9	CAS No.: 95-54-5	Substance: *o*-Phenylenediamine

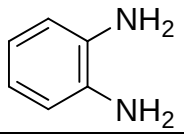
Chemical Substances Control Law Reference No.: 3-185 (Phenylenediamine)

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 3.02×10^{4} mg/1,000 g (20°C), the partition coefficient (1-octanol/water) (log K_{ow}) is 0.15, and the vapor pressure is 9.8×10^{-3} mmHg (=1.3 Pa) (20°C). Biodegradability (aerobic degradation) is judged to be difficult and bioaccumulation is thought to be low. The substance does not have any hydrolyzable groups.

This substance is designated as a Priority Assessment Chemical Substance and phenylenediamines are 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 use of this substance is as a raw material for agricultural chemicals, corrosion inhibitors, rubber chemicals, pharmaceuticals, and pigments. The production and import quantity in fiscal 2011 was 2,465 t, and the production and import category under the PRTR Law is more than 100 t.

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2. Exposure assessment

Total release of phenylenediamine to the environment in fiscal 2011 under the PRTR Law was approximately 3.7 t, of which approximately 2.2 t or 58% of overall releases were reported. The major destination of reported releases was public freshwater bodies. In addition, approximately 34 t was transferred to waste materials, and approximately 1.9 t was transferred to sewage. Industry types with large reported releases were the plastic products manufacturing industry for the atmosphere and the chemical industry alone for public water bodies. 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 98.3%. In regions where the largest estimated releases were to the atmosphere, the predicted proportion distributed to water bodies was 98.2%.

The maximum expected concentration of exposure to humans via inhalation could not be obtained. The mean annual value for atmospheric concentration in fiscal 2011 was calculated by using a plume-puff model on the basis of releases (as phenylenediamine) to the atmosphere reported according to the PRTR Law; this model predicted a maximum level of 0.022 μg/m^3. The maximum expected oral exposure was estimated to be less than 0.0006 μg/kg/day on the basis of calculations from data for public freshwater bodies. When releases (as phenylenediamine) 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 0.0028 μg/L. Using this estimated concentration for rivers to calculate oral exposure gave 0.00011 μg/kg/day. The risk of exposure to this substance by intake from an environmental medium via food is considered slight, given the low bioaccumulation of the substance expected on basis of its physicochemical properties.

The predicted environmental concentration (PEC), which indicates exposure to aquatic organisms, was around less than 0.015 μg/L for both public freshwater bodies and seawater. When releases (as phenylenediamine) 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 taking into consideration only dilution gave a maximum value of 0.0028 μg/L.

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3. Initial assessment of health risk

This substance may cause irritation to eyes and minor irritation to skin and respiratory tract. It may affect blood, and methemoglobin may be produced in blood. Cyanosis, confusion, convulsions, dizziness, headache, nausea and loss of consciousness may occur by its inhalation exposure or ingestion. Its contact with skin may cause redness, while its contact with eyes may cause redness and 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 40 mg/kg/day (for suppressed body weight increase and the increased responses to tail nerve stimulation) 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 4 mg/kg/day was identified to be the reliable lowest dose of the substance and its 'non-toxic level*'. As for its inhalation exposure, its 'non-toxic level*' could not be identified.

With regard to oral exposure to the substance, both its mean and maximum exposure levels were predicted to be below about 0.0006 μg/kg/day, when its intakes through freshwater from public water bodies were assumed. The MOE (Margin of Exposure) would be above 670,000 when calculated from its 'non-toxic level*' of 4 mg/kg/day and its maximum exposure level suggested by animal experiments, and divided by a factor of 10 to convert animal data to human data. In addition, its maximum exposure was calculated to be 0.00011 μg/kg/day from its concentrations in river water with effluents (mixture of isomers) from operators discharging the substance in high concentrations, reported in FY 2011 under the PRTR Law. The MOE would be 3,600,000 when calculated from this 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, no further action would be required at this moment to assess health risk from its inhalation exposure.

With regard to inhalation exposure to the substance, its health risk could not be assessed as its 'non-toxic level*' could not be identified nor its exposure concentrations were not known. If 100% absorption were assumed, its 'non-toxic level*' for oral exposure would be converted to a 'non-toxic level*' of 13 mg/m^3 for its inhalation exposure. The MOE would be 59,000 when calculated for referencefrom this level and its maximum (annual mean) concentration of 0.022 μg/m^3 in the ambient air near the operators discharging it in high concentrations in their emissions (mixture of isomers) as reported in FY 2011 under the PRTR Law, and divided by a factor of 10 to convert animal data to human data. 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*' 4 mg/kg/day	Rat	Suppressed body weight increase & increase of responses to tail nerve stimulation	Drinking water	— μg/kg/day	MOE	—	×	○
				Fresh water	<0.0006 μg/kg/day	MOE	>670,000	○	
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 821 μg/L for growth inhibition in the green alga *Pseudokirchneriella subcapitata*, a 48-h EC_{50} of 1,400 μg/L for immobilization in the crustacean *Daphnia magna*, a 96-h LC_{50} of 4,600 μg/L for the fish species *Oryzias latipes* (medaka), and a 60-h IGC_{50} of 48,240 μg/L for 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 8.2 μg/L was obtained.

With regard to chronic toxicity, the following reliable data were obtained: a 72-h of NOEC 371 μg/L for growth inhibition in the green alga *P. subcapitata*, and a 21-d NOEC of 83 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 0.83 μg/L was obtained.

The value of 0.83 μg/L obtained from the chronic toxicity to the crustacean was used as the PNEC for this substance.

The PEC/PNEC ratio was less than 0.02 for both freshwater bodies and seawater. In addition, the maximum river concentration (as phenylenediamine) estimated by using releases reported according to the PRTR Law and taking only dilution into consideration gives 0.0028 μg/L, resulting in a ratio to PNEC of less than 0.1. Accordingly, further work on this substance 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)			
Crustacean *Daphnia magna*	Chronic	NOEC reproductive inhibition	100	0.83	Freshwater	<0.015	<0.02	○	○
					Seawater	<0.015	<0.02		

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5. Conclusions

	Conclusions		Judgment
Health risk	Oral exposure	No need of further work at present.	○
	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.