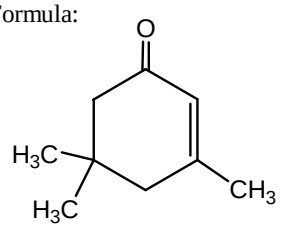
2	CAS No.：78-59-1	Substance: Isophorone

Chemical Substances Control Law Reference No.: 3-2381 and 3-2389

PRTR Law Cabinet Order No.:

Structural Formula:



Molecular Formula: $C_9H_{14}O$

Molecular Weight: 138.21

1. General information

The aqueous solubility of this substance is 1.2 x 10^4 (20°C, 25°C) - 1.45 x 10^4 (25°C) mg/L and the partition coefficient (1-octanol/water) (log Kow) is 1.67. The vapor pressure is 0.3 mmHg (= 40 Pa) (20°C). This substance is determinated to be persistent, also to be non or not highly bioaccumulative. In addition, this substance does not have hydrolyzable groups.

The substance is mainly used for special paints, painting ink, solvents for resins and polymers, chemical intermediates, and major solvents for specific herbicides. The domestic production from FY 1996 to FY 2005 is estimated to be 4,500 tons/yr.

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2. Exposure assessment

As isophorone is not 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), release and transfer quantities could not be obtained. When predictions of distribution ratios by medium were made using the Mackay-Type Level III Fugacity Model, in the event of equal release to the atmosphere, water, and soil, the distribution ratio was highest for soil and water.

No predicted maximum exposure concentration for inhalation exposure to human beings could be established because data for both ambient air and indoor air could not be obtained. The highest estimated oral exposure was calculated to be approximately 0.0013 μg/kg/day based on previous data regarding freshwater bodies. The risk of exposure to this substance through food in environmental media is considered to be low.

The previous predicted environmental concentration (PEC), which indicated exposure to aquatic organisms, was estimated to be approximately 0.032 and 0.028 μg/L for freshwater and seawater bodies, respectively.

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3. Initial assessment of health risk

The substance is irritating to the eyes and the respiratory tract, and may have effects on central nervous system. Contact with eyes may cause redness, pain and blurred vision. The inhalation or ingestion may result in burning sensation, sore throat, cough, dizziness, headache, nausea and shortness of breath. Additionally, by ingestion, it may cause abdominal pain.

There was insufficient information regarding the carcinogenicity of the substance. For this reason, an initial assessment of the substance was conducted based on information of non-carcinogenic effects.

A no observed adverse effect level (NOAEL) of 150 mg/kg/day (no effect even at the highest dose) was obtained for oral exposure from the medium- and long-term toxicity testing for dogs. The NOAEL was divided by 10, because of the experimental period being short, and a value of 15 mg/kg/day was derived as the 'Non-toxic level*'.

A lowest-observed-adverse-effect-level (LOAEL) for the inhalation exposure of 209 mg/m^3 (depression of body weight gain, decrease in liver weight, etc.) was obtained from the medium- and long-term toxicity testing for rats. The

LOAEL was adjusted to 37 mg/m^3 taking into account the exposure situations. As this was a LOAEL, it was divided by 10, and because of the short experimental period, the value was further divided by 10, and a value of 0.37 mg/m^3 was derived as the 'Non-toxic level*'.

With regard to oral exposure, in case of intakes of freshwater in the public water bodies, the predicted maximum exposure was approximately 0.0013 μg/kg/day. The margin of exposure (MOE) of 1,200,000 was derived from the 'Non-toxic level*' of 15 mg/kg/day divided by the predicted maximum dose, and divided by 10, because the 'Non-toxic level*' was established by means of animal testing. As the exposure to this substance through food intakes was estimated minor, even when the exposure through freshwater in the public water bodies and food are combined, it would not greatly affect the MOE values. Accordingly, further action for assessment of its health risk from oral exposure to this substance would not be required at present.

Concerning inhalation exposure, because the exposure concentrations have not been estimated, its health risk can not be identified. The half-life of the substance in the atmosphere was estimated 2.7-27 hrs, and the substance released into the atmosphere was estimated to distribute mostly into the media other than the atmosphere. However, the substance is listed as a potential hazardous air pollutant, and has relatively high production volume. The discharge of the substance has not been surveyed. Accordingly, it would be required to collect information on inhalation exposure to this substance in the ambient air for its health risk assessment.

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*' 15 mg/kg/day	Dogs	no effect even at the highest dose	Drinking water	— μg/kg/day		MOE	—	×	○
				Freshwater	0.0013 μg/kg/day		MOE	1,200,000	○	
Inhalation	'Non-toxic level*' 0.37 mg/m^3	Rats	depression of body weight gain , decrease in liver weight, etc.	Ambient air	— 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 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, reliable information of a 72-hour median effective concentration (EC_{50}) growth inhibition value 234,000 μg/L was found for the algae *Pseudokirchneriella subcapitata*, a 48-hour EC_{50} immobilization value 224,000 μg/L was found for the crustacea *Daphnia magna* (water flea), and a 96-hour median lethal concentration (LC_{50}) value of 140,000 μg/L was found for the fish *Cyprinodon variegatus* (Cyprinodontidae). Accordingly, an assessment factor of 100 was used, and a predicted no effect concentration (PNEC) of 1,400 μg/L was obtained based on the acute toxicity values. With regard to chronic toxicity, reliable information of a 72-hour no observed effect concentration (NOEC) growth inhibition value of 43,000 μg/L was found for the algae *P. subcapitata*, a 21-day NOEC reproduction value exceeding 100,000 μg/L was found for the crustacea *D. magna*, and a 32-day NOEC growth inhibition value of 9,880 μg/L was found for the fish *Pimephales promelas* (fathead minnow). Accordingly, an assessment factor of 10 was used, and a PNEC value of 990 μg/L was obtained based on the chronic toxicity values. As the PNEC for the substance, a value of 990 μg/L obtained from the chronic toxicity for the fish was used.

The PEC/PNEC ratio was 0.00003 for both freshwater and seawater bodies. 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)		
Fish (fathead minnow)	Chronic	NOEC growth inhibition	10	990	Freshwater	0.032	0.00003	○
					Seawater	0.028	0.00003	

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5. Conclusions

	Conclusions		Judgment
Health risk	Oral exposure	No need for further work.	○
	Inhalation exposure	Risk assessment for the ambient air is not feasible, but collection of information is required.	(▲)
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.