5	CAS No.: 101-80-4	Substance: 4,4'-Diaminodiphenylether

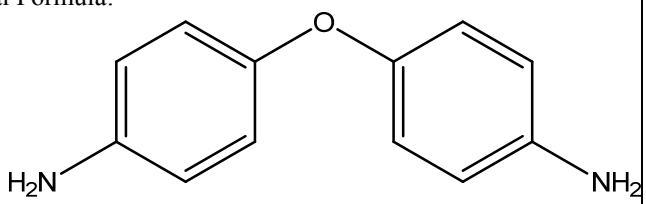
Chemical Substances Control Law Reference No.: 3-854

PRTR Law Cabinet Order No.: 1-143

Molecular Formula: $C_{12}H_{12}N_2O$

Molecular Weight: 200.24

Structural Formula:



1. General information

The aqueous solubility of this substance is 48 mg/L (20°C, pH=6.49–6.71), the partition coefficient (1-octanol/water) (log K_{ow}) is 1.36 (pH=7.4), and the vapor pressure is 0.98 mmHg (=130 Pa) (25°C). Biodegradability (aerobic degradation) is characterized by a BOD degradation rate of 7.6%, and its half-life for hydrolysis is 844-h (25°C) at pH 4; the substance is stable at pH 7 and pH 9.

This substance is a Class 1 Designated Chemical Substance under the PRTR Law.

The main use of this substance is as a raw material for polyimides, polyamide imides, and polyamides. It is also used as a raw material for polymers such as epoxies and urethanes as well as a crosslinking agent for polymers. The production and import quantities in fiscal 2014 were not disclosed because the number of reporting businesses was less than two. 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 2014 under the PRTR Law was 0 t. In addition, approximately 103 t was transferred to waste materials. Predictions of proportions distributed to individual media by using a Mackay-type level III fugacity model indicate that if equal quantities were released to the atmosphere, water bodies, and soil, the proportion distributed to water bodies would be largest.

Information to determine the maximum expected inhalation exposure could not be obtained. Data from public freshwater bodies yielded a maximum expected oral exposure of around 0.00013 μg/kg/day. The exposure level 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, is around less than 0.0032 μg/L for public freshwater bodies, and generally less than 0.0032 μg/L for seawater.

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3. Initial assessment of health risk

No information was available on acute symptoms in human. This substance is not irritating to the skin in guinea pigs but is mildly irritating to the eyes in rabbits. Methemoglobinemia was reported in rats exposed to this substance by ingestion.

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. However, the carcinogenicity was taken into consideration for this risk assessment, because there is sufficient evidence in experimental animals for the carcinogenicity of this substance.

The LOAEL of 10 mg/kg/day for oral exposure (based on inhibition of body weight gain, decreased level of methemoglobin and liver diseases), determined from long-term toxicity tests in rats, was divided by a factor

of 10 to account for uncertainty in using a LOAEL. The calculated value of 1.0 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 0.00013 μg/kg/day, approximately. The MOE (Margin of Exposure) would be over 150,000, when calculated from the predicted maximum exposure level and the 'non-toxic level*'of 1.0 mg/kg/day, and subsequently divided by a factor of 10 to account for extrapolation from animals to humans, and by another factor of 5 to take into consideration the carcinogenicity in animals. Since exposure to the substance in environmental media via food is presumed to be limited, including this concentration 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 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 t in FY 2014 and there was no case where the substance was detected in the water bodies. Moreover, the reported values of the substance's vapor pressure are not so high despite their large variation, and the half-life is as short as several hours in the air. Given these facts, the concentration of the substance in ambient air is not likely to become a major concern. 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*' 1.0 mg/kg/day	Rats	Inhibition of body weight gain, decreased level of methemoglobin and liver diseases	Drinking water	— μg/kg/day	MOE	—	×	○
				Public Freshwater bodies	<0.00013 μg/kg/day	MOE	>150,000	○	
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 21,700 μg/L for growth inhibition in the green algae *Pseudokirchneriella subcapitata*, a 48-h LC_{50} of 920 μg/L for the crustacean *Daphnia magna*, and a 96-h LC_{50} of more than 52,000 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 9.2 μg/L was obtained.

With regard to chronic toxicity, the following reliable data was obtained: a 72-h NOEC of less than 3,750 μg/L for growth inhibition in the green algae *P. subcapitata*. Accordingly, based on this chronic toxicity value and an assessment factor of 100, a PNEC of less than 37 μg/L was obtained.

The definitive value of 9.2 μg/L obtained from the acute toxicity to the crustacean was used as the PNEC

for this substance.

The PEC/PNEC ratio is less than 0.0003 for both freshwater bodies and seawater; accordingly, further work is considered unnecessary at this time.

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)			
Crustacean *Daphnia magna*	Acute	LC_{50} mortality	100	9.2	Freshwater	<0.0032	<0.0003	○	○
					Seawater	<0.0032	<0.0003		

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5. Conclusions

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

［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.