3	CAS No: 4170-30-3	Substance: Crotonaldehyde

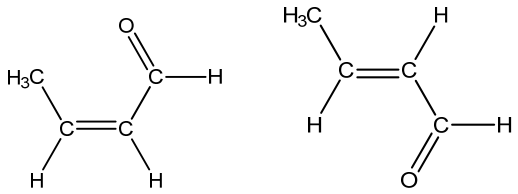
Chemical Substances Control Law Reference No.: 2-524

PRTR Law Cabinet Order: 1-375

Molecular Formula: C_4H_6O

Molecular Weight: 70.09

Structural Formula:



cis-isomer *trans*-isomer

1. General information

The aqueous solubility of this substance is 1.81×10^5 mg/L (20°C), the partition coefficient (1-octanol/water) (log K_{ow}) is 0.60 (calculated value), and the vapor pressure is 36.9 mmHg (= 4.92×10^3 Pa) (25°C, *trans*-isomer). Biodegradability (aerobic degradation) is judged to be good. The substance does not have any hydrolyzable groups.

This substance is designated as 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). The main uses of this substance are as a raw material for butanol, crotonic acid, sorbic acid, and various other chemicals, and as a pharmaceutical ingredient. The production and import quantity was not disclosed in fiscal 2011 or 2012 because the number of reporting businesses was not more than two, but was 2,000 t in fiscal 2010. The production and import category under the PRTR Law is more than 100 t.

---

2. Exposure assessment

Total release to the environment in fiscal 2012 under the PRTR Law was approximately 0.48 t, and all releases were reported. The major destination of reported releases was public water bodies. The sole source of reported releases 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 public water bodies in particular, the predicted proportion distributed to water bodies was 99.8%. In regions where the largest estimated releases were to the atmosphere, the predicted proportion distributed to water bodies was 52.7%, while that distributed to the atmosphere was 45.4%.

The maximum expected concentration of exposure to humans via inhalation could not be obtained for ambient air but was 18 μg/m^3 for indoor air. However, past ambient air concentration indicated around 0.23 μg/m^3. The mean annual value for atmospheric concentration in fiscal 2012 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 0.00095 μg/m^3. The maximum expected oral exposure was estimated to be around 0.0084 μg/kg/day on the basis of calculations from data for public freshwater bodies. However, the maximum expected exposure calculated from data for public freshwater bodies and past data for food was around less than 4 μg/kg/day, although reports of values higher than this for oral exposure via food also exist. This substance is formed in vivo, and is formed in many foods by enzymatic and non-biological (self oxidation, heat treatment) transformations. When releases to public freshwater bodies in fiscal 2012 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 0.03 μg/L. Using this estimated concentration for rivers to calculate oral exposure gave 0.0012 μg/kg/day.

The predicted environmental concentration (PEC), which indicates exposure to aquatic organisms, was around

0.21 μg/L for public freshwater bodies and around 0.19 μg/L for seawater. When releases to public freshwater bodies in fiscal 2012 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 0.03 μg/L.

---

3. Initial assessment of health risk

This substance is lachrymatory and its vapors cause severe irritation to the skin and respiratory tract. This substance is corrosive to the eyes. When ingested, abdominal pain, burning sensation, diarrhea, nausea and vomiting may occur, while burning sensation, coughing, breathing difficulty, shortness of breath and sore throat may occur when inhaled. Pulmonary edema or death may be caused if exposed to high concentrations of its vapors. Contact of the substance with the skin may cause redness, burning sensation and pain, while contact with the eyes may cause redness, pain and severe eye burns.

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

With regard to the oral exposure to the substance, the LOAEL of 2 mg/kg/day (based on mutated liver cell nests), obtained for mid-term and long-term toxicity tests on rats, was divided by a factor of 10 for the use as a LOAEL. The outcome of 0.2 mg/kg/day was considered to be the reliable lowest dose of the substance and was identified as its 'non-toxic level*'. As for the inhalation exposure, the LOAEL of 8.6 mg/m^3 (based on nasal damage), obtained for mid-term and long-term toxicity tests on rats, was adjusted according to the test conditions to obtain an exposition of 1.5 mg/m^3 and was divided by a factor of 10, for the use as a LOAEL. The outcome of 0.15 mg/m^3 was considered to be the reliable lowest dose of the substance and was identified as its 'non-toxic level*'.

Concerning the oral exposure, the predicted maximum exposure concentration in freshwater and public water bodies was approximately 0.0084 μg/kg/day. The MOE (Margin of Exposure) of 2,400 was derived from the substance's 'non-toxic level*' of 0.2 mg/kg/day and the predicted maximum exposure concentration, after the division by a factor of 10 to convert animal data to human data. In addition, the MOE of 17,000 was derived from the maximum exposure level of 0.0012 μg/kg/day; derived itself from the concentrations in effluents from high discharging plants, predicted according to the reported data in FY 2012 under the PRTR Law. Besides, the MOE of more than 5 was derived from the oral exposure level of below 4 μg/kg/day approximately, calculated from the maximum exposure level of 0.23 μg/m^3 according to the data on exposure through food intake (reported in 1998). Therefore, collection of further information would be required to assess the health risk for the oral exposure to this substance.

Regarding the inhalation exposure to the substance, the absence of information on exposure concentrations in ambient air did not allow the health risk assessment. The MOE of 65 was derived from the predicted maximum exposure level of 0.23 μg/m^3 (reported in 1998) and, the division by a factor of 10 to convert animal data to human data. In addition, the MOE of 16,000 was derived from the maximum concentration in ambient air in the high discharging plants area, calculated according to the reported emissions in FY 2012 under the PRTR Law. However, health risks are likely to be underestimated with the atmospheric concentrations predicted from the reported data, as the substance is generated by combustion. Meanwhile, the MOE of 1 was derived from the maximum exposure concentration in indoor air of 18 μg/m^3. Therefore, collection of further information is required to assess the health risk for inhalation exposure to this substance in ambient air, and the substance is considered to be a candidate for further assessment concerning inhalation exposure in indoor air.

Toxicity				Exposure assessment		Result of risk assessment			Judgment
Exposure Path	Risk assessment benchmark	Animal	Criteria for diagnoses (endpoint)	Exposure medium	Predicted maximum exposure dose and concentration				
Oral	'Non-toxic level* 0.2 mg/kg/day	Rat	Mutated liver cell nests	Drinking water	— μg/kg/day	MOE	—	×	(▲)
				Freshwater	0.0084 μg/kg/day	MOE	2,400	○	
Inhalation	'Non-toxic level*' 0.15 mg/m^3	Rat	Nasal cavity damage	Ambient air	— μg/m^3	MOE	—	×	(▲)
				Indoor air	18 μg/m^3	MOE	1	■	■

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

With regard to acute toxicity, the following reliable data were obtained: a 72-h EC_{50} of 597 μg/L for growth inhibition in the green alga *Pseudokirchneriella subcapitata*, a 48-h EC_{50} of 995 μg/L for swimming inhibition in the crustacean *Daphnia magna*, and a 96-h LC_{50} of 72 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 0.72 μg/L was obtained.

With regard to chronic toxicity, the following reliable data were obtained: a 72-h NOEC of 42 μg/L for growth inhibition in the green alga *P. subcapitata*, a 21-d NOEC of 20 μg/L for reproductive inhibition in the crustacean *D. magna*, and a 41-d NOEC of 24.7 μg/L for growth inhibition in the fish species *O. latipes* (medaka). Accordingly, based on these chronic toxicity values and an assessment factor of 10, a PNEC of 2 μg/L was obtained.

The value of 0.72 μg/L obtained from the acute toxicity to the fish species was used as the PNEC for this substance.

The PEC/PNEC ratio is 0.3 for both freshwater bodies and for seawater; accordingly, efforts to collect data on this substance are needed. Regarding this substance, efforts are needed to measure environmental concentrations by taking information on release sources into consideration.

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)			
Fish (medaka)	Acute	LC_{50} mortality	100	0.72	Freshwater	0.21	0.3	▲	▲
					Seawater	0.19	0.3		

---

5. Conclusions

	Conclusions		Judgment
Health risk	Oral exposure	Further information collection would be required for risk characterization.	(▲)
	Inhalation exposure (Ambient air)	Further information collection would be required for risk characterization.	(▲)
	Inhalation exposure (Indoor air)	The substance is considered to be a candidate 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

（○）: 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.