1	CAS No. 1330-20-7 (xylene) 95-47-6 (*o*-xylene) 108-38-3 (*m*-xylene) 106-42-3 (*p*-xylene)	Substance: Xylene

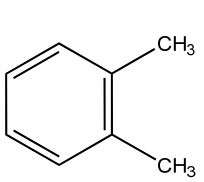
Chemical Substances Control Law Reference No.: 3-3 (Xylene)

PRTR Law Cabinet Order No.: 80 (Xylene)

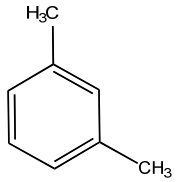
Molecular Formula: C_8H_{10}

Molecular Weight: 106.17

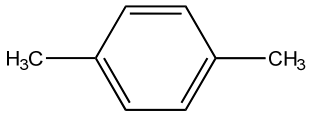
Structural formula:



o-xylene



m- xylene



p-xylene

1.General information

The aqueous solubilities of these substances are 171 mg/1000 g (*o*-isomer, 25°C), 161 mg/1000 g (*m*-isomer, 25°C) and 181 mg/1000 g (*p*-isomer, 25°C); the partition coefficients (1-octanol/water) (log Kow) are 3.12 (*o*-isomer, pH unknown), 3.20(*m*-isomer, pH unknown), and 3.15 (*p*-isomer, pH unknown); and the vapor pressures are 880 Pa(*o*-isomer, 25°C), 1130 Pa (*m*-isomer, 25°C, 1190 Pa (*p*-isomer, 25°C). Xylene is readily biodegradable (aerobic degradation), and the substance (*o*-, *m*-, *p*-isomers) does not have any hydrolyzable groups.

From the perspectives of human health and ecological effects, xylene is designated as both Priority Assessment Chemical under the Chemical Substances Control Law and a Class 1 Chemical Substance under the PRTR Law. The main uses of the petrochemical known as mixed xylene are as solvents and thinners in products such as oil-based paints, adhesives, printing inks, and agricultural chemicals. The main use of *o*-xylene is as a raw material for phthalic anhydride. The main use of *p*-xylene is as a raw material for terephthalic acid. The main use of *m*-xylene is as a raw material for isophthalic acid, which is itself used as a raw material for plasticizers and polyester resin. *m*-Xylene is also converted into *o*-xylene and *p*-xylene for further use. In addition, the production and import quantity of xylenes in fiscal 2022 was 3,999,802 t.

2.Exposure assessment

Total release to the environment in fiscal 2022 under the PRTR Law was approximately 52,000 t, of which approximately 20,000 t, or 38% of overall releases, were notified. The major destination of notified releases was the atmosphere. Further, approximately 6.2 t was transferred to sewage and approximately 7400 t was transferred to waste materials. The major notified emission sources to the atmosphere were the industries of shipbuilding and repair, marine engine manufacturing, transportation equipment manufacturing, metal products manufacturing, general machinery manufacturing, electrical machinery manufacturing, and plastic products manufacturing. The major emission sources to water bodies were petroleum and coal products manufacturing and the chemical industry. The largest release among releases to the environment including those unnotified was to the atmosphere.

The maximum expected concentration of exposure to humans via inhalation was around 8.0 μg/m^3 based on ambient atmospheric air quality data and around 140 μg/m^3 based on indoor air quality data. Further, the mean annual value for atmospheric concentration in fiscal 2022 was calculated by use of a plume-puff model on the basis of releases to the atmosphere notified under the PRTR Law for fiscal 2022: this model predicts a maximum level of 200 μg/m^3 (as xylene) but there is a possibility of a higher atmospheric concentration estimate if releases from mobile sources are considered.

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3. Initial assessment of health risk

Since this substance has been designated as one of the “monitored substances” for water pollution, the initial assessment of this substance did not cover the health risk via oral exposure.

Xylene irritates the eyes and skin and may cause effects on the central nervous system, regardless of isomers. Inhalation

will cause dizziness, drowsiness, headache and nausea. Ingestion will cause burning sensation and abdominal pain in addition to the same symptoms as inhalation. Contact with the skin will cause dry skin and redness. Contact with the eyes will cause redness and pain. There are reports on the mixture of isomers that presented the lowest lethal dose of 50 mg/kg and the lowest lethal concentration of 10,000 ppm (43,400 mg/m^3) after inhalation for 6 hours in humans. Another report presented the lowest lethal concentration of 6,125 ppm (26,580 mg/m^3) in humans after inhalation of *o*-xylene for 12 hours.

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

The LOAEL of 14 ppm for inhalation exposure (based on irritation of the eyes and nose, and effects on the central nervous system), determined from epidemiologic studies, was adjusted according to exposure conditions to obtain 2.8 ppm, and subsequently divided by a factor of 10 to account for uncertainty in using a LOAEL. The calculated value of 0.28 ppm (1.2 mg/m^3) was deemed the lowest reliable concentration and was identified as the 'non-toxic level' of the substance for inhalation exposure.

Regarding inhalation exposure, the predicted maximum exposure concentrations were approximately 8.0 μg/m^3 in ambient air and 140 μg/m^3 in indoor air, respectively. The MOE would be 150 which is calculated from the predicted maximum exposure concentration in ambient air and the 'non-toxic level' of 1.2 mg/m^3. This would lead to the health risk judgment that the collection of further information would not be required to assess the health risk of this substance via inhalation in ambient air. On the other hand, the MOE would be 9 which is calculated from the predicted maximum exposure concentration in indoor air and the 'non-toxic level' of 1.2 mg/m^3. This would lead to the health risk judgment that this substance would be a candidate for further work. The maximum concentration (annual mean) in ambient air near the operators that are releasing a large amount of the substance was estimated to be 200 μg/m^3 based on the releases into air reported in FY 2022 under the PRTR Law. The MOE for reference would be 6 which is calculated from the estimated maximum concentration (annual mean) in ambient air and the 'non-toxic level' of 1.2 mg/m^3. 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, while this substance would be a candidate for further work to assess the health risk via inhalation in indoor air. Regarding the health risk via indoor air inhalation, it should be noted that the studies in Japan have suggested the association between exposure to this substance and developmental neurotoxicity in children.

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'	(−) mg/kg/day	(−)	(−)	Drinking water	(−)	μg/kg/day	MOE	(−)	(−)
					Groundwater	(−)	μg/kg/day	MOE	(−)	
Inhalation	'Non-toxic level'	1.2 mg/m^3	Humans	Irritation of the eyes and nose, and effects on the central nervous system	Ambient air	8.0	μg/m^3	MOE	150	▲
					Indoor air	140	μg/m^3	MOE	9	■

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. Conclusions

	Conclusions		Judgment
Health risk	Oral exposure	Not covered by this assessment	(−)
	Inhalation exposure (Ambient air)	Requiring information collection	▲
	Inhalation exposure (Indoor air)	Candidate for further work	■

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

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