9	CAS No.: 127-19-5	Substance: *N*,*N*-Dimethylacetamide

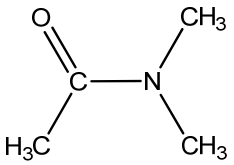
Chemical Substances Control Law Reference No.: 2-723

PRTR Law Cabinet Order No.: 1-213

Molecular Formula: C_4H_9NO

Molecular Weight: 87.12

Structural Formula:



1. General information

The aqueous solubility of this substance is $>1\times10^6$ mg/L (20°C), the partition coefficient (1-octanol/water) (log K_{ow}) is –0.796 (25°C), and the vapor pressure is 0.56 mmHg (=75 Pa) (25°C). Biodegradability (aerobic degradation) is judged to be good. Further, this substance does not hydrolyze.

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

The main uses of this substance are as a reaction solvent (elimination reactions), as a refining solvent, as a resin solvent, as a paint stripper, and in pharmaceutical-related applications (solvent for substances that are hard to dissolve). It is also used as an agricultural chemical (pesticide) auxiliary material. The production and import quantity in fiscal 2014 was 10,000 t, and the production and import category under the PRTR Law was more than 100 t.

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2. Exposure assessment

Total release to the environment in fiscal 2014 under the PRTR Law was approximately 520 t, of which approximately 450 t or 87% of overall releases were reported. The major destination of reported releases was the atmosphere. In addition, 34 t was transferred to sewage and approximately 3,400 t to waste materials. Industries with large reported releases were the chemical industry for the atmosphere, and the chemical industry and the medical equipment and device manufacturing industry for public water bodies. The largest releases to the environment, including those unreported, were to the atmosphere.

A multi-media model used to predict the proportions distributed to individual media in the environment indicates that in regions where the largest quantities are estimated to have been released to the environment overall or the atmosphere in particular, the predicted proportion distributed to the atmosphere is 99.9%. In regions where the largest quantities were estimated to have been released to public water bodies and soil, the predicted proportion distributed to the atmosphere is 99.7%.

The maximum expected concentration of exposure to humans via inhalation, based on ambient atmospheric data, was around 0.22 μg/m^3. Furthermore, the mean annual value for the atmospheric concentration in fiscal 2014 was calculated by using a plume-puff model based on releases to the atmosphere reported according to the PRTR Law: this model predicts a maximum level of 77 μg/m^3.

The maximum expected oral exposure was estimated to be around 2.9 μg/kg/day based on calculations from data for public freshwater bodies. In contrast, when releases to public freshwater bodies in fiscal 2014 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 729 μg/L. Using this estimated concentration for rivers to calculate oral exposure gave 29 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

73 μg/L for public freshwater bodies, and around 0.037 μg/L for seawater. When releases to public freshwater bodies in fiscal 2014 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 729 μg/L.

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3. Initial assessment of health risk

This substance causes headache and nausea, if inhaled, and causes headache, nausea, abdominal cramps and diarrhea, if ingested. Contact with the skin causes redness. The substance on the skin may be absorbed to cause the same symptoms as inhalation.

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 for oral exposure of 100 mg /kg/day (based on inhibition of body weight gain and increased weight of the liver), 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 10 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 NOAEL for inhalation exposure of 18 ppb (based on increased weight of the liver and kidneys, hepatic fatty degeneration and exacerbation of nephropathy), determined from long-term toxicity tests in rats, was adjusted according to exposure conditions. The calculated value of 3.2 ppm (11 mg/m^3) was deemed to be the lowest reliable concentration and was identified as the 'non-toxic level*' of the substance for inhalation exposure.

With regard to oral exposure, assuming the substance is absorbed via public freshwater bodies, the predicted maximum exposure level would be 2.9 μg/kg/day, approximately. The MOE (Margin of Exposure) would be 69, when calculated from the predicted maximum exposure level and the 'non-toxic level*'of 10mg/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. For comparison, the maximum exposure level was calculated to be 29 μg/kg/day. This value derives from the estimated concentration in the effluents from the high discharging plants, according to the releases reported in FY 2014 under the PRTR Law. The MOE would be 7, when calculated from this level. Since exposure to the substance in environmental media via food is presumed to be limited, including the concentration in the calculation would not change the MOE significantly. Therefore, collection of information would be required to assess the health risk of this substance via oral exposure.

With regard to inhalation exposure, the predicted maximum exposure concentration in ambient air was 0.22 μg/m^3, approximately. The MOE would be 1,000, when calculated from the predicted maximum exposure concentration and the 'non-toxic level*'of 11 mg/m^3, 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. For comparison, the maximum concentration (annual mean) in ambient air near the operators releasing large amount of the substance was estimated to be 77 μg/m^3 based on the releases reported in FY 2014 under the PRTR Law. The MOE would be 3, when calculated from this concentration. Therefore, collection of further information would 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*' 10 mg/kg/day	Rats	Inhibition of body weight gain and increased weight of the liver.	Drinking water	— μg/kg/day	MOE	—	×	▲
				Public Freshwater bodies	2.9 μg/kg/day	MOE	69	▲	
Inhalation	'Non-toxic level*' 11 mg/m^3	Rats	Increased weight of the liver and kidneys, hepatic fatty degeneration and exacerbation of nephropathy	Ambient air	0.22 μg/m^3	MOE	1,000	○	(▲)
				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 more than 500,000 μg/L for growth inhibition in the green algae *Desmodesmus subspicatus*, a 48-h EC_{50} of more than 500,000 μg/L for immobilization in the crustacean *Daphnia magna*, and a 96-h LC_{50} of more than 500,000 μg/L for the fish species *Leuciscus idus* (golden orfe). A PNEC value could not be set based on these acute toxicity values because they are values obtained from limit tests that investigated the presence of effects at a designated concentration.

With regard to chronic toxicity, the following reliable data was obtained: a 72-h of NOEC 500,000 μg/L for growth inhibition in the green algae *D. subspicatus*. A PNEC value could not be set based on this chronic toxicity value because it is a value obtained from limit tests that investigated the presence of effects at a designated concentration.

However, if the lowest chronic toxicity value of 500,000 μg/L obtained for the algae is divided by an assessment factor of 100, the provisional PNEC value becomes 5,000 μg/L. Using this value, the PEC/provisional PNEC ratio is smaller than 0.1 for both freshwater bodies and seawater. Furthermore, when releases to public freshwater bodies in fiscal 2014 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 729 μg/L, and the ratio of this value to the provisional PNEC is 0.15, which is slightly in excess of 0.1. Accordingly, further work is considered unnecessary at this time. Further, the maximum concentration in rivers estimated from reported releases and the maximum value (PEC) in public freshwater bodies are values for the same location.

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)			
—	—	—	—	—	Freshwater	73	—	×	○
					Seawater	0.037	—		

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5. Conclusions

	Conclusions		Judgment
Health risk	Oral exposure	Requiring information collection.	▲
	Inhalation exposure	Collection of further information would 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

（○）: 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.