12	CAS No.: 106-50-3	Substance: *p*-Phenylenediamine

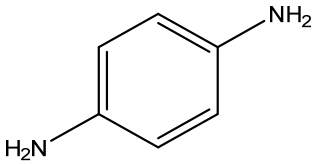
Chemical Substances Control Law Reference No.: 3-185 (Phenylenediamine), 5-4998（Oxidation base-10）

PRTR Law Cabinet Order No.: 1-348 (Phenylenediamine)

Molecular Formula: $C_6H_8N_2$

Molecular Weight: 108.14

Structural Formula:



1. General information

The aqueous solubility of this substance is 3.57×10^4 mg/1000 g (24°C), the partition coefficient (1-octanol/water) (log K_{ow}) is −0.30, and the vapor pressure is <1 mmHg (<133 Pa) (21°C). This substance does not biodegrade easily and bioaccumulation is thought to be low.

This substance is classified as a Class 1 Designated Chemical Substance under the PRTR Law. The main uses of this substance are as a raw material for azo dyestuffs, hair dyes, rubber vulcanizers, and para-aramid fibers. The production and import quantity of phenylenediamine in fiscal 2017 was 1000 t. The production and import quantity under the PRTR Law was more than 100 t.

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2. Exposure assessment

Total release to the environment in fiscal 2017 under the PRTR Law was approximately 3.5 t, of which approximately 3.3 t or 95% was reported. The major destination of reported releases was public water bodies

In addition, approximately 42 t was transferred to waste materials and 0.16 t was transferred to sewage. Industries with large reported releases were the plastic product manufacturing industry for the atmosphere, and the chemical and plastic product manufacturing industries for public water bodies. 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, the predicted proportion distributed to the public water bodies would be 99.6%. Where the largest quantities were estimated to have been released to the atmosphere, the predicted proportion distributed to the public water bodies would be 96.4%.

The maximum expected concentration of exposure to humans via inhalation could not be determined because ambient atmospheric and indoor air quality data could not be obtained. The mean annual value for the atmospheric concentration of phenylenediamine in fiscal 2017 was calculated by use of a plume-puff model on the basis of releases to the atmosphere reported according to the PRTR Law; this model predicts a maximum level of 0.0028 μg/m^3 . Further, this estimate assumes that all reported releases of phenylenediamine were in the form of *p*-phenylenediamine and is based on reports of *p*-phenylenediamine releases (including those that reported 0 kg) for the period 2001–2009, which is prior to the revision of substances classified under the PRTR Law.

The maximum expected oral exposure was calculated to be around less than 0.00064 μg/kg/day assuming intake solely from public freshwater bodies. However, when releases of phenylenediamine to public freshwater bodies in fiscal 2017 reported under 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 0.039 μg/L. Using this estimated concentration for rivers to calculate oral exposure gives 0.0016 μg/kg/day. Further, this estimate assumes that all reported releases of phenylenediamine were in the form of *p*-phenylenediamine and is based on reports of

p-phenylenediamine releases (including those that reported 0 kg) for the period 2001–2009, which is prior to the revision of substances classified under the PRTR Law. Further, when transfer to sewage is included in the previous calculation, a maximum value of 1.0 μg/L is obtained, and the resulting oral exposure becomes 0.040 μg/kg/day. The risk of exposure to this substance by intake from an environmental medium via food is considered slight, given its nonexistent or low bioaccumulation.

The predicted environmental concentration (PEC), which indicates exposure to aquatic organisms, was reported to be around less than 0.016 μg/L for both public freshwater bodies and seawater. When releases of phenylenediamine to public freshwater bodies in fiscal 2017 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 gives a maximum value of 0.039 μg/L. Further, this estimate assumes that all reported releases of phenylenediamine were in the form of *p*-phenylenediamine and is based on reports of *p*-phenylenediamine releases (including those that reported 0 kg) for the period 2001–2009, which is prior to the revision of substances classified under the PRTR Law. Further, when transfer to sewage is included in the previous calculation, a maximum value of 1.0 μg/L is obtained.

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3. Initial assessment of health risk

This substance is irritating to the eyes. Ingestion of the substance causes abdominal pain, cyanosis, convulsions, drowsiness, labored breathing, shortness of breath, vomiting and weakness. Inhalation causes cough, dizziness, headache and labored breathing, and may cause the same symptoms as ingestion including cyanosis. Contact with the skin causes redness. Contact with the eyes may cause redness, pain, swelling of the eyelids, blurred vision and loss of vision.

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 of 4 mg/kg/day for oral exposure (based on increase in the relative weight of liver and kidneys), determined from toxicity tests in rats, was divided by a factor of 10 to account for extrapolation to chronic exposure. The calculated value of 0.4 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, assuming the substance is absorbed via public freshwater bodies, the predicted maximum exposure level would be less than 0.00064 μg/kg/day, approximately. The MOE (Margin of Exposure) would exceed 63,000, when calculated from the predicted maximum exposure level and the 'non-toxic level' of 0.4 mg/kg/day, and subsequently divided by a factor of 10 to account for extrapolation from animals to humans. This would lead to the health risk judgment that no further work would be required at present. In addition, the MOE for reference would be 25,000, when calculated from the estimated maximum exposure level of 0.0016 μg/kg/day. This maximum exposure level was estimated according to the concentration in effluents from the high discharging plants reported as phenylenediamines in FY 2017 under the PRTR Law. When transfers to sewage are considered, the maximum exposure level would be 0.040 μg/kg/day, giving an MOE of 1,000. Since exposure to the substance in environmental media via food is presumed to be limited in spite of data unavailability, including it in the calculation would not change the MOE significantly. Therefore, as a comprehensive judgment, 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 concentrations, the health risk could not be assessed. However, the MOE would be 46,000, when calculated from the tentative 'non-toxic level' for inhalation exposure of 1.3 mg/m^3 and the concentration in ambient air of 0.0028 μg/m^3, and subsequently divided by a factor of 10 to account for extrapolation from animals to humans. The tentative 'non-toxic level' for inhalation exposure above was derived from the conversion of the 'non-toxic level' for oral exposure, assuming that 100% of the inhaled

substance is absorbed. The concentration in ambient air was estimated as the maximum concentration (annual mean) in ambient air near the operators releasing large amount of the substance based on the releases to air reported as phenylenediamines in FY 2017 under the PRTR Law. Therefore, as a comprehensive judgment, collection of further information would not be required to assess the health risk of this substance via inhalation in ambient air.

Toxicity				Exposure assessment		MOE		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' 0.4 mg/kg/day	Rats	Increase in the relative weight of liver and kidneys.	Drinking water	- μg/kg/day	MOE	-	○
				Public Freshwater bodies	<0.00064 μg/kg/day	MOE	>63,000	
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 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 177 μg/L for growth inhibition in the alga *Raphidocelis subcapitata*, a 48-h EC_{50} of 150 μg/L for swimming inhibition in the crustacean *Daphnia magna*, a 96-h LC_{50} of 66 μg/L for the fish *Oryzias latipes* (medaka), and a 60-h IGC_{50} of 74,060 μg/L for population growth inhibition in the ciliate *Tetrahymena pyriformis*. Accordingly, based on these acute toxicity values and an assessment factor of 100, a predicted no effect concentration (PNEC) of 0.66 μg/L was obtained.

With regard to chronic toxicity, the following reliable data were obtained: a 72-h NOEC of 8 μg/L for growth inhibition in the alga *R. subcapitata* and a 21-d NOEC of 4.14 μg/L for reproductive inhibition in the crustacean *D. magna*. Accordingly, based on these chronic toxicity values and an assessment factor of 100, a PNEC of 0.041 μg/L was obtained.

The value of 0.041 μg/L obtained from the chronic toxicity to the crustacean was used as the PNEC for this substance.

The PEC/PNEC ratio is less than 0.4 for freshwater bodies and seawater. The ecological risk could not be determined because this value straddles the criterion classification.

However, when releases of phenylenediamine to public freshwater bodies in fiscal 2017 reported under 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 0.039 μg/L, and the ratio of this value to the PNEC is 0.9. Further, when transfer to sewage is included in the previous calculation, a maximum value of 1.0 μg/L is obtained, and the ratio of this value to the PNEC is 24; accordingly, based on a comprehensive review of the above findings, efforts to collect data are needed, and environmental concentration data needs to be augmented taking into consideration major emission sources.

Hazard assessment (basis for PNEC)			Assessment coefficient	Predicted no effect concentration PNEC (μg/L)	Exposure assessment		PEC/ PNEC ratio	Comprehensive judgment
Species	Acute/ chronic	Endpoint			Water body	Predicted environmental concentration PEC (μg/L)		
Crustacean *Daphnia magna*	Chronic	NOEC Reproductive inhibition	100	0.041	Freshwater	<0.016	<0.4	▲
					Seawater	<0.016	<0.4	

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5. Conclusions

	Conclusions		Judgment
Health risk	Oral exposure	No need for further work.	○
	Inhalation exposure	No need for further work.	○
Ecological risk	Requiring information collection.		▲

［Risk judgments］○: No need for further work ▲: Requiring information collection
■: Candidates for further work ×: Impossibility of risk characterization