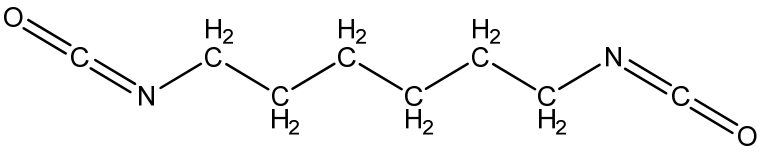


13	CAS No.: 822-06-0	Substance: Hexamethylene diisocyanate
<p>Chemical Substances Control Law Reference No.: 2-2863  PRTR Law Cabinet Order No.: 1-391  Molecular Formula: C<sub>8</sub>H<sub>12</sub>N<sub>2</sub>O<sub>2</sub>      Structural Formula:  Molecular Weight: 168.19</p> 		
<p><b>1. General information</b></p> <p>The aqueous solubility and partition coefficient (1-octanol/water) (log K<sub>ow</sub>) of this substance were not calculated using a model because the substance hydrolyzes. The vapor pressure is 5.3×10<sup>-3</sup> mmHg (0.7 Pa) (20°C). Biodegradability (aerobic degradation) is judged to be good. Its half-life for hydrolysis is 5 min (20°C; initial concentration, 200 mg/L) and 10 min. (20°C; initial concentration, 2 mg/L).</p> <p>This substance is designated as a Priority Assessment Chemical Substance and 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). Its main use is as a curing agent in the manufacture of polyurethane resin. The production and import quantity in fiscal 2013 was 36,761 t. The production and import category under the PRTR Law is more than 100 t.</p> <hr/> <p><b>2. Exposure assessment</b></p> <p>Total release to the environment in fiscal 2013 under the PRTR Law was approximately 0.52 t, and all releases were reported. All reported releases were assumed to be to the atmosphere. In addition, approximately 15 t was transferred to waste materials and 0.0003 t was transferred to sewage. The industry type with large reported releases was the chemical industry. The largest release among releases to the environment including unreported ones was to the atmosphere. A multi-media distribution prediction was not carried out because the required physicochemical properties could not be obtained.</p> <p>The maximum expected concentration of exposure to humans via inhalation, based on general environmental atmospheric data, was around 0.00018 µg/m<sup>3</sup>. The mean annual value for the atmospheric concentration in fiscal 2013 was calculated by using a plume-puff model on the basis of releases to the atmosphere reported according to the PRTR Law; this model predicted a maximum level of 0.10 µg/m<sup>3</sup>. The maximum expected oral exposure to humans could not be obtained. The likelihood of exposure to this substance by intake from an environmental medium is considered nonexistent for normal activities when taking into consideration its high hydrolyzability, PRTR data, etc.</p> <p>The predicted environmental concentration (PEC), which indicates exposure to aquatic organisms, could not be set because water quality data could not be obtained. Taking into consideration the high hydrolyzability of this substance and PRTR data, etc., the likelihood of exposure to aqueous organisms for this substance from water is considered nonexistent for normal activities.</p> <hr/> <p><b>3. Initial assessment of health risk</b></p> <p>This substance is irritating to the eyes, skin and respiratory tract. Exposure to the substance far above the acceptable concentration may cause respiratory sensitization. Inhalation exposure to this substance causes burning sensation, coughs, labored breathing, shortness of breath and sore throat. Contact with skin causes redness, skin burns and blisters, and contact with the eyes causes redness, pain and swelling of the eyelids.</p> <p>As sufficient information on the carcinogenicity of the substance was not available, the initial assessment was</p>		

conducted on the basis of information on its non-carcinogenic effects.

The 'non-toxic level\*' of the substance for oral exposure could not be identified.

The NOAEL of 0.005 ppm for inhalation exposure (based on degeneration of the olfactory epithelium), determined from medium-term and long-term toxicity tests in rats, was adjusted for exposure conditions. The obtained value of 0.00089 ppm (0.0061 mg/m<sup>3</sup>) 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, owing to lack of identified 'non-toxic level\*' and exposure levels, the health risk could not be assessed. Nonetheless, considering that the total amount of the substance released to the environment was 0.517 t; that all of it was emitted to ambient air, and that the substance undergoes rapid hydrolysis in water, collection of further information would not 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 0.00018 µg/m<sup>3</sup>, approximately. The MOE (Margin of Exposure) would be 3,400, when calculated from the predicted maximum exposure concentration and the 'non-toxic level\*' of 0.0061 mg/m<sup>3</sup>, 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 to ambient air was estimated to be 0.10 µg/m<sup>3</sup> on the basis of the data reported in FY 2013 under the PRTR Law. The MOE would be 6, when calculated from this value and the 'non-toxic level\*'. Therefore, collection of information on inhalation exposure 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*' — mg/kg/day	—	—	Drinking water	— µg/kg/day	MOE	—	×	(○)
				Groundwater	— µg/kg/day	MOE	—	×	
Inhalation	'Non-toxic level*' 0.0061 mg/m <sup>3</sup>	Rat	Degeneration of the olfactory epithelium	Ambient air	0.00018 µg/m <sup>3</sup>	MOE	3,400	○	(▲)
				Indoor air	— µg/m <sup>3</sup>	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.

#### 4. Initial assessment of ecological risk

This substance is used as a curing agent for polyurethane resin. Total release to the environment reported under the PRTR law was approximately 0.52 t, with all being released to the atmosphere. The possibility of detecting releases of this substance to the atmosphere in public water bodies is considered to be nonexistent, given its high hydrolyzability (half-life of 5–10 min) and concentration in typical atmospheric environments.

Release of this substance to the environment from the quantity transferred to waste materials (i.e., approximately 15 t shipped from factories that handle the substance) is unclear. However, the likelihood of exposure to this substance by intake from an aqueous medium is considered nonexistent for normal activities when taking into consideration the high hydrolyzability of this substance (half-life of 5–10 min).

In addition, the toxicity value for this substance obtained from toxicity test findings for aqueous organisms is thought to indicate the toxicity of its hydrolysis products, and not reflect the actual toxicity of the substance.

Accordingly, an initial assessment of ecological risk to aqueous organisms for this substance was not conducted.

A separate evaluation of the need for an initial assessment of the ecological risk of this substance's hydrolysis products is considered necessary. Furthermore, among the hydrolysis products of this substance, an initial assessment of ecological risk was conducted for hexamethyl diamine (alternative name: 1,6-hexane diamine, CAS No.: 124-09-4) in the fourth revision. This indicated that "risk cannot be judged" because a predicted environmental concentration (PEC) could not be set (the PNEC of 42 µg/L obtained from the NOEC for reproductive inhibition in the crustacean *Daphnia magna* was adopted).

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**5. Conclusions**

	Conclusions		Judgment
Health risk	Oral exposure	Although risk to human health could not be confirmed, collection of further information would not be required.	(○)
	Inhalation exposure	Further information collection would be required for risk characterization.	(▲)
Ecological risk	Initial assessment of ecological risk to aqueous organisms for this substance was not carried out. Another evaluation of the need for an initial assessment of ecological risk of substance's hydrolysis products considered necessary.		(-)

[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.