1	CAS No: 504-29-0	Substance: 2-Aminopyridine

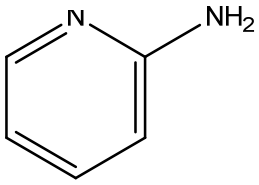
Chemical Substances Control Law Reference No.: 5-724 (2- or 4- Aminopyridine), 9-106

PRTR Law Cabinet Order No.:

Molecular Formula: $C_5H_6N_2$

Molecular Weight: 94.11

Structural Formula:



1. General information

The aqueous solubility of this substance is $>1 \times 10^6$ mg/L (20°C), the partition coefficient (1-octanol/water) (log K_{ow}) is 0.48, and the vapor pressure is 0.8 mmHg (=106.7 Pa) (25°C) (extrapolated value). The biodegradability (aerobic degradation) is characterized by a BOD degradation rate of 0%, and bioaccumulation is thought to be nonexistent or low.

The main uses of this substance is as intermediates for pharmaceuticals (antihistamines) and agricultural chemicals. The production and import quantity in fiscal 2015 was not disclosed because the number of reporting businesses was less than two.

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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 using a Mackay-type level III fugacity model indicated that if equal quantities were released to the atmosphere, water bodies, and soil, the proportion distributed to soil would be largest.

The maximum expected concentration of exposure to humans via inhalation, based on ambient atmospheric data, was around less than 0.000051 μg/m^3. The predicted maximum oral exposure calculated from public freshwater body data was around 0.00019 μg/kg/day. The risk of exposure to this substance by intake from an environmental medium via food is considered slight, given its low bioaccumulation.

The predicted environmental concentration (PEC), which indicates exposure to aquatic organisms, is around 0.0048 μg/L for public freshwater bodies and 0.012 μg/L for seawater.

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3. Initial assessment of health risk

The substance is irritating to the eyes and skin, and may cause effects on the central nervous system. It causes convulsions, dizziness, headache, nausea, shortness of breath and weakness, if inhaled or ingested. These symptoms may also be caused by absorption via skin. Contact with the eyes or skin causes redness.

As sufficient information on the carcinogenicity of the substance was not available, the initial assessment was conducted on the basis of information on its non-carcinogenic effects.

With regard to oral exposure, owing to the lack of the identified ‘non-toxic level*’, the health risk could not be assessed. Assuming that 100% of the ingested substance is absorbed, the ‘non-toxic level*’ for oral exposure, derived from the conversion of 0.45 mg/m^3 for inhalation exposure, would be 0.14 mg/kg/day. 0.45 mg/m^3 was obtained by adjusting TLV-TWA of 1.9 mg/m^3, which was determined on the basis of evidence on human health effects, for continuous exposure. Assuming the substance is absorbed via public freshwater bodies, the predicted maximum exposure level would be 0.00019 μg/kg/day, approximately. The MOE （Margin of Exposure） would be 740,000, when

calculated from the predicted maximum exposure level and the converted ‘non-toxic level*’ for oral exposure. Alternatively, the ‘non-toxic level*’, derived from the LOAEL for oral exposure to the isomer of the substance (4-aminopyridine) of 0.07 mg/kg/day (based on perioral paresthesias, dizziness, light-headedness, etc.) divided by a factor of 10, would be 0.007 mg/kg/day. The MOE would be 37,000, when calculated from the predicted maximum exposure level and isomer’s LOAEL-derived ‘non-toxic level*’. Since exposure to the substance in environmental media via food is presumed to be limited, including this concentration value in the calculation would not change the MOE significantly. Therefore, collection of further information would not be required to assess the health risk of this substance via oral exposure.

With regard to inhalation exposure, owing to the lack of the identified ‘non-toxic level*, the health risk could not be assessed. The MOE would be over 8,800,000, when calculated from the predicted maximum exposure concentration of less than 0.000051 μg/m^3, approximately and the value of 0.45 mg/m^3 obtained by adjusting TLV-TWA for continuous exposure. Alternatively, assuming that 100% of the ingested substance is absorbed, the ‘non-toxic level*’ for inhalation exposure, derived from the conversion of isomer’s LOAEL-derived ‘non-toxic level*’ for oral exposure of 0.007 mg/kg/day, would be 0.023 mg/m^3. The MOE would be over 450,000, when calculated from the predicted maximum exposure concentration and the converted ‘non-toxic level*’ for inhalation exposure. Therefore, collection of further information would not be required to assess the health risk of this substance via inhalation in ambient air.

Toxicity				Exposure assessment		Result of risk assessment			Judgment
Exposure Path	Criteria for risk assessment	Animal	Criteria for diagnoses (endpoint)	Exposure medium	Predicted maximum exposure dose and concentration				
Oral	‘Non-toxic level*’ — mg/kg/day	—	—	Drinking water	— μg/kg/day	MOE	—	×	(○)
				Public Freshwater bodies	0.00019 μg/kg/day	MOE	—	×	
Inhalation	‘Non-toxic level*’ — mg/m^3	—	—	Ambient air	≤0.000051 μg/m^3	MOE	—	×	(○)
				Indoor air	— μg/m^3	MOE	—	×	×

Non-toxic level *

- When a LOAEL is available, it is divided by 10 to obtain a NOAEL-equivalent level.
- When an adverse effect level for the short-term exposure is available, it is divided by 10 to obtain a level equivalent to an adverse effect level for the long-term exposure.

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4. Initial assessment of ecological risk

With regard to acute toxicity, the following reliable data were obtained: a 72-h EC_{50} of 12,000 μg/L for growth inhibition in the green algae *Pseudokirchneriella subcapitata*, a 48-h EC_{50} of 35,000 μg/L for immobilization in the crustacean *Daphnia magna*, a 96-h LC_{50} of 11,000 μg/L for the fish species *Oryzias latipes* (medaka), and a 60-h IGC_{50} of 370,440 μg/L for reproductive inhibition in the ciliate *Tetrahymena thermophila*. Accordingly, based on these acute toxicity values and an assessment factor of 100, a predicted no effect concentration (PNEC) of 110 μg/L was obtained.

With regard to chronic toxicity, the following reliable data were obtained: a 72-h NOEC of 2,100 μg/L for growth inhibition in the green algae *P. subcapitata*. Accordingly, based on these chronic toxicity values and an assessment factor of 100, a PNEC of 21 μg/L was obtained.

The value of 21 μg/L obtained from the chronic toxicity to the green algae species was used as the PNEC for this substance.

The PEC/PNEC ratio is 0.0002 for freshwater bodies and 0.0006 for seawater; accordingly, 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	Judgment based on PEC/PNEC ratio	Assessment result
Species	Acute/ chronic	Endpoint			Water body	Predicted environmental concentration PEC (μg/L)			
Green algae	Chronic	NOEC Growth inhibition	100	21	Freshwater	0.0048	0.0002	○	○
					Seawater	0.012	0.0006		

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5. Conclusions

	Conclusions		Judgment
Health risk	Oral exposure	Although risk to human health could not be confirmed, collection of further information would not be required.	(○)
	Inhalation exposure	Although risk to human health could not be confirmed, collection of further information would not be required.	(○)
Ecological risk	No need of further work at present.		○

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

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

（○）: Although risk to human health could not be confirmed, collection of further information would not be required.

（▲）: Further information collection would be required for risk characterization.