1 CAS No.: 103-90-2

Substance: Acetaminophen

Chemical Substances Control Law Reference No.: 3-678 (Hydroxyacetylaminobenzene)

PRTR Law Cabinet Order No.:

Molecular Formula: C₈H₉NO₂

Molecular Weight: 151.16





1.General information

The aqueous solubility of this substance is 1.3×10^4 mg/1,000 g (25°C), the partition coefficient (1-octanol/water) (log K_{ow}) is 0.46 (pH unknown), and the vapor pressure is 2.59×10^{-4} Pa (25°C) (estimated by MPBVPWIN). Its biodegradability (aerobic degradation) is 57% based on oxygen consumption. Further, this substance is believed to not hydrolyze under ambient environmental conditions because it does not possess any hydrolyzable groups.

The main usage of this substance is as a raw material for pharmaceuticals, where it is used in aminophenol-based antipyretics for treating indications such as headache, earache, symptomatic neuralgia, lower back pain, myalgia, tendon pain, bruising, sprains, and reducing fever and pain in acute upper respiratory tract infections. The substance is also used for as an anti-inflammatory drug for veterinary use (antipyretic for bacterial pneumonia in pigs, with certain drugs not suitable for lactating pigs). The production volume in Japan in 2016 was 700 t. The production volume as pharmaceuticals in 2021 was 442.3 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 0.079 t, of which 0.036 t or 46% were notified releases. All notified releases were to public water bodies. Further, and 0.032 t was transferred to sewage, and approximately 8.5 t was transferred to waste. The pharmaceuticals industry was the major notifier of releases. The major destination of releases, including both notified and unnotified releases, was public water bodies.

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 would be 98.2%.

In terms of water quality, data for setting the predicted environmental concentration (PEC) as a conservative value for assessment could not be obtained for this substance. However, a maximum concentration of about $0.025 \ \mu g/L$ was reported for freshwater bodies and a maximum concentration of about $0.054 \ \mu g/L$ was reported for seawater, albeit for public water bodies covering limited areas. River concentrations using discharge volumes into public freshwater bodies based on the PRTR Law in fiscal 2021 were not estimated because there were no environmental reference points, nor auxiliary points, located downstream of discharging business establishments. Transfer to sewage was reported in fiscal 2021. Accordingly, when releases to public freshwater bodies estimated from this reported transfer to sewage 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 0.050 $\mu g/L$.

3.Initial assessment of ecological risk

With regard to acute toxicity, the following reliable data were obtained: a 72-h EC₅₀ of 317,400 μ g/L for growth inhibition in the green alga *Raphidocelis subcapitata*, a 48-h EC₅₀ of 3,500 μ g/L for swimming inhibition in the crustacean *Daphnia magna*, a 96-h LC₅₀ exceeding 100,000 μ g/L for the fish *Oryzias latipes* (medaka) and *Danio rerio* (zebrafish), and a 48-h

 LC_{50} of 319,000 µg/L for the rotifer *Plationus patulus*. Accordingly, based on the acute toxicity value of the crustacean and an assessment factor of 100, a predicted no effect concentration (PNEC) of 35 µg/L was obtained.

With regard to chronic toxicity, the following reliable data were obtained: a 7-d NOEC of 22,500 μ g/L for growth inhibition in the duckweed *Lemna minor*, an 8-d NOEC of 210 μ g/L for reproductive inhibition in the crustacean *Ceriodaphnia dubia*, a 90-d NOEC of 9,500 μ g/L for embryo to post-hatch survival and growth inhibition in *O. latipes* (medaka) fry, and a 6-d NOEC of 5,000 μ g/L for reproductive inhibition on the rotifer *Plationus patulus*. Accordingly, based on these chronic toxicity values and an assessment factor of 10, a PNEC of 21 μ g/L was obtained.

The value of 21 μ g/L obtained from the chronic toxicity to the crustacean 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.

Albeit a survey of limited areas of public water bodies, there are reports of a maximum concentration of about 0.025 μ g/L for freshwater bodies and a maximum of about 0.054 μ g/L for seawater. The ratios of these values to the PNEC are 0.001 for freshwater bodies and 0.003 for seawater. In addition, when releases to public freshwater bodies estimated from the reported transfer to sewage in fiscal 2021 under 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 0.050 μ g/L, and the ratio of this value to the PNEC was 0.002.

Accordingly, <u>based on a comprehensive review of the above findings</u>, further work is considered unnecessary at this <u>time</u>.

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Hazard assessment (basis for PNEC)				Predicted no effect	Exposure assessment		NEC/	
Species	Acute/ chronic	Endpoint	coefficient	concentration PNEC (µg/L)	Water body	Predicted environmental concentration PEC (µg/L)	PEC/ PNEC ratio	judgment
Crustacean Ceriodaphnia dubia	Chronic	NOEC Reproductive inhibition	10	21	Freshwater	—	_	0
	Chilome				Seawater	_		
4. Conclusions								
		Conclusions						Judgment
Ecological 1	risk No ne	No need for further work.						

 $[Risk judgments] \bigcirc$: No need for further work

▲: Requiring information collection

■: Candidates for further work

×: Impossibility of risk characterization