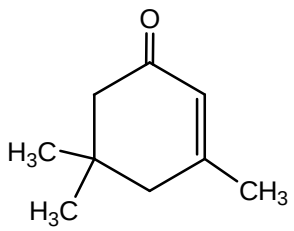
2	CAS No.: 78-59-1	Substance: Isophorone

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

PRTR Law Cabinet Order No.:

Molecular Formula: $C_9H_{14}O$ Structural formula:

Molecular Weight: 138.21



1. General information

The aqueous solubility of this substance is 1.45×10^4 mg/L (25°C), the partition coefficient (1-octanol/water) (log K_{ow}) is 1.67, and the vapor pressure is 0.3 mmHg (=40 Pa) (20°C). Biodegradability (aerobic degradation) is not good, and bioaccumulation is thought to be nonexistent or low. Furthermore, The substance does not have any hydrolyzable groups.

The main uses are as a solvent for specialty coatings, printing inks, resins and polymers; as an important solvent for chemical intermediates and specific herbicides; and as a raw material for isophorone diamine and isophorone diisocyanate. The production quantity in 2005 was 4,500 t (estimate), and the production (shipments) and import quantity in fiscal 2007 was 1,000 to <10,000 t/y.

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2. Exposure assessment

Because this substance 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. Predictions of distribution by medium using a Mackay-type level III fugacity model indicated that if equal quantities were released to the atmosphere, water bodies, and soil, the proportions distributed to soil and water bodies would be greater.

The predicted maximum exposure to humans via inhalation, based on general environmental atmospheric data, was less than around 0.031 μg/m^3.

Data for setting the predicted maximum oral exposure to humans could not be obtained. Further, albeit past data, public freshwater body data indicated an exposure of around 0.0013 μg/kg/day. In addition, oral exposure based on the isophorone concentration in purchased food and ingestion quantity by food group was 0.028 μg/kg/day. Summing this oral exposure with exposure calculated from public freshwater bodies data gives 0.029 μg/kg/day. Further, one cannot rule out the possibility that this substance detected in purchased food exists as a natural component of plant ingredients. Data exists based on public freshwater body measurements made more than 10 years ago, but taking into consideration trends in production and import quantities for this substance, the probability of marked increases in concentration is considered to be low. The risk of exposure to this substance by intake from an environmental medium via food is considered slight based on estimates of oral exposure using estimated concentrations in fish species.

Data for setting the predicted environmental concentration (PEC), which indicates exposure to aquatic organisms, could not be obtained. Further, albeit past data, a PEC of around 0.032 μg/L was reported for public freshwater bodies and around 0.028 μg/L for seawater. Data exists based on public freshwater body measurements made more than 10 years ago, but the probability of marked increases is considered to be low.

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3. Initial assessment of health risk

This substance is irritable to the eyes and respiratory tract and may affect the central nervous system. Contact with the substance can cause redness and pain in the eyes and blurred vision. Symptoms of poisoning via the inhalation route include burning sensation, sore throat, cough, dizziness, headache, nausea and shortness of breath, while those via the oral route include abdominal pain as well.

As sufficient information was not available on the carcinogenicity of the substance, an initial assessment was conducted on the basis of information on its non-carcinogenic effects.

With regard to oral exposure to the substance, a NOAEL of 150 mg/kg/day (no effect observed even at the highest dose) obtained from mid-term and long-term toxicity tests in dogs was divided by 10 due to the short test periods. 15 mg/kg/day derived was deemed as a plausible value for the lowest dose of the substance and was identified as its 'non-toxic level*'. As for inhalation exposure, a LOAEL of 209 mg/m^3 (for suppressed body weight increase, reduced liver weight, etc.) obtained from mid-term and long-term toxicity tests in rats was divided by 10 due to short test periods, and was further divided by 10 as is always the case with a LOAEL. 0.37 mg/m^3 derived was deemed as a plausible value for the lowest concentration dose of the substance and was identified as its 'non-toxic level*'.

As for oral exposure, the absence of information available on exposure concentrations did not allow for a health risk assessment. For reference, however, it was reported in 1995 that intakes of freshwater from public water bodies would result in oral exposure to the substance of up to approximately 0.0013 μg/kg/day when calculated from its concentrations in river water. The MOE would be 1,200,000 when calculated from the 'non-toxic level*' of 15 mg/kg/day and divided by 10 due to the need to convert the 'non-toxic level*' obtained from the animal experiments to a human equivalent dose. As historical production trends were not indicative of considerable changes in concentrations in the environment since 1955, remarkable changes in the MOE would not be likely. The exposure from food intakes would be 0.028 μg/kg/day when calculated from the concentrations in food. When calculated from the exposure from intakes of freshwater, the total exposure would be 0.029 μg/kg/day and a MOE of 52,000 would be derived. Examination of measurements of concentrations in fish indicated the exposure through food intakes from the environment would be minor. When intakes from freshwater were assumed, remarkable changes in the MOE would not be likely. Collection of information, therefore, would not be required to assess health risk from oral exposure to this substance.

With regard to inhalation exposure to the substance, the predicted maximum concentration in the ambient air was less than 0.031μg/m^3. The MOE would be greater than 12,000 when calculated from the 'non-toxic level*' of 0.37 mg/m^3 and the predicted maximum exposure concentration and divided by 10 due to the need to convert the 'non-toxic level*' obtained from the animal experiments to a human equivalent dose. Therefore, no further action would be required at the moment to assess health risk from inhalation exposure to this substance in the ambient air.

Information of toxicity				Exposure assessment		Result of risk Exposure 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 Groundwater	— —	μg/kg/day μg/kg/day	MOE MOE	— —	× ×	(○)
Inhalation	'Non-toxic level * ' 0.37 mg/m^3	Rats	Suppressed body weight increase, reduced liver weight, etc.	Ambient air Indoor air	< 0.031 —	μg/m^3 μg/m^3	MOE MOE	> 1,200 —	○ ×	○ ×

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, the following reliable data were obtained: a 72-h EC_{50} of 234,000 µg/L for growth inhibition in the green algae *Pseudokirchneriella subcapitata*, a 48-h EC_{50} of 224,000 µg/L for swimming inhibition in the crustacean *Daphnia magna*, and a 96-h LC_{50} of 140,000 µg/L for the fish species *Cyprinodon variegatus* (sheepshead minnow). Accordingly, based on these acute toxicity values and an assessment coefficient of 100, a predicted no effect concentration (PNEC) of 1,400 µg/L was obtained.

With regard to chronic toxicity, the following reliable data were obtained: a 72-h NOEC of 43,000 µg/L for growth inhibition in the green algae *P. subcapitata*, a 21-d NOEC of more than 100,000 µg/L for reproductive inhibition in the crustacean *D. magna*, and a 32-d NOEC of 9,880 µg/L for growth inhibition in the fish species *Pimephales promelas* (fathead minnow). Accordingly, based on these chronic toxicity values and an assessment coefficient of 10, a predicted no effect concentration (PNEC) of 990 µg/L was obtained. The value of 990 µg/L obtained from the chronic toxicity to the fish species was used as the PNEC for this substance.

Risk could not be judged because data for setting the predicted environmental concentration (PEC), which indicates exposure to aquatic organisms, could not be obtained. However, albeit past data, concentrations of around 0.032 µg/L for public freshwater bodies and around 0.028 µg/L for seawater have been reported, and calculations of the ratio of public freshwater body concentration to the PNEC gives 0.00003 for both freshwater bodies and seawater. While public freshwater bodies concentrations for this substance have not been obtained in recent years, the likelihood of concentrations having increased markedly is considered low based on production quantity and import quantity trends. Accordingly, it is thought there is little need to collect further data regarding this substance.

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	End point			Water body	Predicted environmental concentration PEC (µg/L)			
Fish species fathead minnow	Chronic	NOEC Growth inhibition	10	990	Freshwater	–	–	×	○
					Seawater	–	–		

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5. Conclusions

	Conclusions		Judgment
Health risk	Oral exposure	Though a risk characterization cannot be determined, there would be little necessity of collecting information.	(○)
	Inhalation exposure	No need for further work.	○
Ecological risk	Minimal need to collect data.		○

［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.