1	CAS No. 78-84-2	Substance: Isobutyraldehyde

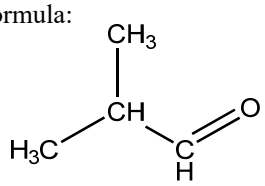
Chemical Substances Control Law Reference No.: 2-494 (Alkanal (C = 4–19))

PRTR Law Cabinet Order No.:

Molecular Formula: C_4H_8O

Molecular Weight: 72.11

Structural formula:



1.General information

The aqueous solubility of this substance is 1.00×10^5 mg/1,000g (20°C), the partition coefficient (1-octanol/water) (log K_{ow}) is 0.398 (pH unknown), and the vapor pressure is 2.30×10^4 Pa at (25°C). The biodegradability (aerobic degradation) is characterized by a BOD degradation rate of 81%, and biodegradability is judged to be good. Further, this substance is believed to not hydrolyze under ambient environmental conditions because it does not possess any hydrolyzable groups.

The main usages of this substance are as a raw material for neopentylglycol and a raw material for organic synthesis. This substance is a designated food additive. This substance occurs naturally in fruits and vegetables as an aromatic component. It is also widely present in alcoholic beverages (brandy, whiskey, etc.) and processed foods such as bread. The production and import quantity in fiscal 2020 was 32,510 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 22 t and all releases were notified. The major destination of notified releases was the atmosphere. In addition, approximately 0.26 t was transferred to waste materials. The major source of notified releases to the atmosphere and public water bodies was the chemical industry. 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 95.1%. Where the largest quantities were estimated to have been released to public water bodies, the predicted proportion distributed to water bodies would be 94.4%.

The maximum expected concentration of exposure to humans via inhalation, based on ambient atmospheric data, was around less than 2.2 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 2.8 μg/m^3.

Data for potable water, groundwater, public freshwater bodies, food, and soil to assess oral exposure could not be obtained. However, the concentration of this substance in public freshwater bodies is believed to be low given there were 0 kg of notified releases to public freshwater bodies in fiscal 2021 under the PRTR Law. The exposure to this substance by intake from an environmental medium via food is considered slight, given the low bioaccumulation of the substance expected on the basis of its physicochemical properties.

Exposure to aquatic organisms based on water quality data could not be estimated. Further, no releases to public freshwater bodies were notified in fiscal 2021 under the PRTR Law and as such, public freshwater body concentrations originating from discharging plants are believed to be low. However, notified releases to seawater were 1,900 kg.

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3. Initial assessment of health risk

This substance irritates the eyes. The substance at very high concentrations irritates the upper respiratory tract as well. Inhalation of this substance will cause sore throat, cough, burning sensation, headache, dizziness, nausea, and vomiting. Ingestion will cause abdominal cramps and aspiration risk in addition to the same symptoms as inhalation. Contact with the

skin will cause redness. Contact with the eyes 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 60 mg/kg/day for oral exposure (based on hyperplasia of squamous epithelium in limiting ridge of forestomach/glandular stomach), determined from toxicity tests in rats, was divided by a factor of 10 to account for extrapolation to chronic exposure. The calculated value of 6 mg/kg/day was deemed the lowest reliable dose and was identified as the 'non-toxic level' of the substance for oral exposure. The LOAEL of 500 ppm for inhalation exposure (based on squamous metaplasia in the nasal cavity), determined from toxicity tests in rats, was adjusted according to exposure conditions to obtain 89.3 ppm and subsequently divided by a factor of 10 to account for uncertainty in using a LOAEL. The calculated value of 8.9 ppm (26 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. Since the release of this substance to public freshwater bodies was reported to be 0 kg in FY 2021 under the PRTR Law, the concentrations in public freshwater bodies derived from the discharging operators would not be high. In addition, exposure to the substance in environmental media via food is presumed to be limited, despite the lack of exposure level via food. 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 2.2 μg/m^3. The MOE (Margin of Exposure) would exceed 1,200 which is calculated from the predicted maximum exposure concentration and the 'non-toxic level' of 26 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 2.8 μg/m^3, based on the releases to air reported in FY 2021 under the PRTR Law. The MOE for reference would be 930 which is calculated from the estimated maximum concentration (annual mean) in ambient air and the 'non-toxic level' of 26 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*'	6 mg/kg/day	Rats	Hyperplasia of squamous epithelium in limiting ridge of forestomach/glandular stomach	Drinking water	- μg/kg/day	MOE	-	○
					Groundwater	- μg/kg/day	MOE	-	
Inhalation	'Non-toxic level*'	26 mg/m^3	Rats	Squamous metaplasia in the nasal cavity	Ambient air	<2.2 μg/m^3	MOE	>1,200	○
					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 83,700 μg/L for growth inhibition in the green alga *Desmodesmus subspicatus*, a 48-h EC_{50} of 277,000 μg/L for swimming inhibition in the crustacean *Daphnia magna*, and a 96-h LC_{50} of 23,000 μg/L for the fish *Pimephales promelas* (fathead minnow). Accordingly, based on this

acute toxicity value and an assessment factor of 100, a predicted no effect concentration (PNEC) of 230 μg/L was obtained.

Reliable data for chronic toxicity could not be obtained. Accordingly, the value of 230 μg/L obtained from the acute toxicity to the fish 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.

Further, no releases to public freshwater bodies were notified in fiscal 2021 under the PRTR Law and as such, public freshwater body concentrations originating from discharging plants are believed to be low. However, notified releases to seawater were 1,900 kg and as such, concentrations in the vicinity of discharge sources may be high. Accordingly, based on a comprehensive review of the above findings, efforts to collect data are considered necessary. Efforts are required to understand the environmental data for the substance including past PRTR data trends.

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)		
Fish *Pimephales promelas*	Acute	LC_{50} Mortality	100	230	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	Requiring information collection.		▲

［Risk judgments］ ○: No need for further work ▲: Requiring information collection
■: Candidates for further work ×: Impossibility of risk characterization