12	CAS No: 526-73-8	Substance: 1,2,3-Trimethylbenzene

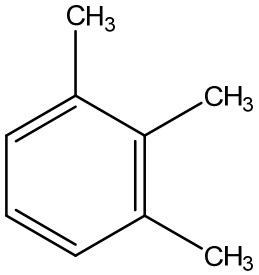
Chemical Substances Control Law Reference No.: 3-7 (Tri or tetramethylbenzene), 3-3427 (Trialkyl (C=1–4) benzene)

PRTR Law Cabinet Order No.:

Molecular Formula: C_9H_{12}

Molecular Weight: 120.19

Structural Formula:



1. General information

The aqueous solubility of this substance is 70 mg/1,000 g (25℃), the partition coefficient (1-octanol/water) (log K_{ow}) is 3.55, and the vapor pressure is 1.69 mmHg (=225 Pa) (25°C).

Biodegradability (aerobic degradation) is characterized by a BOD degradation rate of 0%, and bioaccumulation is judged to be non-existent or low. Furthermore, the substance does not have any hydrolyzable groups.

The main use of this substance is as a solvent. The production and import quantity for trimethylbenzene and tetramethylbenzene in fiscal 2014 was less than 1,000 t.

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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. Releases of this substance to the atmosphere have been estimated from the volatile organic compound (VOC) inventory, and estimated releases were 1 t in fiscal 2011. Furthermore, annual releases to the atmosphere during gasoline refueling were estimated to be 0.5 t in fiscal 2011 based on the sales volume of gasoline in Tokyo Metropolis in fiscal 2011.

Predictions of proportions distributed to individual media by using a Mackay-type level III fugacity model indicate that if equal quantities are 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 0.58 μg/m^3, and around 46 μg/m^3 based on indoor air data. In addition, the predicted maximum exposure was 1.4 μg/m^3 based on past data for the ambient atmosphere. The maximum expected oral exposure was estimated to be around 0.00044 μg/kg/day based on calculations from data for public freshwater bodies. The exposure level to this substance by intake from an environmental medium via food is considered slight, based on its low bioaccumulation.

The predicted environmental concentration (PEC), which indicates exposure to aquatic organisms, is around 0.011 μg/L for public freshwater bodies, and around less than 0.0048 μg/L for seawater

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3. Initial assessment of health risk

This substance is irritating to the eyes, skin and respiratory tract, and may cause effects on the central nervous system. If this liquid is swallowed, aspiration into the lungs may result in chemical pneumonitis. Inhalation of the substance causes confusion, dizziness, headache, vomiting, drowsiness, coughs and sore throat. Contact with

the skin causes redness and contact with the eyes causes redness and pain.

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

The LOAEL for oral exposure of 40 mg/kg/day (based on relative liver weight increase), determined from medium-term toxicity tests in rats, was divided by a factor of 10 to account for extrapolation from sub-chronic to chronic exposure and by another factor of 10 to account for uncertainty in using a LOAEL. The calculated value of 0.40 mg/kg/day was deemed to be the lowest reliable dose and was identified as the 'non-toxic level*' for oral exposure.

The NOAEL for inhalation exposure of 25 ppm (based on disturbances in rotarod performance and increase in bronchial goblet cells), determined from medium-term toxicity tests in rats, was adjusted according to exposure conditions to obtain 4.5 ppm (22 mg/m^3) and subsequently divided by a factor of 10 to account for extrapolation from sub-chronic to chronic exposure. The calculated value of 2.2 mg/ m^3 was deemed to be the lowest reliable concentration and was identified as the 'non-toxic level*' for inhalation exposure.

With regard to oral exposure, assuming the substance is absorbed via public freshwater bodies, the predicted maximum exposure level would be 0.00044 μg/kg/day, approximately. The MOE (Margin of Exposure) would be 91,000, when calculated from the predicted maximum exposure level and the 'non-toxic level*'of 0.40 mg/kg/day, and subsequently divided by a factor of 10 to account for extrapolation from animals to humans. Since exposure to the substance in environmental media via food is presumed to be limited, including this concentration in the calculation would not change the MOE significantly. Therefore, no further work would be required at present to assess the health risk of this substance via oral exposure.

With regard to inhalation exposure, the predicted maximum exposure concentration was 0.58 μg/m^3 in ambient air, approximately. The MOE would be 380, when calculated from the predicted maximum exposure concentration and the 'non-toxic level*' of 2.2 mg/m^3, and subsequently divided by a factor of 10 to account for extrapolation from animals to humans. As for indoor air, the predicted maximum exposure concentration was 46 μg/m^3. The MOE would be 5, when calculated from this concentration. Therefore, this substance is a candidate for further work to assess the health risk via inhalation in indoor air, while collection of further information would not be required regarding ambient air.

Toxicity				Exposure assessment		Result of risk assessment			Judgment
Exposure Path	Criteria for risk assessment	Animal	Criteria for diagnoses (endpoint)	Exposure medium	Predicted maximum exposure dose and concentration				
Oral	'Non-toxic level*' 0.40 mg/kg/day	Rats	Relative liver weight increase	Drinking water	— μg/kg/day	MOE	—	×	○
				Public Freshwater bodies	0.00044 μg/kg/day	MOE	91,000	○	
Inhalation	'Non-toxic level*' 2.2 mg/m^3	Rats	Disturbances in rotarod performance and increase in bronchial goblet cells	Ambient air	0.58 μg/m^3	MOE	380	○	○
				Indoor air	46 μg/m^3	MOE	5	■	■

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 48-h EC_{50} of 5,700 μg/L for growth inhibition in the green algae *Pseudokirchneriella subcapitata*, a 48-h EC_{50} of 2,700 μg/L for immobilization in the crustacean *Daphnia magna*, and a 96-h LC_{50} of 7,800 μg/L for the fish species *Oryzias latipes* (medaka). Accordingly, based on these acute toxicity values and an assessment factor of 100, a predicted no effect concentration (PNEC) of 27 μg/L was obtained.

With regard to chronic toxicity, the following reliable data was obtained: a 48-h NOEC of 380 μg/L for growth inhibition in the green algae *P. subcapitata*. Accordingly, based on this chronic toxicity value and an assessment factor of 100, a PNEC of 3.8 μg/L was obtained.

The value of 3.8 μg/L, obtained from the chronic toxicity to the green algae, was used as the PNEC for this substance.

The PEC/PNEC ratio is 0.003 for freshwater bodies and less than 0.001 for seawater; accordingly, further work 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	Judgment based on PEC/PNEC ratio	Assessment result
Species	Acute/ chronic	Endpoint			Water body	Predicted environmental concentration PEC (μg/L)			
Green algae	Chronic	NOEC growth inhibition	100	3.8	Freshwater	0.011	0.003	○	○
					Seawater	<0.0048	<0.001		

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5. Conclusions

	Conclusions		Judgment
Health risk	Oral exposure	No need for further work at present.	○
	Inhalation exposure (atmosphere)	No need for further work at present.	○
	Inhalation exposure (room air)	Candidates for further work.	■
Ecological risk	No need for further work at present.		○

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

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

（○）: Although risk to human health could not be confirmed, collection of further information would not be required.

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