3	CAS No. 1069-66-5 (Sodium valproate): 99-66-1 (Valproic acid)	Substance: Sodium valproate

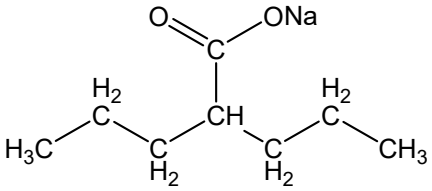
Chemical Substances Control Law Reference No.: 2-611 (Aliphatic monocarboxylic acid (C6−28) light metal salt (Na, K, Li, Ba, Mg, Ca))

PRTR Law Cabinet Order No.:

Molecular Formula: $C_8H_{15}NaO_2$

Molecular Weight: 166.19

Structural formula:



1.General information

The aqueous solubility of this substance is 2.5×10^6 mg/L, the partition coefficient (1-octanol/water) (log Kow) is 0.26 (pH = 7.4, buffered solution), and the vapor pressure is 1.15×10^{-6} Pa (25°C) (estimated value). Biodegradability data could not be obtained. Furthermore for hydrolysis, degradability screening tests indicated a residual rate (as valproic acid) of 94% after 7 days in the dark (preparation concentration: 0.030 ng/mL, pH = 7).

This substance is used as a pharmaceutical agent for the treatment of epilepsy, mania/manic states, and migraines. The production and import quantity in fiscal 2022 was 182.2 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) of valproic acid converted to sodium valproate, which indicates exposure to aquatic organisms, was around 0.028 μg/L for public freshwater bodies and around 0.015 μg/L for seawater.

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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} exceeding 86,800 μg/L for growth inhibition in the green alga *Raphidocelis subcapitata*, a 48-h EC_{50} exceeding 86,800 μg/L for swimming inhibition in the crustacean *Daphnia magna*, and a 96-h EC_{50} of 30,500 μg/L for teratogenesis in the embryos of the African clawed frog *Xenopus laevis*. Accordingly, based on this acute toxicity value and an assessment factor of 1000, a predicted no effect concentration (PNEC) for sodium valproate exceeding 100 μg/L was obtained.

With regard to chronic toxicity, the following reliable data were obtained: a 72-h NOEC of 86,800 μg/L for growth inhibition in the green alga *R. subcapitata*, and a 6-d NOEC of 876 μg/L for reproductive inhibition in the crustacean *Ceriodaphnia dubia*. Accordingly, based on this chronic toxicity value and an assessment factor of 100, a predicted no effect concentration (PNEC) for sodium valproate of 10 μg/L was obtained.

The value of 10 μg/L for sodium valproate obtained from the chronic toxicity to the crustacean species was used as the PNEC for this substance.

The PEC/PNEC ratio was 0.003 for freshwater bodies and 0.002 for seawater. Accordingly, further work to evaluate ecological risk is considered unnecessary at this time.

Although there are few surveys of water quality data, this substance's PEC/PNEC ratio is sufficiently low. Accordingly, based on a comprehensive review of the above findings, 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	Comprehensive judgment
Species	Acute/ chronic	Endpoint			Water body	Predicted environmental concentration PEC (μg/L)		
Crustacean *Ceriodaphnia dubia*	Chronic	NOEC Reproductive inhibition	100	10	Freshwater	0.028	0.003	○
					Seawater	0.015	0.002	

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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