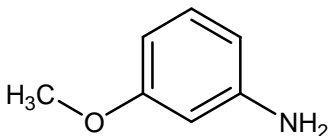| 13	CAS No.: 536-90-3	Substance: 3-Methoxyaniline

Chemical Substances Control Law Reference No.: 3-682 (Aminophenol alkyl [C=1–2] ether)

PRTR Law Cabinet Order No.:

Molecular Formula: C_7H_9NO Structural formula:

Molecular Weight: 123.15

1. General information

The aqueous solubility of this substance is 2.05×10^4 mg/L (25°C), the partition coefficient (1-octanol/water) (log K_{ow}) is 1.01, and the vapor pressure is 0.0750 mmHg (=10.0 Pa) (25°C). The biodegradability (aerobic degradation) is characterized by a BOD degradation rate of 0%, and bioaccumulation is thought to be nonexistent or low. Its half-life for hydrolysis is more than 1 year (pH=4.0, 7.0, 9.0).

This substance is designated as a Type II Monitoring Chemical Substance under the Law Concerning the Examination and Regulation of Manufacture, etc. of Chemical Substances. The main use is as a dyestuff intermediate. The production (shipments) and import quantity in fiscal 1998 for aminophenol alkyl (C=1–2) ethers was 100 to <1,000t/y.

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2. Exposure assessment

Because this substance is not a Class 1 Designated Chemical Substance under the Law Concerning Reporting, etc. of Releases to the Environment of Specific Chemical Substances and Promoting Improvements in Their Management (PRTR Law), release and transfer quantities could not be obtained. Predictions of distribution by medium using a Mackay-type level III fugacity model indicated that if equal quantities were released to the atmosphere, water bodies, and soil, the proportions distributed to soil and water bodies would be greater.

Data for setting the predicted maximum exposure to humans via inhalation could not be obtained. Further, albeit past data, the exposure was less than around 0.5 µg/m^3 based on general environmental atmospheric data.

The predicted maximum oral exposure was estimated to be less than around 0.00064 µg/kg/day based on calculations from data for groundwater. The risk of exposure to this substance by intake from an environmental medium via food is considered slight based on estimates of oral exposure using estimated concentrations in fish species.

The predicted environmental concentration (PEC), which indicates exposure to aquatic organisms, was less than around 0.016 µg/L for public freshwater bodies and seawater.

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3. Initial assessment of health risk

Hematological effects of this substance may produce methemoglobin. Signs and symptoms of poisoning via the inhalation route include blue lips, finger nails and skin, confusion, convulsions, dizziness, headache, nausea and unconsciousness. Similar symptoms can be caused by oral exposure to the substance.

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

With regard to oral exposure to the substance, a LOAEL of 2.4 mg/kg/day (for splenic extramedullary hematopoiesis in spleen observed) obtained from mid-term and long-term toxicity tests in rats was divided by 10 due to the short test periods and was further divided by 10 as is always the case with a LOAEL. 0.024 mg/kg/day derived was deemed as a plausible value for the lowest dose of the substance and was identified as its 'non-toxic level*'. As for inhalation

exposure, its 'non-toxic level*' could not be identified.

As to oral exposure to the substance, when intakes of groundwater were assumed, the predicted maximum exposure was approximately less than 0.00064 µg/kg/day. The MOE was 3,800 when calculated from the 'non-toxic level*' of 0.024 mg/kg/day and the predicted maximum exposure divided by 10 due to the need to convert the 'non-toxic level*' from the animal experiments to a human equivalent dose. As the exposure to this substance through food intakes was estimated to be minor, even when the exposure through groundwater and food were combined, the MOE would not be greatly affected. Therefore, no further action to assess health risk from oral exposure to this substance would be required at present.

With regard to inhalation exposure to the substance, the absence of information available on 'non-toxic levels*' and exposure concentrations did not allow for a health risk assessment. For reference, however, its 'non-toxic level*' for oral exposure, if 100% absorption were assumed, would be equivalent to its 'non-toxic level*' of 0.08 mg/m^3 for inhalation exposure. When combined with the maximum concentration of approximately less than 0.5 µg/m^3 reported in 1990 for the ambient air, the MOE would be greater than 16. As information on historical production and import trends for the substance was not available, changes in concentration in the environment since the last report could not be estimated. Discussion would be required on the necessity of collection of information on historical production and import trends and identification of potential inhalation exposure levels of the substance in the ambient air to assess health risk. Review of detection limits would be among those to be discussed.

Information of toxicity				Exposure assessment		Result of risk Exposure assessment			Judgment
Exposure Path	Criteria for risk assessment	Animal	Criteria for diagnoses (endpoint)	Exposure medium	Predicted maximum exposure quantity and concentration				
Oral	'Non-toxic level *' 0.024 mg/kg/day	Rats	Splenic extramedullary hematopoiesis in spleen	Drinking water	— µg/kg/day	MOE	—	×	○
				Groundwater	< 0.00064 µg/kg/day	MOE	> 3,800	○	
Inhalation	'Non-toxic level *' — mg/m^3	—	—	Ambient air	— 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 level equivalent to NOAEL.
・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 10,000 µg/L for growth inhibition in the green algae *Pseudokirchneriella subcapitata*, a 48-h EC$_{50}$ of 110 µg/L for swimming inhibition in the crustacean *Daphnia magna*, and a 96-h LC$_{50}$ of 161,000 µg/L for the fish species *Oryzias latipes* (medaka). Accordingly, based on these acute toxicity values and an assessment coefficient of 100, a predicted no effect concentration (PNEC) of 1.1 µg/L was obtained. The value of 1.1 µg/L obtained from the acute toxicity to the crustacean was used as the PNEC for this substance because reliable chronic toxicity data could not be obtained.

The PEC/PNEC ratio was less than 0.01 for both freshwater bodies and seawater. Accordingly, further work is thought to be 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	End point			Water body	Predicted environmental concentration PEC (µg/L)			
Crustacean *Daphnia magna*	Acute	EC$_{50}$ swimming inhibition	100	1.1	Freshwater	<0.016	<0.01	○	○
					Seawater	<0.016	<0.01		

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5. Conclusions

		Conclusions	Judgment
Health risk	Oral exposure	No need for further work	○
	Inhalation exposure	Further information collection would be required for risk characterization.	(▲)
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

　　　（○）: Though a risk characterization cannot be determined, there would be little necessity of collecting information.

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