6	CAS No.: 87-59-2	Substance: 2,3-Dimethylaniline

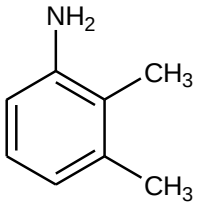
Chemical Substances Control Law Reference No.: 3-129 (dialkyl (C =1-5) aniline)

PRTR Law Cabinet Order No.: 2-42 (Cabinet Order No. after revision*: 2-50)

Structural Formula:

Molecular Formula: $C_8H_{11}N$

Molecular Weight: 121.18



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

1. General information

The aqueous solubility of this substance is 1.4×10^3 mg/L (25°C, calculated value), the partition coefficient (1-octanol/water) (log K_{ow}) is 1.84, and the vapor pressure is 0.075 mmHg (=10 Pa) (25°C). The biodegradability (aerobic degradation) is characterized by a BOD degradation rate of 3%, and bioaccumulation is thought to be nonexistent or low. The substance does not have any hydrolyzable groups.

This substance is designated as a Type II and III Monitoring Chemical Substance under the Law Concerning the Examination and Regulation of Manufacture, etc. of Chemical Substances. It was also designated as a Class 2 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). The main application is as a raw material for the manufacture of antipyretic, anti-inflammatory analgesics (mefenamic acid). The production and import category under the PRTR Law is 10 t. Japanese producers stopped producing this substance in 2004, and there have been no sales since 2005. An estimated 30–40 t was imported around 2005.

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2. Exposure assessment

Because this substance is not a Class 1 Designated Chemical Substance under the PRTR Law, release and transfer quantities could not be obtained. 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.

In terms of human exposure, general environmental atmospheric data from the past was less than around 0.5 μg/m^3. In addition, there is a report of less than 0.00076 μg/m^3 for data from a limited area (Kawasaki City). The predicted maximum oral exposure was estimated to be less than around 0.00028 μg/kg/day based on calculations from data for groundwater. The risk of exposure to this substance by intake from an environmental medium via food is considered slight.

The predicted environmental concentration (PEC), which indicates exposure to aquatic organisms, was less than around 0.007 μg/L for both public freshwater bodies and seawater.

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3. Initial assessment of health risk

Diminished consciousness is caused as a result of exposure to high levels of this substance and MetHb may possibly be generated. Inhalation exposure causes dizziness, lethargy, headache and nausea while oral exposure causes cyanosis on the lips, nail beds and skin, dizziness, lethargy, headache, nausea and loss of consciousness.

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 12 mg/kg/day for the splenic hemosiderosis was obtained for oral exposure from its mid-term and long-term toxicity tests for rats. This LOAEL was divided by 10 as is always the case with LOAEL, and divided again by 10 due to their short test periods, to produce 0.12 mg/kg/day as its 'non-toxic level.*' As for inhalation exposure, its 'non-toxic level*' could not be identified.

As for its oral exposure, its maximum exposure was estimated to be less than around 0.00028 μg/kg/day, when intakes of groundwater were assumed. Its margin of exposure (MOE) would be more than 43,000 when calculated from its 'non-toxic level*' of 0.12 mg/kg/day and its estimated maximum exposure, and then divided by 10 due to the fact that 'non-toxic level*' was obtained from animal experiments. Since risk associated with exposure to this substance through food intakes from the environment is presumed to be minimal, this exposure will not increase MOE significantly, and no further action will be required at the moment to assess health risk from oral exposure to this substance.

As for inhalation exposure to this substance, its 'non-toxic level' could not be identified, and its health risk could not be assessed.

The 'non-toxic level' for its oral exposure, if 100% absorption is assumed for it, turns to be the 'non-toxic level' of 0.4 mg/m^3 for its inhalation exposure. When combined with its estimated maximum concentration of around 0.5 μg/m^3 in the ambient air, MOE will be calculated to be 80. Calculation on the basis of the maximum concentration of less than 0.00076 μg/m^3 estimated from the latest report for some location will produce MOE of more than 53,000. Collection of information on its inhalation exposure to assess health risk associated with its 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*' 0.12 mg/kg/day	Rats	Splenic hemosiderosis	Drinking water	– μg/kg/day	MOE	–	×	○
				Groundwater	< 0.00028 μg/kg/day	MOE	> 43,000	○	
Inhalation	'Non-toxic level*' – mg/m^3	–	–	Ambient air	< 0.5 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 41,400 μg/L for growth inhibition in the green algae *Pseudokirchneriella subcapitata;* a 48-h EC_{50} of 8,900 μg/L for swimming inhibition in the crustacean *Daphnia magna*; a 96-h median lethal concentration (LC_{50}) of more than 94,000 μg/L for the fish species *Oryzias latipes* (medaka); and a 48-h median inhibition of growth concentration (IGC_{50}) of 327,000 μg/L for growth inhibition of the ciliated freshwater protozoan *Tetrahymena pyriformis*. Accordingly, based on these acute toxicity values and an assessment factor of 100, a predicted no effect concentration (PNEC) of 89 μg/L was obtained. With regard to chronic toxicity, the following reliable data were obtained: a 72-h no observed effect concentration (NOEC) of 4,320 μg/L for growth inhibition in the green algae *P. subcapitata*, and a 21-d NOEC of 100 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 1 μg/L was obtained. The value of 1 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 0.007 for both freshwater bodies and seawater. Accordingly, further work is

thought to be unnecessary at this time.

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	1	Freshwater	<0.007	<0.007	○
					Seawater	<0.007	<0.007	

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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	No need for further work.		○

［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.