1	CAS No.: 21145-77-7, 1506-02-1	Substance: 6-Acetyl-1,1,2,4,4,7-hexamethyltetralin

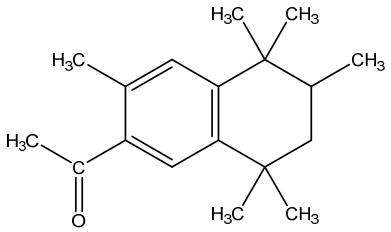
Chemical Substances Control Law Reference No.: 4-1179

PRTR Law Cabinet Order No.:

Molecular Formula: $C_{18}H_{26}O$

Molecular Weight: 258.40

Structural Formula:



1.General information

The aqueous solubility of this substance is 1.22 mg/L (pH=7) (25°C), the partition coefficient (1-octanol/water) (log K_{ow}) is 5.4, and the vapor pressure is 5.12×10^{-4} mmHg (= 0.0682 Pa)(25°C). The biodegradability (aerobic degradation) is characterized by a BOD degradation rate of 0%. Further, the substance does not possess any hydrolyzable groups.

The main use of this substance is as a compound perfume for perfumery and cosmetics; it is also particularly effective as a softener for soaps, detergents and textiles. The production and import quantity in fiscal 2016 was less than 1,000 t.

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2. Exposure assessment

Because this substance is not classified as a Class 1 Designated Chemical Substance under the PRTR Law, release and transfer quantities could not be obtained. Predictions of proportions distributed to individual media by use of a Mackay-type level III fugacity model indicate that if equal quantities were released to the atmosphere, water bodies, and soil, the proportion distributed to soil would be largest.

The maximum expected concentration of exposure to humans via inhalation could not be determined because ambient atmospheric and indoor air quality data could not be obtained.

Data for potable water, ground water, food and soil to assess oral exposure could not be obtained. Thereupon, assuming intake solely from public freshwater bodies, the maximum expected oral exposure was predicted to be around 0.0092 μg/kg/day. Further, data related to food could not be obtained. Therefore, maximum concentrations for fish species (0.00075 μg/g) and shellfish species (0.0021 μg/g) were used along with average daily intakes (63.4 g/capita/day for fish species and 2.2 g/capita/day for shellfish species) to calculate a reference value for exposure by intake from an environmental medium via food of 0.0010 μg/kg/day. Adding this to the oral exposure calculated from freshwater data gives around 0.010 μg/kg/day

The predicted environmental concentration (PEC), which indicates exposure to aquatic organisms, was reported to be around 0.23 μg/L for public freshwater bodies and around 0.012 μg/L for seawater.

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3. Initial assessment of health risk

No information was available on acute symptoms in humans. Signs of sluggishness and piloerection were observed in rats within a few hours after oral administration of this substance. Following these symptoms, hematuria, encrustations around eyes and nostrils and signs of emaciation were observed.

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

The NOAEL of 1.5 mg/kg/day for oral exposure (based on anemia, prolonged prothrombin time, etc.), determined from medium-term toxicity tests in rats, was divided by a factor of 10 to account for extrapolation from sub-chronic to chronic exposure. The calculated value of 0.15 mg/kg/day was deemed to be the lowest reliable dose and was identified as the 'non-toxic level*' of the substance for oral exposure. The 'non-toxic level*' for inhalation exposure could not be identified.

With regard to oral exposure, assuming the substance is absorbed via public freshwater bodies, the predicted maximum exposure level would be 0.0092 μg/kg/day, approximately. The MOE (Margin of Exposure) would be 1,600, when calculated from the predicted maximum exposure level and the 'non-toxic level*'of 0.15 mg/kg/day, and subsequently divided by a factor of 10 to account for extrapolation from animals to humans. Alternatively, assuming the substance is absorbed via public freshwater bodies and food including fish and shellfish, the exposure level would be 0.010 μg/kg/day, and the MOE calculated from this level would be 1,500. Therefore, no further work would be required at present to assess the health risk of this substance via oral exposure.

With regard to inhalation exposure, owing to the lack of identified 'non-toxic level*' and exposure concentrations, the health risk could not be assessed. Average concentrations of this substance in ambient air reported by Western studies did not exceed 0.003 μg/m^3 and maximum concentrations in indoor air ranged from 0.077 to 0.11μg/m^3. Assuming that 100% of the inhaled substance is absorbed, the 'non-toxic level*' for inhalation exposure, derived from the conversion of the 'non-toxic level*' for oral exposure, would be 0.50 mg/m^3. The MOE would be 450, when calculated from a provisional exposure concentration of 0.11 μg/m^3 and the converted 'non-toxic level*' for inhalation exposure, and subsequently divided by a factor of 10 to account for extrapolation from animals to humans. Therefore, collection of further information would not 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*'	0.15	mg/kg/day	Rats	Anemia, prolonged prothrombin time, etc.	Drinking water	-	μg/kg/day	MOE	-	○
						Public freshwater bodies	0.0092	μg/kg/day	MOE	1,600	
Inhalation	'Non-toxic level*'	-	mg/m^3	-	-	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 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} exceeding 835 μg/L for growth inhibition in the green alga *Pseudokirchneriella subcapitata*, a 48-h LC_{50} of 710 μg/L for the crustacean *Acartia tonsa*, a 96-h LC_{50} of 1,490 μg/L for the fish species *Lepomis macrochirus* (blue gill), and a 120-h EC_{50} of 397 μg/L for swimming inhibition in the oligochaete *Lumbriculus variegatus*. Accordingly, based on these acute toxicity values and an assessment factor of 100, a predicted no effect concentration (PNEC) of 7.1 μg/L was obtained.

With regard to chronic toxicity, the following reliable data were obtained: a 72-d NOEC of 381 μg/L for growth inhibition in the green alga *P. subcapitata*, a 21-d NOEC of 196 μg/L for reproductive inhibition in the crustacean *Daphnia magna*, a 36-d NOEC of 35 μg/L for growth inhibition in the fish species *Pimephales promelas* (fathead minnow), and a 34-d NOEC of 35 μg/L for developmental anomaly in the fish species *Danio rerio* (zebrafish).

Accordingly, based on these chronic toxicity values and an assessment factor of 10, a PNEC of 3.5 μg/L was obtained.

The value of 3.5 μg/L obtained from the chronic toxicity to the fish species was used as the PNEC for this substance.

The PEC/PNEC ratio is 0.07 for freshwater bodies and 0.003 for seawater; accordingly, further work is considered unnecessary at this time.

Hazard assessment (basis for PNEC)			Assessment coefficient	Predicted no effect concentration PNEC (μg/L)	Exposure assessment		PEC/ PNEC ratio	Assessment result
Species	Acute/ chronic	Endpoint			Water body	Predicted environmental concentration PEC (μg/L)		
Fish *Pimephales promelas* ／*Danio rerio*	Chronic	NOEC Growth inhibition／ NOEC Development inhibition	10	3.5	Freshwater	0.23	0.07	○
					Seawater	0.012	0.003	

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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	No need for further work.		○

［Risk judgments］ ○: No need for further work ▲: Requiring information collection

■: Candidates for further work ×: Impossibility of risk characterization

（▲）: Further efforts to collect data required based on comprehensive review of existing relevant data

（■）: Candidate for further work based on comprehensive review of existing data