8	CAS No: 102-81-8	Substance: 2- (Di-*n*-butylamino) ethanol

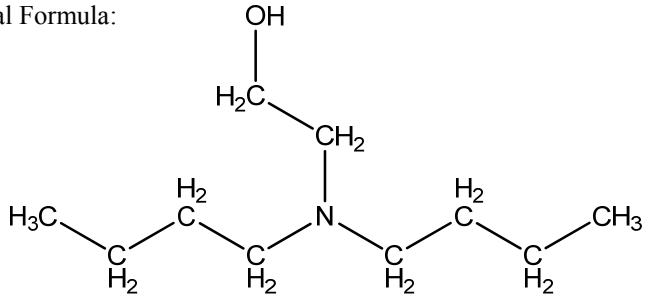
Chemical Substances Control Law Reference No.: 2-353 (*N*,*N*-Dialkyl (or hydroxyethyl)-*N*-(2-hydroxyalkyl) amine)

PRTR Law Cabinet Order No.:

Molecular Formula: $C_{10}H_{23}NO$

Molecular Weight: 173.30

Structural Formula:



1. General information

The aqueous solubility of this substance is 4×10^3 mg/L (20°C, pH=11.1), the partition coefficient (1-octanol/water) (log K_{ow}) is 1.86 (25°C, pH=9.2), and the vapor pressure is 0.038 mmHg (=5 Pa) (20°C, extrapolated value). Biodegradability (aerobic degradation) is judged to be difficult, and it has been judged to not be highly bioaccumulative.

The main uses of this substance are as a synthetic raw material for textile leveling agents, as a lubricant, as a catalyst for foaming of urethanes, as a raw material for emulsifiers, and as an emulsifier in its own right. The production and import quantity of *N*,*N*-dialkyl (or hydroxyethyl)-*N*-(2-hydroxyalkyl) amine) in fiscal 2014 was less than 1000 t.

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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 2009 under the PRTR Law was approximately 0.16 t, of which approximately 0.14 t or 89% of overall releases were reported. The major destination of reported releases was public water bodies. In addition, 0.017 t was transferred to sewage and approximately 2.7 t was transferred to waste materials. Industries with large reported releases were the electrical machinery manufacturing industry and the chemical industry for the atmosphere, and the electrical machinery manufacturing industry for public water bodies. The largest releases to the environment including unreported releases were to water bodies.

A multi-media model used to predict the proportions distributed to individual media in the environment indicates for fiscal 2009 that in regions where the largest quantities are estimated to be released to the environment overall or the atmosphere and public water bodies in particular, the predicted proportion distributed to the public water bodies is 97.3%.

The maximum expected concentration of exposure to humans via inhalation, based on ambient atmospheric data, was generally less than 0.018 μg/m^3. However, because this substance was removed from the Class 1 Designated Chemical Substance list as a result of the revision of substances regulated by the PRTR Law , the mean annual value for the atmospheric concentration was calculated by using a plume-puff model based on releases to the atmosphere using the most recent available data from fiscal 2009: this model predicts a maximum level of 0.0058 μg/m^3.

The maximum expected concentration of oral exposure to humans, based on public freshwater body data, was generally less than 0.001 μg/kg/day. In contrast, when releases to public freshwater bodies in fiscal 2009

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 4.4 μg/L. Using this estimated concentration for rivers to calculate oral exposure gave 0.18 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 generally 0.025 μg/L for public freshwater bodies, and generally less than 0.043 μg/L for seawater. When releases to public freshwater bodies in fiscal 2009 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 4.4 μg/L.

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3. Initial assessment of health risk

This substance affects the central nervous system, which may result in convulsions and respiratory failure. The substance can act as a cholinesterase inhibitor, which may result in death. It is corrosive to the eyes and skin, and causes pain, redness and deep burns. The vapor is irritating to the respiratory tract, and causes coughs, sore throat, nausea, convulsions, dizziness, labored breathing, pupillary constriction, muscle cramp, excessive salivation, sweating and unconsciousness, if inhaled. It is corrosive and causes abdominal pain, burning sensation, shock or collapse, abdominal cramps, diarrhea and vomiting, if ingested. In addition to these symptoms, oral exposure to this substance occasionally causes 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.

The NOAEL for oral exposure of 100 mg/kg/day (based on inhibition of body weight gain, vacuolation of the epithelium in renal collecting tubules, etc.), determined from medium-term toxicity tests in rats, was divided by a factor of 10 to account for extrapolation from sub-chronic to chronic exposure. 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 22 ppm (based on inhibition of body weight gain), determined from medium-term toxicity tests in rats, was adjusted according to exposure conditions to obtain 3.9 ppm (28 mg/m^3) and subsequently divided by a factor of 10 to account for extrapolation from sub-chronic to chronic exposure. The calculated value of 2.8 mg/m^3 was deemed to be the lowest reliable concentration and 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 less than 0.001 μg/kg/day, approximately. The MOE (Margin of Exposure) would be over 1,000,000, when calculated from the predicted maximum exposure level and the ‘non-toxic level*’of 10 mg/kg/day, and subsequently divided by a factor of 10 to account for extrapolation from animals to humans. In addition, the maximum exposure level was calculated to be 0.18 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 2009 under the PRTR Law. The MOE would be 5,600, 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, no further work would be required at present to assess the health risk of this substance via oral exposure.

With regard to inhalation exposure, the predicted maximum exposure concentration was approximately less than 0.018 μg/m^3 in ambient air. The MOE would be over 16,000, when calculated from the predicted maximum

exposure concentration and the 'non-toxic level*' of 2.8 mg/m^3, and subsequently divided by a factor of 10 to account for extrapolation from animals to humans. In addition, the maximum concentration (annual mean) in ambient air near the operators releasing large amount of the substance was estimated to be 0.0058 μg/ m^3 based on the releases reported in FY 2009 under the PRTR Law. The MOE would be 48,000, when calculated from this concentration. Therefore, no further work would be required at present 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, vacuolation of the epithelium in renal collecting tubules, etc.	Drinking water	— μg/kg/day	MOE	—	×	○
				Public Freshwater bodies	<0.001 μg/kg/day	MOE	>1,000,000	○	
Inhalation	'Non-toxic level*' 2.8 mg/m^3	Rats	Inhibition of body weight gain.	Ambient air	<0.018 μg/m^3	MOE	>16,000	○	○
				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 21,400 μg/L for growth inhibition in the green algae *Pseudokirchneriella subcapitata*, a 48-h EC_{50} of 73,700 μg/L for immobilization in the crustacean *Daphnia magna*, and a 96-h LC_{50} of 29,200 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 210 μg/L was obtained.

With regard to chronic toxicity, the following reliable data were obtained: a 72-h NOEC of 3,200 μg/L for growth inhibition in the green algae *P. subcapitata*, and a 21-d NOEC of 4,380 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 32 μg/L was obtained.

The value of 32 μg/L obtained from the chronic toxicity to the green algae was used as the PNEC for this substance.

The PEC/PNEC ratio is less than 0.0008 for freshwater bodies and 0.001 for seawater. Further, when releases to public freshwater bodies in fiscal 2009 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 4.4 μg/L. The ratio of this value and PNEC is 0.14, which is slightly more than 0.1. The production and import quantity of this substance is less than 1,000 t and not tending to increase on an annual basis. Furthermore, the value of 3,200 μg/L for chronic toxicity value to the algae formed the basis of the PNEC value and this is by no means an indication of high toxicity; 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)			
Green algae	Chronic	NOEC growth inhibition	100	32	Freshwater	<0.025	<0.0008	○	○
					Seawater	0.043	0.001		

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5. Conclusions

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