2	CAS No.: 108-68-9	Substance: 3,5-Xylenol

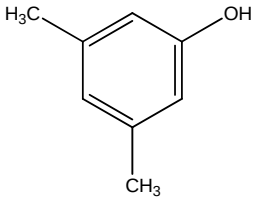
Chemical Substances Control Law Reference No.: 3-521 (Diaryl (C=1–5) phenol), 4-57 (Poly (1–3) alkyl (C=1–3) poly (1–3) hydroxypoly (1–5) phenol)

PRTR Law Cabinet Order No.:

Molecular Formula: $C_8H_{10}O$

Molecular Weight: 122.16

Structural Formula:



1. General information

The aqueous solubility of this substance is 4.88×10^3 mg/L (25°C), the partition coefficient (1-octanol/water) (log K_{ow}) is 2.35, and the vapor pressure is 0.020 mmHg (=2.7Pa) (25°C). Biodegradability (aerobic degradation) is judged to be difficult, and the substance does not have any hydrolyzable groups.

The main uses of this substance are in agricultural chemicals (pesticides, herbicides), in pharmaceuticals (disinfectants, vitamins), as an industrial reagent (antioxidants, lubricant additives), in polymers (plasticizers, coatings, laminates), and as a dye raw material. The production and import quantity in fiscal 2014 was 30,000 t as dialkyl (C=1–5) phenol.

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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. Predictions of proportions distributed to individual media by using a Mackay-type level III fugacity model indicated 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 could not be obtained. However, past ambient atmospheric data from an environmental study that surveyed a limited area reported concentrations less than 0.0014 μg/m^3.

Information to determine the maximum expected oral exposure could not be obtained. However, past data from public freshwater bodies yielded a maximum expected exposure of around 0.0030 μg/kg/day. The exposure level to this substance by intake from an environmental medium via food is considered slight, given the low bioaccumulation expected on the basis of its physicochemical properties.

Data for setting the predicted environmental concentration (PEC), which indicates exposure to aquatic organisms, could not be obtained. Further, past data indicated concentrations around 0.076 μg/L for public freshwater bodies and generally less than 0.005 μg/L for seawater.

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3. Initial assessment of health risk

This substance is corrosive to the skin and eyes, and is also corrosive by ingestion. It is irritating to the respiratory tract, and causes coughs, dizziness and headache, if inhaled. It causes burning sensation, abdominal pain, nausea, vomiting, diarrhea, dizziness, headache and shock or collapse, if ingested. Contact with the eyes causes redness, pain and severe deep burns. Contact with the skin causes burning sensation and skin burns. The substance on the skin may be absorbed to cause dizziness and some other effects.

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 NOAEL for oral exposure of 30 mg/kg/day (based on salivation and inhibition of body weight gain), determined from medium-term toxicity tests in rats, was divided by a factor of 10 to account for extrapolation from sub-acute to chronic exposure. The calculated value of 3.0 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 'non-toxic level*' for inhalation exposure could not be identified.

With regard to oral exposure, owing to lack of identified exposure levels, the health risk could not be assessed.

Based on the concentrations in public freshwater bodies reported in 2001, the maximum exposure level of the substance was 0.0030 μg/kg/day. The MOE (Margin of Exposure) would be 100,000, when calculated from this level and the 'non-toxic level*' of 3.0 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, collection of further information would not be required to assess the health risk of the substance via oral exposure.

With regard to inhalation exposure, owing to lack of identified 'non-toxic level*' and exposure levels, the health risk could not be assessed. Assuming that 100% of the ingested substances is absorbed, the 'non-toxic level*' for inhalation exposure, derived from the conversion of oral exposure concentration, would be 10 mg/m^3. The maximum exposure concentration in ambient air in a restricted area is reported to be less than 0.0014 μg/m^3. The MOE would be over 710,000, when calculated from this concentration and the converted 'non-toxic level*' for inhalation exposure, and subsequently divided by a factor of 10 to account for extrapolation from animals to humans. Therefore, collection of further information would not be required to assess the health risk of this substance via inhalation in 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*' 3.0 mg/kg/day	Rats	Salivation and inhibition of body weight gain	Drinking water	— μg/kg/day	MOE	—	×	(○)
				Public Freshwater bodies	— μg/kg/day	MOE	—	×	
Inhalation	'Non-toxic level*' - mg/m^3	—	—	Ambient air	— μg/m^3	MOE	—	×	(○)
				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.

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4. Initial assessment of ecological risk

With regard to acute toxicity, the following reliable data were obtained: a 24-h IC_{50} of 22,000 μg/L for immobilization in the crustacean *Daphnia magna*, a 96-h TLm of 22,000 μg/L for mortality in the fish species *Carassius auratus* (goldfish), and a 48-h IGC_{50} of 94,200 μg/L for reproductive inhibition in the ciliate *Tetrahymena pyriformis*. Accordingly, based on these acute toxicity values and an assessment factor of 1,000, a predicted no effect concentration (PNEC) of 22 μg/L was obtained. Reliable chronic toxicity data could not be obtained.

The value of 22 μg/L, obtained from the acute toxicity to the crustacean and the fish species, was used as the PNEC for this substance.

Information to determine the predicted environmental concentration (PEC), which indicates exposure to aquatic organisms, could not be obtained. However, past data yielded a value of around 0.076 μg/L for public freshwater and a value of generally less than 0.005 μg/L for seawater, indicating a PEC/PNEC ratio of less than 0.1.

No reports exist concerning marked increases in production and import quantities for this substance since fiscal 2001 or increases in releases to the environment. Accordingly, 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	Judgment based on PEC/PNEC ratio	Assessment result
Species	Acute/ chronic	Endpoint			Water body	Predicted environmental concentration PEC (μg/L)			
Crustacean *Daphnia magna*/ Fish *Carassius auratus*	Acute	IC_{50} immobilization / TLm mortality	1,000	22	Freshwater	—	—	×	○
					Seawater	—	—		

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5. Conclusions

	Conclusions		Judgment
Health risk	Oral exposure	Although risk to human health could not be confirmed, collection of further information would not be required.	(○)
	Inhalation exposure	Although risk to human health could not be confirmed, collection of further information would not be required.	(○)
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.