2	CAS No.: 123-30-8	Substance: *p*-Aminophenol

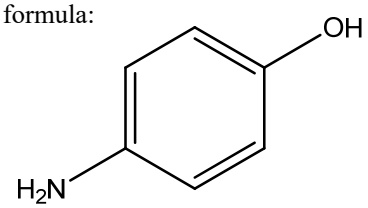
Chemical Substances Control Law Reference No.: 3-675 (Aminophenol), 5-3026 (Oxidation base-6)

PRTR Law Cabinet Order No.: 1-23

Molecular Formula: C_6H_7NO

Molecular Weight: 109.13

Structural formula:



1. General information

The aqueous solubility of this substance is 1.55×10^4 mg/1,000 g (20℃), the partition coefficient (1-octanol/water) (log K_{ow}) is 0.04 (pH=7.4), and the vapor pressure is 0.0750 mmHg (=10.0 Pa) (20℃). The biodegradability (aerobic degradation) of this substance is characterized by a BOD degradation rate of 6%, and it is not believed to be highly bioaccumulative.

This substance is designated as 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). The main uses of this substance are as pharmaceutical intermediate (acetaminophen antipyretic analgesic), an intermediate for sulfur dyes, a rubber antioxidant, an oxidation dye for furs, and as a photographic developing agent. The production and import quantity of aminophenol in fiscal 2015 was 1,000 t. The production and import category under the PRTR Law is more than 100 t.

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2. Exposure assessment

Total release to the environment in fiscal 2015 under the PRTR Law was 0.065 t, and almost all releases were reported. All reported releases were to public water bodies. In addition, 0.077 t was transferred to sewage and approximately 0.71 t was transferred to waste materials. The main source of reported releases was the chemical industry. The largest releases to the environment including unreported releases were 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 public water bodies in particular, the predicted proportion distributed to water bodies was 96.3%.

Information to determine the maximum expected inhalation exposure could not be obtained.

The maximum expected oral exposure was estimated to be generally 0.00048 μg/kg/day based on calculations from data for public freshwater bodies. In contrast, when releases to public freshwater bodies in fiscal 2015 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 0.0082 μg/L. Calculating oral exposure to humans by using this estimated river concentration gave 0.00033 μg/kg/day. Further, the transfer to sewage was much larger than releases to public freshwater bodies. When transfer to sewage was 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 0.79 μg/L, and the resulting oral exposure was 0.032 μg/kg/day. The risk of exposure to this substance by intake from an environmental medium via food is considered slight, given its low bioaccumulation.

The predicted environmental concentration (PEC), which indicates exposure to aquatic organisms, was about 0.012 μg/L. Data for setting the PEC for seawater could not be obtained, however past data reported a value of 0.033 μg/L.

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3. Initial assessment of health risk

No information was available on acute symptoms in humans. Lethargy and piloerection were observed in rats exposed to this substance by ingestion.

As sufficient information on the carcinogenicity of this 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 10 mg/kg/day (based on nephropathy), determined from toxicity tests in rats, 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, assuming the substance is absorbed via public freshwater bodies, the predicted maximum exposure level would be 0.00048 μg/kg/day, approximately. The MOE (Margin of Exposure) would be 2,100,000, when calculated from the predicted maximum exposure level and the 'non-toxic level*'of 10 mg/kg/day, and subsequently divided by a factor of 10 to account for extrapolation from animals to humans. In addition, the maximum exposure level was calculated to be 0.00033 μg/kg/day. This value derives from the estimated concentration in the effluents from the high discharging plants, according to the releases reported in FY 2015 under the PRTR Law. The MOE would be 3,000,000, when calculated from this level. When transfers to sewage are taken into consideration, the maximum exposure level would be 0.032μg/kg/day. The MOE would be 31,000, when calculated from this level. Since exposure to the substance in environmental media via food is presumed to be limited, including the concentration value in the calculation would not change the MOE significantly. Therefore, no further work would be required at present to assess the health risk of this substance via oral exposure.

With regard to inhalation exposure, owing to the lack of identified 'non-toxic level*' and exposure levels, the health risk could not be assessed. The total release of the substance to the environment was reported to be 0.065 t in FY 2015 under the PRTR Law. However, the air emission of the substance was reported to be 0 t, and predictions of the multimedia fugacity model indicated that proportion distributed to air was little. 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*' 10 mg/kg/day	Rats	Nephropathy	Drinking water	- μg/kg/day	MOE	-	×	○
				Public Freshwater bodies	0.00048 μg/kg/day	MOE	2,100,000	○	
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 72-h EC_{50} of 100 μg/L for growth inhibition in the green algae *Pseudokirchneriella subcapitata*, a 48-h EC_{50} of 96 μg/L for immobilization in the crustacean *Daphnia magna*, and a 48-h LC_{50} of 502 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 0.96 μg/L was obtained.

With regard to chronic toxicity, the following reliable data were obtained: a 72-h NOEC of 25 μg/L for growth inhibition in the green algae *P. subcapitata*, and a 41-d NOEC of 64 μg/L for growth inhibition in the fish species *Oryzias latipes* (medaka). Accordingly, based on these chronic toxicity values and an assessment factor of 100, a predicted no effect concentration (PNEC) of 0.25 μg/L was obtained.

The value of 0.25 μg/L obtained from the chronic toxicity to the green algae species was used as the PNEC for this substance.

The PEC/PNEC ratio is 0.05 for freshwater, while risk could not be assessed for seawater. Further, albeit past data, a value of 0.033 μg/L has been reported for seawater. The ratio of this value to PNEC is 0.13. In addition, when releases to public freshwater bodies in fiscal 2015 estimated from transfer to sewage 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 0.79 μg/L, suggesting the possibility that locations with concentrations higher than PNEC exist. Accordingly, efforts to collect data on this substance are needed, as are further measurements of environmental concentrations by taking emission sources into consideration.

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)			
Green algae	Chronic	NOEC Growth inhibition	100	0.25	Freshwater	0.012	0.05	○	▲
					Seawater	—	—		

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5. Conclusions

	Conclusions		Judgment
Health risk	Oral exposure	No need for further work.	○
	Inhalation exposure	Although risk to human health could not be confirmed, collection of further information would not be required.	(○)
Ecological risk	Requiring information collection.		▲

［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.