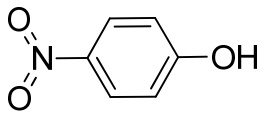
8	CAS No.: 100-02-7	Substance: *p*-Nitrophenol

Chemical Substances Control Law Reference No.: 3-777 (Nitrophenol)

PRTR Law Cabinet Order No.: 2-72

Molecular Formula: $C_6H_5NO_3$ Structural Formula:

Molecular Weight: 139.11



1. General information

The aqueous solubility of this substance is 1.56×10^4 mg/1,000 g (20°C), the partition coefficient (1-octanol/water) (log K_{ow}) is 1.38 (pH=7.4), and the vapor pressure is 2.36×10^{-3} mmHg (=0.315 Pa) (20°C). Biodegradability (aerobic degradation) is not good and bioaccumulation is thought to be non-existent or low. The substance does not have any hydrolyzable groups.

This substance is designated as a Class 2 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). The main use of this substance is as a raw material for *p*-phenetidine (itself used in dyestuffs) and pharmaceuticals as well as for reagents (indicators) and agricultural chemicals (bactericides). The production and import category under the PRTR Law is 1 t to <100 t. The production and import quantity as nitrophenol in fiscal 2011 was less than 1,000 t.

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2. Exposure assessment

This substance was classified as a Class 1 Designated Chemical Substance prior to revision of substances regulated by the PRTR Law. Total release to the environment in fiscal 2009 under the PRTR Law was approximately 0.25 t, of which approximately 0.25 t, or 99% of overall releases were reported. The major destination of reported releases was public water bodies. In addition, approximately 42 t was transferred to waste materials, and 0.003 t was transferred to sewage. The main source of reported releases was the chemical industry. The largest release among releases to the environment including those unreported was to water bodies. A multi-media model used to predict the proportions distributed to individual media in the environment indicated that in regions where the largest quantities were estimated to have been released to the environment overall or to public water bodies in particular, the predicted proportion distributed to water bodies was 96.2%.

The maximum expected concentration of exposure to humans via inhalation could not be obtained. However, past general atmospheric data indicated around 0.064 μg/m^3. The maximum oral exposure could not be obtained. The maximum expected oral exposure was estimated to be less than 0.024 μg/kg/day on the basis of calculations from past data for public freshwater bodies. When releases to public freshwater bodies in fiscal 2011 reported according to the PRTR Law were divided by the ordinary water discharge of the national river channel structure database, estimating the concentration in rivers by taking into consideration only dilution gave a maximum value of 0.0009 μg/L. Using this estimated concentration for rivers to calculate oral exposure gave 0.000036 μg/kg/day.

The risk of exposure to this substance by intake from an environmental medium via food is considered slight, based on past estimates of oral exposure obtained by using estimated concentrations in fish species.

The predicted environmental concentration (PEC), which indicates exposure to aquatic organisms, could not be obtained. However, albeit past data, values of less than around 0.6 μg/L for public freshwater bodies and generally less than 0.6 μg/L for seawater have been obtained.

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rivers by taking into consideration only dilution gave a maximum value of 0.0009 μg/L.

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3. Initial assessment of health risk

This substance may cause irritation to eyes and respiratory tract. When exposed, methemoglobin may be produced in blood. Its inhalation exposure may cause cyanosis, coughing, burning sensation, confusion, convulsion, dizziness, headache, nausea, sore throat, loss of consciousness and weakness, while its oral exposure may cause, in addition to these symptoms, abdominal pain, sore throat and vomiting. Contact of the substance with skin may cause redness, and the symptoms as observed in the case of poisoning through its inhalation exposure may also occur when it is absorbed. Its contact with eyes may cause pain.

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

With regard to oral exposure to the substance, a NOAEL of 25 mg/kg/day (for decreased survival rates) obtained from its mid-term and long-term toxicity tests on rats was divided by a factor of 10 due to their short test periods. Outcome of 2.5 mg/kg/day was identified to be the reliable lowest dose of the substance and its 'non-toxic level*'. As for its inhalation exposure, a NOAEL of 5 mg/m^3 (for cataract) obtained from its mid-term and long-term toxicity tests on rats was adjusted for their durations to provide 0.89 mg/m^3 for its intermittent to continuous exposure, and this was further divided by a factor of 10 due to their short test periods. Outcome of 0.089 mg/m^3 was identified to be the reliable lowest dose of the substance and its 'non-toxic level*'.

With regard to oral exposure to the substance, its health risk could not be assessed as its exposure levels were not known. Its maximum exposure level was estimated to be below about 0.024 μg/kg/day from its maximum exposure level in public freshwater bodies (as reported in 1994). The MOE (Margin of Exposure) would be above 10,000 when calculated from this level and its 'non-toxic level*'. In addition, its maximum exposure level was calculated to be 0.000036 μg/kg/day from its concentrations in river water with effluents from operators discharging the substance in high concentrations reported in FY 2009 under the PRTR Law. The MOE would be 6,900,000 when calculated from this level for reference. As exposure to the substance in the environment through food intakes would be limited, the MOE would not change significantly even when this exposure was included. Therefore, collection of further information would not be required to assess potential health risk from its oral exposure.

With regard to inhalation exposure to the substance, its health risk could not be assessed as its exposure concentrations were not known. The MOE would be 140 when calculated from its maximum concentration of about 0.064 μg/m^3 in the ambient air, estimated from its emissions (reported in 1994), and its 'non-toxic level*' of 0.089 mg/m^3 from animal experiments, and divided by a factor of 10 to convert animal data to human data. In addition, its release to the environment was 0 t in FY 2009, and its predicted allocations among media suggest that the substance would hardly be in the ambient air even if it is released. Therefore, collection of further information would not be required to assess health risk from its inhalation exposure in the 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*' 2.5 mg/kg/day	Rat	Decreased survival rates	Drinking water	— μg/kg/day	MOE	—	×	(○)
				Freshwater	— μg/kg/day	MOE	—	×	
Inhalation	'Non-toxic level*' 0.089 mg/m^3	Rat	Cataract	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 48-h EC_{50} of 250 µg/L for growth inhibition in the green alga *Pseudokirchneriella subcapitata*, a 96-h LC_{50} of 2,800 µg/L for the crustacean *Gammarus pseudolimnaeus*, a 96-h LC_{50} of 3,800 µg/L for the fish species *Oncorhynchus mykiss* (rainbow trout), and a 24-h EC_{50} of 5,500 µg/L for reproductive inhibition in the ciliate protozoan *Tetrahymena pyriformis*. Accordingly, based on these acute toxicity values and an assessment factor of 100, a predicted no effect concentration (PNEC) of 2.5 µg/L was obtained.

With regard to chronic toxicity, the following reliable data were obtained: a 21-d NOEC of 1,300 µg/L for reproductive inhibition in the crustacean *Daphnia magna*, and an 85-d NOEC of 643 µg/L for growth inhibition in the fish species *Oncorhynchus mykiss* (rainbow trout). Accordingly, based on these chronic toxicity values and an assessment factor of 100, a PNEC of 6.4 µg/L was obtained.

The value of 2.5 µg/L obtained from the acute toxicity to algae was used as the PNEC for this substance.

The predicted environmental concentration (PEC) of this substance could not be obtained As such, a judgment on ecological risk could not be made. Albeit past data, the concentration of this substance in public water bodies was around less than 0.6 µg/L for freshwater bodies and generally less than 0.6 µg/L for seawater. The ratios of these concentrations to PNEC are less than 0.2 for both freshwater bodies and seawater. However, the river concentration estimated by using releases reported according to the PRTR Law and taking only dilution into consideration gives 0.0009 µg/L, resulting in a ratio to PNEC of less than 0.1. Accordingly, further work is considered unnecessary at this time.

Hazard assessment (basis for PNEC)			Assessment factor	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	Acute	EC_{50} growth inhibition	100	2.5	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 of further work at present.		○

［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