4	CAS No. 116836-41-0	Substance: 14-(*R*)-Hydroxy clarithromycin

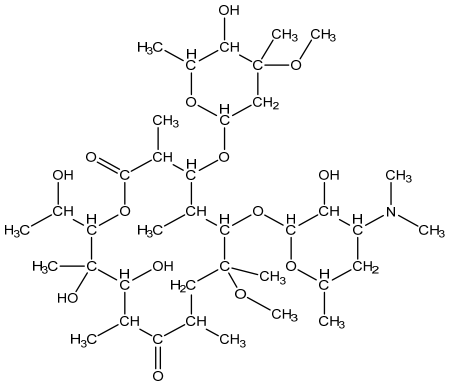
Chemical Substances Control Law Reference No.:

PRTR Law Cabinet Order No.:

Molecular Formula: $C_{38}H_{69}NO_{14}$

Molecular Weight: 763.95

Structural formula:



1.General information

The aqueous solubility of this substance is 5.314 mg/L (25°C) (estimated value), the partition coefficient (1-octanol/water) (log Kow) is 1.64 (estimated value), and the vapor pressure is 4.86×10^{-26} Pa (25°C) (estimated value). Biodegradability data could not be obtained. Furthermore for hydrolysis, degradability screening tests indicated a residual rate of 99% after 7 days in the dark (preparation concentration: 0.10 ng/mL, pH = 7).

No information on the uses of this substance has been obtained. This substance is considered a metabolite of clarithromycin, a 14-membered ring macrolide antibiotic. The production volume of clarithromycin in fiscal 2022 was 48.9 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 0.23 μg/L for public freshwater bodies, and around 0.049 μg/L for seawater. Further, albeit based on a survey for a limited area, a maximum value in seawater of around 0.39 μg/L was obtained was reported.

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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 27.2 μg/L for growth inhibition in the cyanobacterium *Anabaena flos-aquae*, and a 48-h EC_{50} exceeding 2000 μg/L for swimming inhibition the crustacean *Daphnia magna*. Accordingly, based on these acute toxicity values and an assessment factor of 1000, a predicted no effect concentration (PNEC) of 0.027 μg/L was obtained.

With regard to chronic toxicity, the following reliable data were obtained: a 72-h NOEC of 2.7 μg/L for growth inhibition in the cyanobacterium *A. flos-aquae*, and a 21-d NOEC of more than 850 μg/L for the crustacean *D. magna*. Accordingly, based on this chronic toxicity value and an assessment factor of 100, a predicted no effect concentration (PNEC) of 0.027 μg/L was obtained.

The value of 0.027 μg/L obtained from the acute and chronic toxicities to the cyanobacterium was used as the PNEC for this substance.

The PEC/PNEC ratio is 9 for freshwater bodies and 2 for seawater. Accordingly, this substance is considered a candidate

for detailed assessment of ecological risk.

In the 2019 water quality survey, seven freshwater sites and one seawater site exceeded the PNEC. Furthermore, in a survey of public freshwater bodies spanning a limited area, a maximum value of approximately 0.39 μg/L was reported, with a ratio of this value to the PNEC of 14.

Accordingly, this substance is considered a candidate for detailed assessment of ecological risk. When conducting detailed assessments, a review based on augmented toxicity data centered on fish species is necessary. For fish, in addition to 96-hour exposure time testing for acute toxicity, insufficient chronic toxicity test data should also be increased.

In addition, this substance is the clarithromycin metabolite that was judged to be a candidate for detailed assessment of ecological risk in 16th Results of the initial environmental risk assessment of chemicals. This substance and clarithromycin are known to coexist in the environment, and evaluation of simultaneous exposure to clarithromycin and similar substances is considered necessary.

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)		
Cyanobacterium	Acute/ chronic	EC_{50} Growth inhibition / NOEC Growth inhibition	1,000 / 100	0.027	Freshwater	0.23	9	■
					Seawater	0.049	2	

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4. Conclusions

	Conclusions	Judgment
Ecological risk	Candidates for further work.	■

［Risk judgments］ ○: No need for further work ▲: Requiring information collection
■: Candidates for further work ×: Impossibility of risk characterization