2	CAS No.: 303-49-1	Substance: Clomipramine

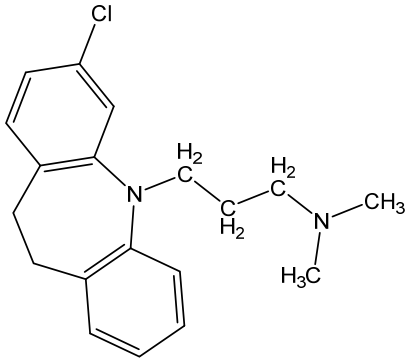
Chemical Substances Control Law Reference No.: 9-372

PRTR Law Cabinet Order No.:

Molecular Formula: $C_{19}H_{23}ClN_2$

Molecular Weight: 314.85

Structural formula:



1. General information

The aqueous solubility of this substance is 0.29 mg/L (25°C) (calculated value), the partition coefficient (1-octanol/water) (log K_{ow}) is 5.19, and the vapor pressure is 2.0×10^{-5} Pa (25°C) (calculated value). Biodegradability data could not be obtained. Further, degradability screening tests found a residual ratio of 91% after 7 days (initial concentration: 2×10^{-3} μg/mL, pH: 7) for hydrolyzability.

The main uses of clomipramine hydrochloride are as a drug for human use (tricyclic antidepressants, treatment of enuresis, treatment of cataplexy) and veterinary drug (nervous system drug). In addition, the sales value of "other nervous system drugs" under the veterinary drug category was JPY450,845,000 in 2020.

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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 predicted environmental concentration (PEC), which indicates exposure to aquatic organisms, was around 0.0015 μg/L for public freshwater bodies, and less than 0.00002 μg/L for seawater.

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3. Initial assessment of ecological risk

With regard to acute toxicity (for clomipramine), the following reliable data were obtained: a 72-h IC_{50} of 3.0 μg/L for growth inhibition in the diatom *Skeletonema marinoi*, a 48-h EC_{50} of 2,460 μg/L for swimming inhibition in the crustacean *Daphnia magna*, and a 36-h EC_{50} of 140 μg/L for embryonic development inhibition in the Pacific oyster *Crassostrea gigas*. While a value that could be used with fish species could not be obtained, the acute toxicity value for carp appeared to exceed the chronic toxicity value. On this account, an assessment value of 100 normally applied when reliable data for three groups of organisms (algae, crustaceans, fish species) was used and a predicted no effect concentration (PNEC) of 0.030 μg/L was obtained.

With regard to chronic toxicity (for clomipramine), the following reliable data were obtained: a 72-h IC_{10} of 1.8 μg/L for the diatom *S. marinoi* and a 30-d NOEC of 9 μg/L for embryonic growth inhibition of the fish *Cyprinus carpio* (carp). Accordingly, based on these chronic toxicity values and an assessment factor of 100, a PNEC of 0.018 μg/L was obtained.

The value of 0.018 μg/L obtained from the chronic toxicity to the diatom was used as the PNEC for this substance.

The PEC/PNEC ratio was 0.08 for freshwater bodies and 0.001 for seawater. Further work to assess the ecological risk this substance is considered unnecessary at this time. While production and import quantities and releases to the environment for this substance have not been obtained, there is little need to collect further data as this time. Accordingly, based on a comprehensive review of the above findings, no further work is required.

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)		
Diatom	Chronic	NOEC Growth inhibition	100	0.018	Freshwater	0.0015	0.018	○
					Seawater	<0.000020	<0.001	

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4. Conclusions

	Conclusions	Judgment
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