3	CAS No.: 7440-22-4 (Silver)	Substance: Silver and its compounds

Chemical Substances Control Law Reference No.:

PRTR Law Cabinet Order No.:1-82 (Silver and its water-soluble compounds)

Chemical symbol: Ag

Atomic Weight: 107.87

1. General information

Silver nitrate is the main silver compound. The aqueous solubility of silver nitrate is 2.34×10^6 mg/1,000g (25°C), and although it is not readily degradable, bioaccumulation is thought to be low.

Silver and its soluble compounds are classified as Class 1 Designated Chemical Substances under the PRTR Law. The main uses of silver are its uses as a raw material for silver nitrate, as an electrical contact material, and as silver solder. In addition, silver nitrate is used as a photosensitive material and in telecommunications devices. The production and import quantity of silver chloride, silver oxide, silver bromide, or silver iodide in fiscal 2015 was not disclosed because the number of reporting businesses was less than two for any of these compounds. The production and import quantity of silver nitrate in fiscal 2015 was less than 1,000 t. The production and import category under the PRTR Law for silver and its water-soluble compounds was more than 100 t.

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2. Exposure assessment

Total release to the environment in fiscal 2015 under the PRTR Law was approximately 6.6 t, of which 5.0 t or 76% were reported. The majority of reported releases were to the atmosphere and public water bodies. In addition, approximately 4.4 t was transferred to landfill, approximately 0.29 t was transferred to sewage, and approximately 1.1 t was transferred to waste materials. Industry types with large reported releases were the nonferrous metals manufacturing and the chemical industry for the atmosphere and nonferrous metals manufacturing for public water bodies. The largest releases to the environment including unreported releases were to water bodies.

Predicting distribution proportions by individual media was not considered appropriate because the chemical forms of silver in the environment are not fully understood. Accordingly, a prediction of distribution proportions by individual media for silver was not carried out.

The maximum expected concentration of exposure to humans via inhalation, based on ambient atmospheric data, was around 0.0033 μg Ag/m^3. The mean annual value for the atmospheric concentration in fiscal 2015 was calculated by using a plume-puff model on the basis of releases to the atmosphere reported according to the PRTR Law (as silver and its water-soluble compounds); this model predicted a maximum level of 0.017 μg Ag/m^3.

Furthermore, the predicted maximum oral exposure calculated from potable water data was less than around 0.0024 μg Ag/kg/day, while that calculated from public fresh water body data was around 0.0048 μg Ag/kg/day. When releases to public freshwater bodies in fiscal 2015 reported under the PRTR Law (as silver and its water-soluble compounds) were divided by the ordinary water discharge of the national river channel structure database, estimating the concentration in rivers by taking into consideration only dilution gave a maximum value of 2.6 μg Ag/L. Using this estimated concentration for rivers to calculate oral exposure gave 0.10 μg Ag/kg/day. The maximum estimated concentration for rivers (2.6 μg Ag/L) and the maximum value for public freshwater bodies (0.12 μg Ag/L) are values for the same location. In addition, reference values of 0.053 μg Ag/kg/day and 0.058 μg Ag/kg/day were obtained for oral exposures based on food data surveyed for a limited area and soil data combined with potable water and public freshwater body data, respectively.

The predicted environmental concentration (PEC), which indicates exposure to aquatic organisms, was around 0.12 μg Ag/L for public water bodies and around 0.017 μg Ag/L for seawater. Exposure was highly like to be anthropogenic in origin and set based on total silver concentrations.

When releases to public freshwater bodies in fiscal 2015 reported under the PRTR Law (as silver and its soluble compounds) were divided by the ordinary water discharge of the national river channel structure database, estimating the concentration in rivers by taking into consideration only dilution gave a maximum value of 2.6 μg Ag/L. Further, the estimated maximum concentration for rivers (2.6 μg Ag/L) and the maximum value for public freshwater bodies (0.12 μg Ag/L) are values for the same location.

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3. Initial assessment of health risk

No information was available on acute symptoms in humans. Inhalation of high amounts of metallic silver vapors may cause lung damage with pulmonary edema. Silver nitrate is corrosive to the eyes, skin and respiratory tract. It is corrosive on ingestion as well. Inhalation exposure causes sore throat, cough, burning sensation, shortness of breath, labored breathing, cyanosis of lips, fingernails and skin, dizziness, headache, nausea, confusion, convulsions and unconsciousness. Oral exposure causes abdominal pain, burning sensation and shock or collapse in addition to the same symptoms as inhalation. Contact with the skin causes pain, redness, skin burns and blisters. Contact with the eyes causes redness, pain, severe deep burns and loss of vision. The lowest lethal dose in humans is reported to be 0.71mg Ag/kg for intravenous administration of colloidal silver, and 140 mg Ag/kg for intrauterine administration of silver nitrate. The lethal dose for oral exposure is estimated to be 10 g approximately, which is considered attributable to corrosiveness of silver nitrate.

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

The LOAEL for oral exposure of 0.13 mg Ag/kg/day (based on Argyria development), determined from the effects observed in humans, was divided by a factor of 10 to account for extrapolation from sub-chronic to chronic exposure, and by another factor of 10 to account for uncertainty in using a LOAEL. The calculated value of 0.0013 mg Ag/kg/day was deemed to be the lowest reliable dose and was identified as the 'non-toxic level*' of the substances for oral exposure. The 'non-toxic level*' for inhalation exposure could not be identified.

With regard to oral exposure, assuming the substances are absorbed via drinking water, the predicted maximum exposure level would be less than 0.0024 μg Ag/kg/day, approximately. The MOE (Margin of Exposure) would be over 540, when calculated from the predicted maximum exposure level and the 'non-toxic level*'of 0.0013 mg Ag/kg/day. Assuming the substances are absorbed via public freshwater bodies, the predicted maximum exposure level would be 0.0048 μg Ag/kg/day. The MOE would be 270, when calculated from this exposure level. For comparison, the maximum exposure level was calculated to be 0.10 μg Ag/kg/day. This value derives from the estimated concentration in the effluents from the high discharging plants, according to the releases reported in FY 2015 under the PRTR Law. The MOE would be 13, when calculated from this level and the 'non-toxic level*'. For additional comparison, the exposure level was calculated to be 0.053 μg Ag/kg/day by integrating the data on food and soil in a restricted area and those on drinking water, and 0.058 μg Ag/kg/day by integrating the data on food and soil and those on public freshwater bodies. The MOEs would be 25 and 22 respectively, when calculated from these levels. Therefore, collection of further information would be required to assess the health risk of silver and its compounds via oral exposure.

With regard to inhalation exposure, owing to the lack of identified 'non-toxic level*', the health risk could not be assessed. Assuming that 100% of the ingested substances is absorbed, the 'non-toxic level*' for inhalation exposure, derived from the conversion of oral exposure concentration, would be 0.0043 mg Ag/m^3. The predicted maximum exposure concentration in ambient air was 0.0033 μg Ag/m^3, approximately. The MOE would be 1,300, when calculated from the predicted maximum exposure concentration and the converted 'non-toxic level*' for inhalation exposure. In addition, the maximum concentration (annual mean) in ambient air near the operators releasing large amount of the substances was estimated to be 0.017 μg Ag/m^3 based on the releases reported in FY 2015 under the PRTR Law. The

MOE would be 250, when calculated from this concentration. Therefore, collection of further information would not be required to assess the health risk of silver and its compounds 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*'	0.0013 mg Ag/kg/day	Humans	Argyria development	Drinking water	<0.0024	μgAg/kg/day	MOE	>540	○	(▲)
					Public Freshwater bodies	0.0048	μgAg/kg/day	MOE	270	○	
Inhalation	'Non-toxic level*'	—	mgAg/m^3	—	—	Ambient air	0.0033	μgAg/m^3	MOE	—	×	(○)
						Indoor air	—	μgAg/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 96-h EC_{50} of 10.3 μg Ag/L for growth inhibition in the green microalga *Chlorella vulgaris*, a 48-h LC_{50} of 0.18 μg Ag/L for the crustacean *Daphnia magna*, a 96-h LC_{50} of 1.48 μg Ag/L for the fish species *Oncorhynchus mykiss* (rainbow trout), and a 96-h LC_{50} of 3.9 μg Ag/L for the insect species *Maccaffertium modestum* (flatheaded mayfly). Accordingly, based on these acute toxicity values and an assessment factor of 100, a predicted no effect concentration (PNEC) of 0.0018 μg Ag/L was obtained.

With regard to chronic toxicity, the following reliable data were obtained: an 11-d NOEC of 1.9 μg Ag/L for growth inhibition in the alga *Champia parvula*, a 21-d NOEC of 0.1 μg Ag/L for reproductive inhibition in the crustacean *D. magna*, a 60-d NOEC of 0.24 μg Ag/L for growth inhibition in the fish species *Oncorhynchus mykiss* (steelhead trout, sea-run variety), and a 14-d NOEC of 0.31 μg Ag/L for moulting inhibition in the insect species *Isonychia bicolor* (brushlegged mayfly). Accordingly, based on these chronic toxicity values and an assessment factor of 10, a predicted no effect concentration (PNEC) of 0.01 μg Ag/L was obtained.

The value of 0.0018 μg Ag/L obtained from the acute toxicity to the crustacean was used as the PNEC for this substance.

The PEC/PNEC ratio was 67 for freshwater bodies and 9 for seawater. Accordingly, these substances are considered to be candidates for detailed assessment. Further, a water quality survey conducted in fiscal 2015 found that the PNEC was exceeded in 12 out of 15 locations. In this assessment, the total silver concentration was taken as the available aqueous silver concentration. On the other hand, OECD guidance document identify dissolved organic carbon (DOC), sulfide ions, and chloride ions, etc., as substances that can affect the toxicity of silver. When carrying out a detailed assessment, attention needs to be paid to variations in toxicity brought about by water quality conditions and the forms in which silver exists in aqueous media.

Hazard assessment (basis for PNEC)			Assessment coefficient	Predicted no effect concentration PNEC (μg Ag/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 Ag/L)			
Crustacean *Daphnia magna*	Acute	LC_{50} Mortality	100	0.0018	Freshwater	0.12	67	■	■
					Seawater	0.017	9		

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5. Conclusions

	Conclusions		Judgment
Health risk	Oral exposure	Further information collection would be required for risk characterization.	(▲)
	Inhalation exposure	Although risk to human health could not be confirmed, collection of further information would not be required.	(○)
Ecological risk	Candidates for further work.		■

［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.