9	CAS No.: 98-73-7	Substance: *p-tert*-Butylbenzoic acid

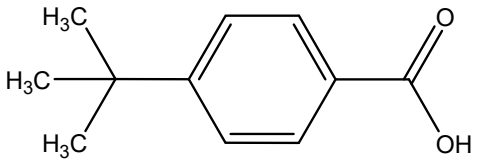
Chemical Substances Control Law Reference No.: 3-1338 (Alkyl (C=3–7) benzoic acid)

PRTR Law Cabinet Order No.:

Molecular Formula: $C_{11}H_{14}O_2$

Molecular Weight: 178.23

Structural Formula:



1.General information

The aqueous solubility of this substance is 300 mg/L (20°C), the partition coefficient (1-octanol/water) (log K_{ow}) is 3.85 (pH=2.0), and the vapor pressure is $<8\times10^{-3}$ mmHg (<1 Pa) (20°C). The biodegradability (aerobic degradation) is characterized by a BOD degradation rate of 4%. In addition, this substance does not possess any hydrolyzable groups.

The main uses of this substance are as a coating resin modifier, corrosion inhibitor, and PVC resin stabilizer. The production and import quantity of alkyl (C=3–7) benzoic acid in fiscal 2018 was 1,000 t.

2.Exposure assessment

Because this substance is not classified as a Class 1 Designated Chemical Substance under the PRTR Law, release and transfer quantities could not be obtained. Predictions of proportions distributed to individual media by use of a Mackay-type level III fugacity model indicate that if equal quantities were released to the atmosphere, water bodies, and soil, the proportion distributed to soil would be largest.

The maximum expected concentration of exposure to humans via inhalation, based on ambient atmospheric data, was around 0.017 μg/m^3.

Data for potable water, ground water, food, and soil to assess oral exposure could not be obtained. Thus, assuming intake solely from public freshwater bodies, a maximum expected concentration of exposure of around 0.0084 μg/kg/day was obtained. Further, food data is not available for these substances. For this reason, oral exposure reference values were estimated using maximum concentrations in fish species (0.024 μg/g) and the average daily intake of fish and shellfish (65.1 g/capita/day) and albeit past data, an oral exposure of around 0.031 μg/kg/day was obtained. Adding this to the oral exposure calculated from freshwater data gives around 0.039 μg/kg/day.

The predicted environmental concentration (PEC), which indicates exposure to aquatic organisms, was reported to be around 0.21 μg/L for both public freshwater bodies and seawater.

---

3. Initial assessment of health risk

No information was available on acute symptoms to the humans caused by this substance. However, rats exposed to an oral dose of this substance displayed excessive salivation, upright flicking of the tail, extended hind limbs, induced convulsions and respiratory gasping, and subsequently they died. The cause of death appeared to be respiratory failure. On necropsy, only congestions of organs were observed in the dead rats, while degeneration of the epithelium of the seminiferous tubules and atrophy of the testes were observed in the surviving rats.

Since sufficient information on the carcinogenicity of the substance was not available, the initial assessment was conducted based on information on its non-carcinogenic effects.

The LOAEL of 6 mg/kg/day for oral exposure (based on increase in the relative weight of liver, as well as necrosis of the renal tubules and papillae and atrophy of testes), determined from toxicity tests in rats, was divided by a factor of 10 to account for uncertainty in using a LOAEL and by another factor of 10 to account for extrapolation to chronic exposure. The calculated value of 0.06 mg/kg/day was deemed to be the lowest reliable dose and was identified as the 'non-toxic level' of the substance for oral exposure. The NOAEL of 1.5 mg/m^3 for inhalation exposure (based on decreased arousal and urinating/defecating), determined from toxicity tests in rats, was adjusted according to exposure conditions to obtain 0.27 mg/m^3 and subsequently divided by a factor of 10 to account for extrapolation to chronic exposure. The calculated

value of 0.027 mg/m^3 was deemed to be the lowest reliable concentration and was identified as the 'non-toxic level' of the substance for inhalation exposure.

Regarding the oral exposure, assuming that the substance is absorbed via public freshwater bodies, the predicted maximum exposure level would be 0.0084 μg/kg/day, approximately. The MOE (Margin of Exposure) would be 710, when calculated from the predicted maximum exposure level and the 'non-toxic level' of 0.06 mg/kg/day, and subsequently divided by a factor of 10 to account for extrapolation from animals to the humans. This would lead to the health risk judgment that no further work would be required. In addition, the MOE for reference would be 150, when calculated from the estimated maximum exposure level of 0.039 μg/kg/day. This exposure level was estimated assuming that the substance is absorbed via fish and public freshwater bodies, due to the lack of exposure level via food. Therefore, as a comprehensive judgment, no further work would be required at present to assess the health risk of this substance via oral exposure.

Regarding the inhalation exposure, the predicted maximum exposure concentration in ambient air was 0.017 μg/m^3, approximately. The MOE would be 160, when calculated from the predicted maximum exposure concentration and the 'non-toxic level' of 0.027 mg/m^3, and subsequently divided by a factor of 10 to account for extrapolation from animals to the humans. This would lead to the health risk judgment that no further work would be required at present, and the same conclusion can be drawn as a comprehensive judgment.

Toxicity				Exposure assessment		MOE		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' 0.06 mg/kg/day	Rats	Increase in the relative weight of liver, necrosis of the renal tubules and papillae and atrophy of testes	Drinking water	- μg/kg/day	MOE	-	○
				Public freshwater bodies	0.0084 μg/kg/day	MOE	710	
Inhalation	'Non-toxic level' 0.027 mg/m^3	Rats	Decreased arousal and urinating/defecating	Ambient air	0.017 μg/m^3	MOE	160	○
				Indoor air	- μg/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.

4.Initial assessment of ecological risk

With regard to acute toxicity, the following reliable data were obtained: a 72-h EC_{50} exceeding 94,000 μg/L for growth inhibition in the alga *Raphidocelis subcapitata* and a 96-h LC_{50} of 33,000 μg/L for the fish species *Carassius auratus* (goldfish). Accordingly, based on these acute toxicity values and an assessment factor of 1,000, a predicted no effect concentration (PNEC) of 33 μg/L was obtained.

With regard to chronic toxicity, the following reliable data was obtained: a 72-h NOEC of 21,000 μg/L for growth inhibition in the alga *R. subcapitata*. Accordingly, based on this chronic toxicity value and an assessment factor of 100, a PNEC of 210 μg/L was obtained.

The value of 33 μg/L obtained from the acute toxicity to the fish was used as the PNEC for this substance.

The PEC/PNEC ratio is 0.006 for both freshwater bodies and seawater; accordingly, further work is considered unnecessary at this time for determining ecological risk. In addition, based on a comprehensive review of the above findings, there is little need to collect new data regarding this substance.

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)		
Fish *Carassius auratus*	Acute	LC_{50} Mortality	1,000	33	Freshwater	0.21	0.006	○
					Seawater	0.21	0.006	

---

5. Conclusions

	Conclusions		Judgment
Health risk	Oral exposure	No need for further work.	○
	Inhalation exposure	No need for further work.	○
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