2	CAS No. 23593-75-1	Substance: Clotrimazole

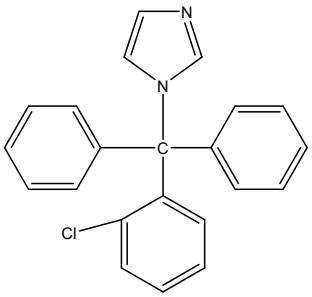
Chemical Substances Control Law Reference No.:

PRTR Law Cabinet Order No.:

Molecular Formula: $C_{22}H_{17}ClN_2$

Molecular Weight: 344.84

Structural formula:



1.General information

The aqueous solubility of this substance is 0.02984 mg/L (25°C) (estimated value) the partition coefficient (1-octanol/water) (log Kow) is 6.26 (estimated value), and the vapor pressure is 2.83×10^{-7} Pa (25°C) (estimated value). Biodegradability data could not be obtained. Furthermore for hydrolysis, degradability screening tests indicated a residual rate of 98% after 7 days in the dark (preparation concentration: 4.0 ng/mL, pH = 7).

This substance is used as a pharmaceutical and veterinary drug. In human medicine, it is used as an antifungal agent. In veterinary medicine, it is used as an antibiotic formulation in combination with agents such as gentamicin sulfate, betamethasone valerate, and mometasone furoate. Based on production volume and imported volume data from the Statistics of Production by Pharmaceutical Industry published by Japan's Ministry of Health, Labour and Welfare, the production volume as a pharmaceutical in fiscal 2021 was 0.035 t, and the imported volume was 0.109 t. The sales volume as a veterinary pharmaceutical in fiscal 2022 was 0.049 t.

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 0.00048 μg/L for public freshwater bodies. Data capable of withstanding assessment of PEC in seawater areas could not be obtained.

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3. Initial assessment of ecological risk

With regard to acute toxicity, the following reliable data were obtained: a 72-h EC_{50} of 260 μg/L for growth inhibition in the green alga *Raphidocelis subcapitata*, and a 48-h LC_{50} exceeding 1000 μg/L in the African clawed frog (embryo) *Xenopus tropicalis*. Accordingly, based on these acute toxicity values and an assessment factor of 1000, a predicted no effect concentration (PNEC) of 0.26 μg/L was obtained.

With regard to chronic toxicity, the following reliable data were obtained: a 72-h NOEC of 0.348 μg/L for growth inhibition in the green alga *R. subcapitata*, and a 21-d NOEC of more than 3.75 μg/L for reproductive inhibition in the crustacean *Daphnia magna*. Accordingly, based on this chronic toxicity value and an assessment factor of 100, a predicted no effect concentration (PNEC) of 0.0034 μg/L was obtained.

The value of 0.0034 μg/L obtained from the chronic toxicity to the alga was used as the PNEC for this substance.

The PEC/PNEC ratio is 0.14 for freshwater bodies. Based on a comprehensive review of the above findings efforts to

collect further data are considered necessary.

Although there is concern that this substance may exhibit high chronic toxicity to algae and other organisms, reliable toxicity data is insufficient.

Accordingly, based on a comprehensive review of the above findings, efforts to collect further data are considered necessary. Toxicity data should be augmented focusing on biota where such information is lacking, while variations in production volumes, import volumes and sales quantities should be monitored.

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)		
Green algae	Chronic	NOEC Growth inhibition	100	0.0034	Freshwater	0.00048	0.14	▲
					Seawater	—	—	

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4. Conclusions

	Conclusions	Judgment
Ecological risk	Requiring information collection.	▲

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

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