22	CAS No.: 101-77-9	Substance: 4,4'-Methylenedianiline

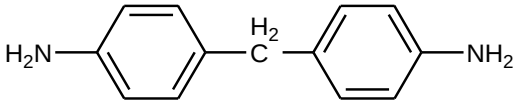
Chemical Substances Control Law Reference No.: 4-40

PRTR Law Cabinet Order No.: 1-340 (Cabinet Order No. after revision*: 1-446)

Structural Formula:

Molecular Formula: $C_{13}H_{14}N_2$

Molecular Weight: 198.26



*Note: No. according to revised order enacted on October 1, 2009.

1. General information

The aqueous solubility of this substance is 1.00×10^3 mg/L (25°C), the partition coefficient (1-octanol/water) (log K_{ow}) is 1.59, and the vapor pressure is 2.15×10^{-8} mmHg (=2.87×10^{-6} Pa) (25°C, extrapolated value). The biodegradability (aerobic degradation) is characterized by a BOD degradation rate of 0%, and bioaccumulation is thought to be nonexistent or low. The substance does not have any hydrolyzable groups.

This substance was 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), and this continues to be the case after the revision of substances regulated by the PRTR Law (enacted on October 1, 2009). It is primarily used as a raw material for diphenylmethane diisocyanate (MDI), which is a key raw material for synthetic resin (polyurethane), as a curing agent for epoxy resins, and also as a raw material for chemicals such as dyestuffs. The production and import quantity in fiscal 2007 was 1,776 t.

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2. Exposure assessment

Total release to the environment in fiscal 2006 under the PRTR Law was 0 t, while 12 t was transfer to waste. Predictions of distribution by medium using a Mackay-type level III fugacity model indicated that if equal quantities were released to the atmosphere, water bodies, and soil, the proportion distributed to soil would be higher.

Data for setting the predicted maximum exposure to humans via inhalation could not be obtained. The predicted maximum oral exposure was estimated to be less than around 0.0024 μg/kg/day based on calculations from data for groundwater and food.

The predicted environmental concentration (PEC), which indicates exposure to aquatic organisms, was less than around 0.04 μg/L for both public freshwater bodies and seawater.

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3. Initial assessment of health risk

This substance may cause effects on the liver, causing hepatic disorders. Inhalation exposure causes abdominal pain, nausea, vomiting, fever and chills while oral exposure may cause jaundice in addition to the symptoms caused by inhalation exposure. Abdominal pain, fever and jaundice are regarded as major symptoms of this substance observed in mass food poisoning incidents caused by baked bread contaminated with this substance. Acute hepatic incidents have been frequently observed in workers dealing with this substance. In these incidents, dermal absorption, rather than inhalation exposure, is regarded as a major cause.

Sufficient information could not be obtained on its carcinogenicity, and its initial assessment was conducted on the basis of data on its non-carcinogenic effects.

Its lowest-observed-adverse-effect-level (LOAEL) of 9 mg/kg/day for fatty degeneration and swelling of livers was obtained for oral exposure from its mid-term and long-term toxicity tests for rats. This LOAEL was divided by 10 to produce 0.9 mg/kg/day as its 'non-toxic level.[*]'

As for its inhalation exposure, its LOAEL of 440 mg/m^3 (for the degeneration of the photoreceptor cells, etc.)

obtained from mid-term and long-term toxicity tests for guinea pigs was adjusted against exposure conditions to produce 52 mg/m^3. It was divided by 10 due to their short test periods, and divided by 10 again as is always the case with LOAEL, to provide 0.52 mg/m^3 as its 'non-toxic level*'.

As for its oral exposure, the predicted maximum exposure was estimated to be less than around 0.0024 μg/kg/day, when intakes of groundwater and food were assumed. Its margin of exposure (MOE) would be more than 7,500 when calculated from its 'non-toxic level*' of 0.9 mg/kg/day and the predicted maximum exposure, and then divided by 10 due to the fact that 'non-toxic level*' was obtained from animal experiments, and divided again by 5 when its carcinogenicity was considered. No further action, therefore, will be required at the moment to assess health risk from oral exposure to this substance.

As for inhalation exposure to this substance, lack of information on its exposure concentration did not allow its risk assessment. This substance is designated as a potential hazardous air pollutant. Its half-life in the atmosphere is 2.1 to 21 hrs. When released to the atmosphere, nearly all of it is expected to go to media other than the ambient air. Total release of this substance to the environment is 0 t. Collection of information on its inhalation exposure to assess health risk associated with its inhalation exposure in the ambient air would not be required.

Information of toxicity				Exposure assessment		Result of risk assessment			Judgment
Exposure Path	Criteria for risk assessment	Animal	Criteria for diagnoses (endpoint)	Exposure medium	Predicted maximum exposure quantity and concentration				
Oral	'Non-toxic level*' 0.9 mg/kg/day	Rats	Hepatic steatosis and swelling, etc.	Drinking water & food	– μg/kg/day	MOE	–	×	○
				Groundwater & food	< 0.0024 μg/kg/day	MOE	>7,500	○	
Inhalation	'Non-toxic level*' 0.52 mg/m^3	Guinea Pigs	Degeneration of receptor cells, etc.	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 level equivalent to NOAEL.
- When an adverse effect level is available for the short-term exposure, 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 median effective concentration (EC_{50}) of 11,600 μg/L for growth inhibition in the green algae *Pseudokirchneriella subcapitata*; a 48-h EC_{50} of 2,470 μg/L for swimming inhibition in the crustacean *Daphnia magna*; and a 96-h median lethal concentration (LC_{50}) of 20,600 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 25 μg/L was obtained.

With regard to chronic toxicity, the following reliable data were obtained: a 72-h no observed effect concentration (NOEC) of 1,830 μg/L for growth inhibition in the green algae *P. subcapitata* and a 21-d NOEC 5.25 μg/L for reproductive inhibition in the crustacean *D. magna*. Accordingly, based on these chronic toxicity values and an assessment factor of 100, a predicted no effect concentration (PNEC) of 0.053 μg/L was obtained. The value of 0.053 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 0.8 for both freshwater bodies and seawater. Accordingly, a judgment cannot be made at this point in time regarding ecological risk. This substance is primarily used as a synthetic resin raw material. Release to public water bodies is 0 t, and release to the environment is 0 t. Transfer to waste is 12 t, and while release to the environment from waste treatment facilities is unknown, the possibility of transfer to water is considered to be low from the viewpoints of releases based on the PRTR Law and actual measured data for water quality. Accordingly, the need for collecting data for the purpose of initial assessment of the ecological risk of this substance to aquatic

organisms is considered low. However, if changes to applications, new public water body concentrations, or releases to public water bodies were to present a potential ecological risk to aquatic organisms, then consideration of collection of data would be required.

Hazard assessment (basis for PNEC)			Assessment factor	Predicted no effect concentration PNEC (μg/L)	Exposure assessment		PEC/ PNEC ratio	Result of assessment
Species	Acute/ chronic	Endpoint			Water body	Predicted environmental concentration PEC (μg/L)		
Crustacean (water flea)	Chronic	NOEC Reproductive inhibition	100	0.053	Freshwater	<0.04	<0.8	×（○）
					Seawater	<0.04	<0.8	

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5. Conclusions

	Conclusions		Judgment
Health risk	Oral exposure	No need for further work.	○
	Inhalation exposure	Though a risk characterization cannot be determined, there would be little necessity of collecting information.	（○）
Ecological risk	Though a risk characterization cannot be determined, there would be little necessity of collecting information.		（○）

［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.