3	CAS No.: 100-37-8	Substance: 2-(Diethylamino)ethanol

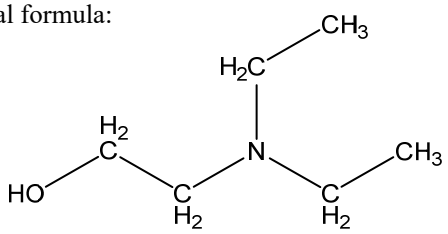
Chemical Substances Control Law Reference No.: 2-297 (*N,N*-Dialkyl (C=1–3)-*N*-ethanolamine),
2-353 (*N,N*-Dialkyl (or hydroxyethyl)-*N*-(2-hydroxyalkyl)amine)

PRTR Law Cabinet Order No.:

Molecular Formula: $C_6H_{15}NO$

Molecular Weight: 117.19

Structural formula:



1.General information

This substance is miscible in water, the partition coefficient (1-octanol/water) (log K_{ow}) is 0.21 (pH unknown), and the vapor pressure is 187 Pa at (25°C). The biodegradability (aerobic degradation) is characterized by a BOD degradation rate of 1%, and while it is a persistent substance, the substance is not judged to be highly bioaccumulative. Further, this substance is not thought to hydrolyze.

The main uses of this substance are as a leveling agent for textile dyeing; a cationization agent (paper-processing agent); a pharmaceutical precursor for antihistamines, antimalarial agents, local anesthetics, and analgesics; as an emulsifier for waxes; a rust inhibitor; a printing ink raw material; a volatilizing agent for azo dyes; an epoxy resin low temperature reaction (polymerization) accelerant; and a urethane foam foaming catalyst. The production and import quantity in fiscal 2021 as *N,N*-dialkyl (C=1–3)-*N*-ethanolamine was less than 10,000 t, while the production and import quantity in fiscal 2021 as *N,N*-dialkyl (or hydroxyethyl)-*N*-(2-hydroxyalkyl) amine was less than 1,000 t.

2.Exposure assessment

This substance was classified as a Class 1 Designated Chemical Substance prior to revision of substances regulated by the PRTR Law. Total release to the environment in fiscal 2021 under the PRTR Law was approximately 0.36 t, of which approximately 0.35 t or 95% were notified. The major destination of notified releases was the atmosphere. In addition, 0.030 t was transferred to sewage and approximately 13 t was transferred to waste materials. The major sources of notified releases to the atmosphere were the pharmaceutical industry and the plastic product manufacturing industry, while the major source of notified releases to public water bodies was the chemical industry. Including unnotified releases, the majority of releases to the environment were to the atmosphere. 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 the atmosphere in particular, the predicted proportion distributed to water bodies would be 98.3%. Where the largest quantities were estimated to have been released to public water bodies, the predicted proportion distributed to water bodies would be 99.1%.

The maximum expected concentration of exposure to humans via inhalation, based on ambient atmospheric data, was less than around 0.040 μg/m^3. Further, the mean annual value for atmospheric concentration in fiscal 2021 was calculated by use of a plume-puff model on the basis of releases to the atmosphere notified under the PRTR Law for fiscal 2021: this model predicts a maximum level of 0.041 μg/m^3.

Data for potable water, ground water, public freshwater bodies, food, and soil to assess oral exposure could not be obtained. However, when notified releases under the PRTR Law to public freshwater bodies in fiscal 2021 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 0.010 μg/L, and the oral exposure calculated thereof was 0.00041 μg/kg/day. Further, when releases to public freshwater bodies estimated from the reported transfer to sewage 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 0.040 μg/L, and a calculated average daily exposure of 0.0016 μg/kg/day. This substance is not judged to be highly bioaccumulative and as such, exposure from an environmental medium via ingestion is believed to be low.

Exposure to aquatic organisms could not be estimated based on water quality data. When releases reported under the PRTR Law in fiscal 2021 to public freshwater bodies estimated from the reported transfer to public freshwater bodies 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 0.010 μg/L. Further, when releases to public freshwater bodies estimated from the reported transfer to sewage 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 0.040 μg/L.

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3. Initial assessment of health risk

This substance severely irritates the skin and the respiratory tract and is corrosive to the eyes. Inhalation of this substance will cause a cough, nausea, sore throat, vomiting, and dizziness. Ingestion will cause abdominal pain and diarrhea. Contact with the eyes will cause redness, pain, and blurred vision. Contact with the skin will cause redness and pain.

Since not enough information was available on the carcinogenicity of the substance, the initial assessment was conducted based on information on its non-carcinogenic effects.

The NOAEL of 17 mg/kg/day for oral exposure (based on tremors and shaking movements of the head), determined from toxicity tests in dogs, was deemed the lowest reliable dose and was identified as the 'non-toxic level' of the substance for oral exposure. The NOAEL of 11 ppm for inhalation exposure (based on hyperplasia and squamous metaplasia of the respiratory epithelium in the nasal cavity), determined from toxicity tests in rats, was adjusted according to exposure conditions to obtain 1.96 ppm and subsequently divided by a factor of 10 to account for extrapolation to chronic exposure. The calculated value of 0.20 ppm (0.96 mg/m^3) was deemed the lowest reliable concentration and was identified as the 'non-toxic level' of the substance for inhalation exposure.

Regarding oral exposure, due to the lack of identified exposure levels, the health risk could not be assessed. The maximum exposure level was estimated to be 0.00041 μg/kg/day according to the concentration in effluents from the high discharging plants based on the releases to public freshwater bodies reported in FY 2021 under the PRTR Law. The MOE (Margin of Exposure) for reference would be 4,100,000 which is calculated from the estimated maximum exposure level and the 'non-toxic level' of 17 mg/kg/day and subsequently divided by a factor of 10 to account for extrapolation from animals to humans. When the transfers to the sewage system were taken into consideration, the maximum exposure level would be 0.0016 μg/kg/day, giving an MOE of 1,100,000. Since exposure to the substance in environmental media via food is presumed to be limited, despite the lack of exposure level via food, including it in the calculation would not change the MOE significantly. Therefore, as a comprehensive judgment, the collection of further information would not be required to assess the health risk of this substance via oral exposure.

Regarding inhalation exposure, both the average exposure concentration and the predicted maximum exposure concentration in ambient air were approximately less than 0.040 μg/m^3. The MOE would exceed 2,400 which is calculated from the predicted maximum exposure concentration and the 'non-toxic level' of 0.96 mg/m^3 and subsequently divided by a factor of 10 to account for extrapolation from animals to humans. This would lead to the health risk judgment that no further work would be required at present. The maximum concentration (annual mean) in ambient air near the operators that are releasing a large amount of the substance was estimated to be 0.041 μg/m^3, based on the releases to air reported in FY 2021 under the PRTR Law. The MOE for reference would be 2,300 which is calculated from the estimated maximum concentration (annual mean) in ambient air and the 'non-toxic level' of 0.96 mg/m^3 and subsequently divided by a factor of 10 to account for extrapolation from animals to humans. Therefore, as a comprehensive judgment, no further work would be required at present.

Toxicity					Exposure assessment		Result of risk assessment		Comprehensive judgment
Exposure Path	Criteria for risk assessment		Animal	Criteria for diagnoses (endpoint)	Exposure medium	Predicted maximum exposure dose and concentration			
Oral	'Non-toxic level*'	17 mg/kg/day	Dogs	Tremors and shaking movements of the head	Drinking water	- μg/kg/day	MOE	-	○
					Groundwater	- μg/kg/day	MOE	-	
Inhalation	'Non-toxic level*'	0.96 mg/m^3	Rats	Hyperplasia and squamous metaplasia of the respiratory epithelium in the nasal cavity	Ambient air	<0.040 μg/m^3	MOE	>2,400	○
					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 44,000 μg/L for growth inhibition in the green alga *Desmodesmus subspicatus*, a 48-h EC_{50} of 165,000 μg/L for swimming inhibition in the crustacean *Daphnia magna*, a 96-h LC_{50} exceeding 1,000,000 μg/L for the fish *Leuciscus idus* (ide) and *Oryzias latipes* (medaka), and a 40-h IGC_{50} of 3,710,000 μg/L for reproductive inhibition in the ciliate *Tetrahymena pyriformis*. Accordingly, based on this acute toxicity value and an assessment factor of 100, a predicted no effect concentration (PNEC) of 440 μg/L was obtained.

With regard to chronic toxicity, the following reliable datum was obtained: a 72-h NOEC of 5,000 μg/L for growth inhibition in the green alga *D. subspicatus*. Accordingly, based on this chronic toxicity value and an assessment factor of 100, a PNEC of 50 μg/L was obtained.

The value of 50 μg/L obtained from the chronic toxicity to the green alga species was used as the PNEC for this substance.

Data for setting the predicted environmental concentration (PEC) could not be obtained for this substance. Accordingly, an assessment of ecological risk could not be made.

When releases to public freshwater bodies notified under the PRTR Law in fiscal 2021 bodies 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 0.010 μg/L. The ratio of this value and PNEC was 0.0002.

Further, when releases to public freshwater bodies estimated from the reported transfer to sewage 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 0.040 μg/L. The ratio of this value to PNEC was 0.0008. Furthermore, based on expert opinion that this type of amine may have a particularly strong effect on chronic toxicity rather than acute toxicity in crustaceans, a QSAR study of chronic toxicity towards crustaceans was conducted, resulting in a QSAR predicted value of 11,000 μg/L. This value is higher than the chronic toxicity towards the alga (5,000 μg/L) that forms the basis of PNEC. Accordingly, even if a reference PNEC value is calculated by referencing the QSAR predicted value for chronic toxicity towards the crustacean, the PNEC value derived from experiments (50 μg/L) remains unchanged. Accordingly, based on a comprehensive review of the above findings, 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	Comprehensive judgment
Species	Acute/ chronic	Endpoint			Water body	Predicted environmental concentration PEC (μg/L)		
Green algae	Chronic	NOEC Growth inhibition	100	50	Freshwater	—	—	○
					Seawater	—	—	

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5. Conclusions

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