



1. General information

The aqueous solubility of this substance is 0.6 mg/L (25°C) and the partition coefficient (1-octanol/water) (log Kow) is 5.10. The vapor pressure is 8.3×10^{-3} mmHg (= 1.1 Pa) (20°C). Degradability (aerobic degradation) in terms of BOD-based degradation percentage is estimated to be 4.5%. This substance is determinated to be moderately bioaccumulative.

It is mainly used for alkylphenol antidegradants, food antioxidants, various plastics, synthetic rubbers, and antioxidants for petroleum products. The total of production and imports in FY 2001 was 1,000 to less than 10,000 tons/yr, and in FY 2004, 1,000 to less than 10,000 tons/yr as trialkyl (or alkenyl, C1-4) phenol.

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2. Exposure assessment

As 2,6-Di-*tert*-butyl-4-methylphenol is not a Class 1 Designated Chemical Substance under the Law concerning Reporting, etc. of Releases to the Environment of Specific Chemical Substances and Promoting Improvements in Their Management (PRTR Law), no information on release and transfer quantities could be obtained. When predictions of distribution ratios by medium were made using the Mackay-Type Level III Fugacity Model, in the event of equal release to the atmosphere, water, and soil, the distribution ratio was highest for soil.

Based on data for the ambient air, the predicted maximum exposure concentration for inhalation exposure to human beings was estimated at approximately 1.2 μg/m^3. The expected maximum concentration in the indoor air was 7.3 μg/m^3. The highest estimated oral exposure was calculated at 1.714 μg/kg/day based on freshwater bodies and food data.

The predicted environmental concentration (PEC), which indicates exposure to aquatic organisms, was estimated to be approximately 0.35 μg/L for freshwater and approximately 0.94 μg/L for seawater public water bodies.

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3. Initial assessment of health risk

The substance irritates the eyes and the skin, and it may cause their redness and pain. By inhalation, it may cause cough and sore throat. By ingestion, it may cause abdominal pain, confusion, dizziness, nausea and vomiting. There is a report that determined the toxic dose lowest (TDLo) in human to be 80 mg/kg (gastritis, nausea or vomiting, coma).

There was insufficient information regarding the carcinogenicity of the substance. For this reason, an initial assessment of the substance was conducted based on information of non-carcinogenic effects.

A no observed adverse effect level (NOAEL) of 25 mg/kg/day (depression of body weight gain and hyperreactivity in thyroid gland) was obtained for oral exposure from the medium- and long-term toxicity testing for rats. For inhalation exposure, the 'Non-toxic level*' could not be estimated.

With regard to oral exposure, in case of intakes of freshwater in the public water bodies and food, the predicted maximum exposure was 1.7 μg/kg/day. The margin of exposure (MOE) of 1,500 was derived from the 'Non-toxic

level*' of 25 mg/kg/day divided by the predicted maximum dose, and divided by 10, because the 'Non-toxic level*' was established by means of animal testing. Accordingly, further action for assessment of its health risk from oral exposure to this substance would not be required at present.

Concerning inhalation exposure, because its 'Non-toxic level*' is not determined, its health risk can not be identified. For reference, assuming that the absorption rate is 100%, the 'Non-toxic level*' for the oral exposure is converted to the 'Non-toxic level*' for the inhalation. The resulting value is 83 mg/m^3. The MOE determined from this figure and the predicted maximum exposure concentration is 6,900 for this substance in the ambient air and 1,100 in the indoor air. Accordingly, there would be little necessity of collecting information on inhalation exposure to this substance in the ambient air for its health risk assessment.

Information of toxicity				Exposure assessment		Result of risk assessment			Judgment
Exposure Path	Criteria for risk assessment	Animal	Criteria for diagnoses (endpoint)	Exposure medium	Predicted maximum exposure quantity and concentration				
Oral	'Non-toxic level*' 25 mg/kg/day	Rats	depression of body weight gain and hyperreactivity in thyroid gland	Drinking water, Food	— μg/kg/day	MOE	—	×	○
				Freshwater, Food	1.7 μg/kg/day	MOE	1,500	○	
Inhalation	'Non-toxic level*' — mg/m^3	—	—	Ambient air	1.2 μg/m^3	MOE	—	×	(○)
				Indoor air	7.3 μg/m^3	MOE	—	×	×

Non-toxic level *

- When a LOAEL is available, it is divided by 10 to obtain a level equivalent to NOAEL.
- When an adverse effect level for the short-term exposure is available, it is divided by 10 to obtain a level equivalent to an adverse effect level for the long-term exposure.

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4. Initial assessment of ecological risk

With regard to acute toxicity, reliable information of a 48-hour median effective concentration (EC_{50}) immobilization value of 835 μg/L was found for the crustacea *Daphnia magna* (water flea), and a 96-hour median lethal concentration (LC_{50}) value of 1,100 μg/L was found for the fish *Oryzias latipes* (medaka). No applicable values for algae were obtained. The acute toxicity level for green algae, *Pseudokirchneriella subcapitata*, was considered to exceed the solubility based on a literature, and therefore, a predicted no effect concentration (PNEC) based on acute toxicity was determined to be 8.4 μg/L with an assessment factor of 100. With regard to chronic toxicity, reliable information of a 21-day no observed effect concentration (NOEC) reproduction value of 69 μg/L was found for the crustacea *D. magna*. No applicable values for algae were obtained. The chronic toxicity level for green algae, *Pseudokirchneriella subcapitata*, was considered comparable to the solubility based on a literature, and therefore, a predicted no effect concentration (PNEC) based on chronic toxicity was determined to be 0.69 μg/L with an assessment factor of 100. As the PNEC for the substance, a value of 0.69 μg/L obtained from the chronic toxicity for the crustacea, was used.

The PEC/PNEC ratio was 0.5 for freshwater bodies and 1.4 for seawater bodies. This substance is thought to be a candidate for further work. With accurate understanding of changes and distribution of environmental concentrations, chronic toxicity studies in algae and fish should be conducted for this substance. In addition, further collection of hazard data on marine organisms should also be considered in terms of the distribution of environmental concentrations.

Hazard assessment (basis for PNEC)			Assessment factor	Predicted no effect concentration PNEC (μg/L)	Exposure assessment		PEC/ PNEC ratio	Result of assessment
Species	Acute / chronic	Endpoint			Water body	Predicted environmental concentration PEC (μg/L)		
Crustacea (water flea)	Chronic	NOEC reproduction	100	0.69	Freshwater	0.35	0.5	■
					Seawater	0.94	1.4	

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5. Conclusions

	Conclusions		Judgment
Health risk	Oral exposure	No need for further work.	○
	Inhalation exposure	Risk cannot be determined. However, there would be little necessity of collecting information.	(○)
Ecological risk	This substance is thought to be a candidate for further work. With accurate understanding of changes and distribution of environmental concentrations, chronic toxicity studies in algae and fish should be conducted for this substance. In addition, further collection of hazard data on marine organisms should also be considered in terms of the distribution of environmental concentrations.		■

[Risk judgments] ○: No need for further work ▲: Requiring information collection

■: Candidates for further work ×: Impossibility of risk characterization

(○) : Though a risk characterization cannot be determined, there would be little necessity of collecting information.

(▲) : Further information collection would be required for risk characterization.