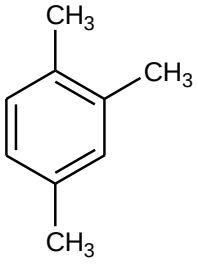
16	CAS No.: 95-63-6	Substance: 1,2,4-Trimethylbenzene

Chemical Substances Control Law Reference No.: 3-7(tri- or tetra-methylbenzene), 3-3427(trialkyl (C=1−4) benzene)
PRTR Law Cabinet Order No.: − (Cabinet Order No. after revision*: 1-296)

Structural Formula:

Molecular Formula: C_9H_{12}
Molecular Weight: 120.19



*Note: No. according to revised order enacted on October 1, 2009.

1. General information

The aqueous solubility of this substance is 57 mg/1000 g (25°C), the partition coefficient (1-octanol/water) (log K_{ow}) is 3.63, and the vapor pressure is 2.3 mmHg (300Pa) (25°C). Biodegradability (aerobic degradation) is not considered to be favorable, and bioaccumulation is thought to be nonexistent or low. The substance does not have any hydrolyzable groups.

Based on a revision of substances regulated by the Law Concerning Reporting, etc. of Releases to the Environment of Specific Chemical Substances and Promoting Improvements in Their Management (PRTR Law) (enacted on October 1, 2009), this substance was newly designated as a Class 1 Designated Chemical Substance. This substance is a component of solvents used in coatings and inks, and it is also found in gasoline. Major applications are for the synthesis of trimellitic acid and vitamin E, as an intermediate for dyestuffs, pigments, and pharmaceuticals, and as a synthetic raw material for pyromellitic acid. The production quantity of this substance as reported by the OECD is 10,000– to <100,000 t/y, and the import quantity is 1,000 to <10,000 t/y.

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2. Exposure assessment

Because this substance was not classified as a Class 1 Designated Chemical Substance prior to revision of substances regulated by the PRTR Law, release and transfer quantities could not be obtained. Predictions of distribution by medium using a Mackay-type level III fugacity model indicated that if equal quantities were released to the atmosphere, water bodies, and soil, the proportions distributed to soil and water bodies would be higher.

The predicted maximum exposure to humans via inhalation, based on general environmental atmospheric data, was approximately 11 μg/m^3. In addition, the predicted maximum exposure for indoor air was around 38 μg/m^3. Data that could calculate the predicted maximum oral exposure could not be obtained. The risk of exposure to this substance by intake from an environmental medium via food is considered slight.

The predicted environmental concentration (PEC), which indicates exposure to aquatic organisms, could not be set because water quality data could not be obtained.

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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. This substance may cause chemical pneumonia if swallowed in its liquid form as it is absorbed into the lungs. Inhalation or oral exposure causes confusion, cough, dizziness, lethargy, headache, sore throat and vomiting. Redness and dryness of the skin and redness and painful irritation in the eyes are caused by contact with this substance.

Sufficient information could not be obtained on its carcinogenicity, and its initial assessment was conducted on the

basis of data on its non-carcinogenic effects.

As for its oral exposure, its no-observed-adverse-effect-level (NOAEL) of 100 mg/kg/day for relative increase of liver weight to body weight obtained from its mid-term and long-term toxicity tests for rats was divided by 10, due to their short test periods, to produce 10 mg/kg/day as its 'non-toxic level*'.

As for its inhalation exposure, its NOAEL of 123 mg/m^3 was obtained not only for effects on behavior (nervous system) but also for degeneration of peribronchial part, from mid-term and long-term toxicity tests for rats. It was adjusted for exposure conditions to provide 22 mg/m^3. This was divided by 10, due to their short test periods, to produce 2.2 mg/m^3 as its 'non-toxic level*'.

As for its oral exposure, lack of information on its exposure concentration did not allow its risk assessment.

1,3,5-trimethylbenzene is its isomer with similar property and for similar use. It is produced/imported more than this substance. When intakes of local freshwater from public water supply are assumed, the predicted maximum exposure to 1,3,5-trimethylbenzene is estimated to be 0.056 μg/kg/day, and reports of its discharges under the Law Concerning Reporting, etc. of Releases to the Environment of Specific Chemical Substances and Promoting Improvements in Their Management suggest its oral exposure of 2.2 μg/kg/day. If these are combined with its 'non-toxic level' of 10 mg/kg/day, and then divided by 10, due to the fact that the 'non-toxic level' has been identified by animal experiments, their MOE (Margin of Exposure) will be 18,000 and 450, respectively. Since risk associated with its exposure through food intakes from the environment is not presumed to be noticeable, MOE will not change significantly even if its additional exposure through food intakes is considered.

Collection of information on its inhalation exposure to assess health risk associated with exposure to it in the ambient air would not be required.

As for its inhalation exposure, the predicted maximum exposure was estimated to be around 11 μg/m^3, when its concentrations in the ambient air were considered. Its margin of exposure (MOE) would be 20, when calculated from its 'non-toxic level*' of 2.2 mg/m^3 and the predicted maximum exposure, and then divided by 10 due to the fact that 'non-toxic level*' was obtained from animal experiments.

On the other hand, when its concentrations in the indoor air were considered, the predicted maximum exposure was estimated to be around 38 μg/m^3 and its margin of exposure (MOE) would be 5.8.

Collection of information would be required on health risk associated with its inhalation exposure in the ambient air. As for health risk associated with its inhalation exposure in the indoor air, on the other hand, this would require detailed assessment.

This substance is contained in paint, printing solvents and gasoline, and this may explain its high exposure concentrations.

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*' 10 mg/kg/day	Rats	Increase in relative liver weight, etc.	Drinking water	– μg/kg/day	MOE	–	×	(○)
				Freshwater	– μg/kg/day	MOE	–	×	
Inhalation	'Non-toxic level*' 2.2 mg/m^3	Rats	Effects on behavior (the nervous system) & degeneration of the peribronchial region	Ambient air	11 μg/m^3	MOE	20	▲	▲
				Indoor air	38 μg/m^3	MOE	5.8	■	■

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 is available for the short-term exposure, 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 data of a 24-h median lethal concentration (LC_{50}) of 12,000 µg/L was obtained for the crustacean *Artemia salina* (brine shrimp). Accordingly, based on this acute toxicity value and an assessment factor of 1,000, a predicted no effect concentration (PNEC) of 12 µg/L was obtained. No data is available regarding chronic toxicity and on this account, 12 µg/L was adopted as the PNEC for this substance. Environmental concentration data could not be obtained, and for this reason, judgment of ecological risk cannot be made.

According to production quantities reported to the OECD, the production quantity of this substance is one-tenth that of the 1,3,5-trimethylbenzene isomer. The river concentration of 1,3,5-trimethylbenzene estimated using reported releases based on the PRTR law is 55 µg/L. Judging from the difference in the production quantity of 1,3,5-trimethylbenzene, the river concentration of this substance is 5.5 µg/L, and the ratio with PNEC is 0.5. Accordingly, reassessment of this substance is considered necessary after measuring its concentration in public water bodies and, if required, obtaining thorough ecological toxicity data.

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)		
Crustacean (brine shrimp)	Acute	LC_{50} Mortality	1,000	12	Freshwater	–	–	× (▲)
					Seawater	–	–	

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5. Conclusions

	Conclusions		Judgment
Health risk	Oral exposure	Impossibility of risk characterization. Collection of information considered unnecessary.	(○)
	Inhalation exposure	Collection of information on exposure in ambient air required; detailed study in indoor air may be required.	■
Ecological risk	Impossibility of risk characterization. Reassessment of this substance is considered necessary after measuring its concentration in public water bodies and, if required, obtaining thorough ecological toxicity data.		(▲)

［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.