23	CAS No.: 90-05-1	Substance: *o*-Methoxyphenol

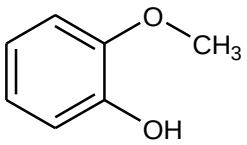
Chemical Substances Control Law Reference No.: 3-567 (Methoxyphenol)

PRTR Law Cabinet Order No.:

Structural Formula:

Molecular Formula: $C_7H_8O_2$

Molecular Weight: 124.14



1. General information

The aqueous solubility of this substance is 2.60×10^4 mg/L (25°C), the partition coefficient (1-octanol/water) (log K_{ow}) is 1.32, and the vapor pressure is 0.103 mmHg (=13.7 Pa) (25°C). Biodegradability (aerobic degradation) is considered to be good. The substance is relatively unaffected by hydrolysis.

The main application of this substance is as a synthetic raw material for pharmaceuticals (guaiacol glycerin ether, potassium guaiacolsulfonate) and flavorings. The production (shipments) and import quantity in 2004 as methoxyphenol was 100 to <1,000 t.

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2. Exposure assessment

Because this substance is not a Class 1 Designated Chemical Substance under the Law Concerning Reporting, etc. of Releases to the Environment of Specific Chemical Substances and Promoting Improvements in Their Management (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 greater.

Data for setting the predicted maximum exposure to humans via inhalation could not be obtained. The predicted maximum oral exposure was estimated to be around 0.0025 μg/kg/day based on calculations from data for public freshwater bodies. 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, was about 0.062 μg/L for public freshwater bodies and generally less than 0.02 μg/L for seawater.

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3. Initial assessment of health risk

This substance and phenol are the major components of wood creosote. Oral exposure causes the same symptoms as those of phenol (burning sensation in the mouth and throat, abdominal pain, tremulousness and collapse). The lethal dose for adults is between 3 to 10 g. In addition, this substance is easily absorbed through the skin. Application within the range of 0.75 to 1.5 g of this substance has no effect, but any double dose within the range may cause chills, sudden decrease in body temperature and torpor.

There was limited information on toxicity of this substance, and information specific to it was not available for its assessment, such as its NOAEL. Sufficient information could not be obtained for its carcinogenicity, and its carcinogenicity in humans could not be assessed. However, toxicity information for wood creosote, which contains this substance, was available. Assuming its effects are solely attributed to this substance, its toxicity was assessed with its threshold presumed, on the basis of information on its non-carcinogenic effects.

No-observed-adverse-effect-level (NOAEL) of 50 mg/kg/day for oral exposure to wood creosote (for reduced survival rate and suppressed body-weight increase) obtained from mid-term and long-term tests for rats was translated, for reference, to ‘non-toxic level’ of 13 mg/kg/day for exposure only to this substance, assuming these effects are

solely attributed to this substance. As for inhalation exposure, its 'non-toxic level*' could not be identified.

As for its oral exposure, its 'non-toxic level*' could not be identified, and its health risk could not be assessed. However, if its 'non-toxic level' of 13 mg/kg/day obtained for reference from information on wood creosote were combined with the predicted maximum exposure of around 0.0025 μg/kg/day estimated for intakes of freshwater in public water bodies, and then divided by 10, due to the fact that the 'non-toxic level' was identified from animal experiments, its margin of exposure (MOE) would be 520,000. Since risk associated with exposure to this substance through food intakes from the environment is presumed to be minimal, this exposure will not increase MOE significantly, and no further action will be required at the moment to assess health risk from oral exposure to this substance.

As for inhalation exposure to this substance, its 'non-toxic level' could not be identified, and its exposure concentrations were yet to be obtained. Its health risk could not be assessed. Its half-life in the atmosphere is 2.2 to 22 hrs. When released to the atmosphere, most of it is expected to go to media other than the ambient air, and collection of information on its inhalation exposure to assess health risk associated with its inhalation exposure in the ambient air would not be required.

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*' – mg/kg/day	–	–	Drinking water	– μg/kg/day	MOE	–	×	(○)
				Freshwater	0.0025 μg/kg/day	MOE	–	×	
Inhalation	'Non-toxic level*' – mg/m^3	–	–	Ambient air	– $\mu g/m^3$	MOE	–	×	(○)
				Indoor air	– $\mu g/m^3$	MOE	–	×	×

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, the following reliable data were obtained: a 72-h median effective concentration (EC_{50}) of 271,000 μg/L for growth inhibition in the green algae *Pseudokirchneriella subcapitata*; a 48-h EC_{50} of 29,100 μg/L for swimming inhibition in the crustacean *Daphnia magna*; and a 96-h median lethal concentration (LC_{50}) of more than 100,000 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 290 μg/L was obtained. With regard to chronic toxicity, the following reliable data were obtained: a 72-h no observed effect concentration (NOEC) of 28,600 μg/L for growth inhibition in the green algae *P. subcapitata* and a 21-d NOEC of 750 μg/L was obtained for reproductive inhibition in the crustacean *D. magna*. Accordingly, based on these chronic toxicity values and an assessment factor of 100, a predicted no effect concentration (PNEC) of 7.5 μg/L was obtained. The value of 7.5 μg/L obtained from the chronic toxicity to the crustacean was used as the PNEC for this substance.

The PEC/PNEC ratio was 0.008 for freshwater bodies and less than 0.003 for seawater. Accordingly, further work is thought to be unnecessary at this time.

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)		
Crustacen (water flea)	Chronic	NOEC Reproductive inhibition	100	7.5	Freshwater	0.062	0.008	○
					Seawater	<0.02	<0.003	

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5. Conclusions

	Conclusions		Judgment
Health risk	Oral exposure	Though a risk characterization cannot be determined, there would be little necessity of collecting information.	(○)
	Inhalation exposure	Though a risk characterization cannot be determined, there would be little necessity of collecting information.	(○)
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

(○) : Though a risk characterization cannot be determined, there would be little necessity of collecting information.

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