8	CAS No.: 75-91-2	Substance: *tert*-Butyl hydroperoxide

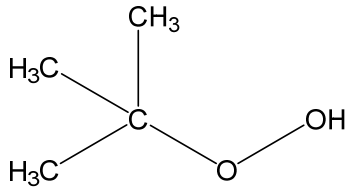
Chemical Substances Control Law Reference No.: 2-224 (*t*-Alkyl (C4–8) hydroperoxide)

PRTR Law Cabinet Order No.: 366

Molecular Formula: $C_4H_{10}O_2$

Molecular Weight: 90.12

Structural Formula:



1.General information

The aqueous solubility of this substance is ≥1×10^5 mg/L (22℃), the partition coefficient (1-octanol/water) (log K_{ow}) is 0.7 (pH=6.34 (average), 25°C, distilled water), and the vapor pressure is 729 Pa (25℃). The biodegradability (aerobic degradation) is characterized by a BOD degradation rate of 0%, the substance is not judged to be highly bioaccumulative. Further, hydrolysis is not observed for this substance (70% aqueous solution) (pH = 4, 7, 9; 50°C; 5 days).

This substance is classified as a Class 2 Designated Chemical Substance under the PRTR Law. The main uses of this substance are as a polymerization initiator for methacrylate, polyethylene, vinyl acetate, ethylene tetrafluoride, styrene, SBR, NBR, etc.; a curing agent for unsaturated polyester and melamine; and a drying agent for varnish and paint. The production and import quantity in fiscal 2021 as *t*-alkyl (C4–8) hydroperoxide was less than 5,000 t.

2.Exposure Assessment

This substance was classified as a Class 1 Designated Chemical Substance prior to revision of substances regulated by the PRTR Law. Total release to the environment in fiscal 2021 under the PRTR Law was approximately 0.52 t, and all releases were notified. The major destination of notified releases was the atmosphere. In addition, approximately 59 t was transferred to waste materials. The sole source of notified releases was the chemical industry. A multi-media model used to predict the proportions distributed to individual media in the environment indicated that in regions where the largest quantities were estimated to have been released to the environment overall or to the atmosphere in particular, the predicted proportion distributed to soil would be 52.6%, and the predicted proportion distributed to water bodies would be 26.0%. Where the largest quantities were estimated to have been released to public water bodies, the predicted proportion distributed to water bodies would be 67.8% and the predicted proportion distributed to soil would be 21.5%.

The maximum expected concentration of exposure to humans via inhalation could not be defined because ambient atmospheric and indoor air quality data could not be obtained. Further, the mean annual value for atmospheric concentration in fiscal 2021 was calculated by use of a plume-puff model on the basis of releases to the atmosphere reported under the PRTR Law: this model predicts a maximum level of 0.15 μg/m^3.

Data for potable water, ground water, public freshwater bodies, food, and soil to assess oral exposure could not be obtained. However, when notified releases under the PRTR Law to public freshwater bodies in fiscal 2021 were divided by the ordinary water discharge of the national river channel structure database, estimating the concentration in rivers by taking into consideration only dilution gave a maximum value of 0.00043 μg/L, and the oral exposure calculated thereof was 0.000017 μg/kg/day. This substance is not judged to be highly bioaccumulative and as such, exposure from an environmental medium via ingestion is believed to be low.

Exposure to aquatic organisms based on water quality data could not be estimated. However, when notified releases under the PRTR Law to public freshwater bodies in fiscal 2021 were divided by the ordinary water discharge of the national river channel structure database, estimating the concentration in rivers by taking into consideration only dilution gave a maximum value of 0.00043 μg/L.

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3. Initial assessment of health risk

This substance is corrosive to the eyes, the skin, and the respiratory tract. Inhalation of this substance will cause burning sensation, cough, and labored breathing. Ingestion will cause abdominal cramps, burning sensation, and weakness. Contact with the skin will cause pain, redness, and blisters. Contact with the eyes will cause redness, pain, and severe deep burns.

While not enough information was available on the carcinogenicity of the substance in humans, squamous cell carcinomas in the nasal cavity were observed in carcinogenicity tests in both sexes of rats exposed to this substance by inhalation. In carcinogenicity tests in mice by application on skin, while treatment with this substance alone produced no tumors, treatment with known carcinogen followed by this substance indicated tumor promoting properties of this substance. Considering the above, an assessment of the carcinogenic risk was deemed necessary as well. Due to the mixed evidence on genotoxicity from studies with positive results and those with negative results, it could not be determined whether this substance is a genotoxic carcinogen, precluding judgment of the existence of a carcinogenic threshold. Therefore, regarding toxicity assuming the existence of thresholds, the 'non-toxic level' was identified based on information on the non-carcinogenic effects of the substance, and carcinogenicity was taken into account in the health risk judgment.

The NOAEL of 21 mg/kg/day for oral exposure (no observed effect dose) determined from reproductive and developmental toxicity tests in rats, was divided by a factor of 10 to account for extrapolation to chronic exposure. The calculated value of 2.1 mg/kg/day was deemed the lowest reliable dose and was identified as the 'non-toxic level' of the substance for oral exposure. The NOAEL of 7.2 mg/m^3 for inhalation exposure (based on the increased unit length labelling index of the transitional epithelium in the maxilloturbinate of the nasal cavity), determined from toxicity tests in rats, was adjusted according to exposure conditions to obtain 1.3 mg/m^3 and subsequently divided by a factor of 10 to account for extrapolation to chronic exposure. The calculated value of 0.13 mg/m^3 was deemed the lowest reliable concentration and was identified as the 'non-toxic level' of the substance for inhalation exposure.

Regarding oral exposure, due to the lack of identified exposure levels, the health risk could not be assessed. The maximum exposure level was estimated to be 0.000017 μg/kg/day according to the concentration in effluents from the high discharging plants based on the releases to public freshwater bodies reported in FY 2021 under the PRTR Law. The MOE (Margin of Exposure) for reference would be 2,500,000 which is calculated from the estimated maximum exposure level and the 'non-toxic level' of 2.1 mg/kg/day and subsequently divided by a factor of 10 to account for extrapolation from animals to humans and by another factor of 5 to take into consideration the carcinogenicity. Since exposure to the substance in environmental media via food is presumed to be limited, despite the lack of exposure level via food, including it in the calculation would not change the MOE significantly. Therefore, as a comprehensive judgment, the collection of further information would not be required to assess the health risk of this substance via oral exposure.

Regarding inhalation exposure, due to the lack of identified exposure concentrations, the health risk could not be assessed. The maximum concentration (annual mean) in ambient air near the operators that are releasing a large amount of the substance was estimated to be 0.15 μg/m^3, based on the releases to air reported in FY 2021 under the PRTR Law. The MOE for reference would be 17 which is calculated from the estimated maximum concentration (annual mean) in ambient air and the 'non-toxic level' of 0.13 mg/m^3 and subsequently divided by a factor of 10 to account for extrapolation from animals to humans and by another factor of 5 to take into consideration the carcinogenicity. Therefore, as a comprehensive judgment, the collection of information would be required to assess the health risk of this substance via inhalation in ambient air, starting from the data on the substance concentration in ambient air near the operators that are releasing a large amount of the substance.

Toxicity					Exposure assessment		Result of risk assessment		Comprehensive judgment
Exposure Path	Criteria for risk assessment		Animal	Criteria for diagnoses (endpoint)	Exposure medium	Predicted maximum exposure dose and concentration			
Oral	'Non-toxic level*'	2.1 mg/kg/day	Rats	No observed effect dose	Drinking water	- μg/kg/day	MOE	-	○
					Groundwater	- μg/kg/day	MOE	-	
Inhalation	'Non-toxic level*'	0.13 mg/m^3	Rats	The increased unit length labelling index of the transitional epithelium in the maxilloturbinate of the nasal cavity	Ambient air	- $\mu g/m^3$	MOE	-	▲
					Indoor air	- $\mu g/m^3$	MOE	-	×

Non-toxic level *

- When a LOAEL is available, it is divided by 10 to obtain a NOAEL-equivalent level.
- 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, the following reliable data were obtained: a 72-h EC_{50} of 1,100 μg/L for growth inhibition in the green alga *Raphidocelis subcapitata*, a 48-h EC_{50} of 14,000 μg/L for swimming inhibition in the crustacean *Daphnia magna*, and a 96-h LC_{50} of 29,610 μg/L for the fish *Pimephales promelas* (fathead minnow). Accordingly, based on the acute toxicity value for the alga and an assessment factor of 100, a predicted no effect concentration (PNEC) of 11 μg/L was obtained.

With regard to chronic toxicity, the following reliable datum was obtained: a 72-h NOEC of 137 μg/L for growth inhibition in the green alga *R. subcapitata*. Accordingly, based on this chronic toxicity value and an assessment factor of 100, a PNEC of 1.3 μg/L was obtained.

The value of 1.3 μg/L obtained from the chronic toxicity to the green alga was used as the PNEC for this substance.

Data for setting the predicted environmental concentration (PEC) could not be obtained for this substance. Accordingly, an assessment of ecological risk could not be made.

When notified releases under the PRTR Law to public freshwater bodies in fiscal 2021 were divided by the ordinary water discharge of the national river channel structure database, estimating the concentration in rivers by taking into consideration only dilution gave a maximum value of 0.00043 μg/L. The ratio of this value to PNEC is 0.0003. Accordingly, further work to assess the ecological risk of this substance is considered unnecessary at this time.

Hazard assessment (basis for PNEC)			Assessment coefficient	Predicted no effect concentration PNEC (μg/L)	Exposure assessment		PEC/ PNEC ratio	Comprehensive judgment
Species	Acute/ chronic	Endpoint			Water body	Predicted environmental concentration PEC (μg/L)		
Green algae	Chronic	NOEC Growth inhibition	100	1.3	Freshwater	—	—	○
					Seawater	—	—	

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5. Conclusions

	Conclusions		Judgment
Health risk	Oral exposure	No need for further work.	○
	Inhalation exposure	Requiring information collection.	▲
Ecological risk	No need for further work.		○

［Risk judgments］○: No need for further work ▲: Requiring information collection
■: Candidates for further work ×: Impossibility of risk characterization