5	CAS No.: 7440-74-6 (Indium)	Substance: Indium and its compounds

Chemical Substances Control Law Reference No.:

PRTR Law Cabinet Order No.: 1-44 (Indium and its compounds)

Element Symbol: In

Atomic Weight: 114.82

1. General information

Indium and indium (III) oxide are insoluble in water. The trihydrate of indium (III) nitrate is soluble in water. The aqueous solubilities of indium (III) chloride and indium (III) sulfate are 1.951×10^6 mg/1,000 g (22°C) and 1.17×10^5 mg/1,000 g (20°C), respectively. Indium trichloride is determined to be persistent but not highly bioaccumulative.

Indium and its compounds are designated as Class 1 Designated Chemical Substances under the Law Concerning Reporting, etc. of Releases to the Environment of Specific Chemical Substances and Promoting Improvements in Their Management (PRTR Law). The main uses of indium include liquid crystal transparent electrodes, bonding agents, compound semiconductors, phosphors, low melting point alloys, and battery materials. The main uses of indium compounds are: as a raw material of transparent electrode materials for indium (III) chloride; as a raw material of ITO for indium (III) oxide; as an electronic material and InP monocrystal raw material for indium (III) phosphide; and as a raw material to manufacture indium oxide, indium nitrate, and indium sulfate, as well as a battery electrode material for indium (III) hydroxide. The production and import quantity of indium oxide in fiscal 2010 was less than 1,000 t. The production and import category of indium and its compounds under the PRTR Law is more than 100 t.

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2. Exposure assessment

Total release of indium and its compounds to the environment in fiscal 2010 under the PRTR Law was approximately 0.69 t, of which approximately 0.66 t or 96% of overall releases were reported. The major destination of reported releases was public freshwater bodies. In addition, 40 t was transferred to waste materials and 0.003 t was transferred to sewage. Industry types with large reported releases were the non-ferrous metal manufacturing industry for the atmosphere, and the non-ferrous metal manufacturing industry and the chemical industry for public water bodies. The largest release among releases to the environment including those unreported was to water bodies. Predicting the proportions distributed to individual media was not considered appropriate because the chemical forms of indium in the environment are not fully understood. Accordingly, indium proportions distributed to individual media were not predicted.

The maximum expected concentration of exposure to humans via inhalation, based on general environmental atmospheric data, was generally around 0.00035 μg/m^3. The mean annual value for atmospheric concentration in fiscal 2010 was calculated by using a plume-puff model based on reported releases to the atmosphere according to the PRTR Law; this model predicted a maximum level of 0.059 μg/m^3.

The maximum expected oral exposure was estimated to be less than 0.00006 μg/kg/day on the basis of calculations from data for public freshwater bodies. However, a maximum expected oral exposure of around 0.0022 μg/kg/day was calculated from data for public freshwater bodies (filtrate) in a limited survey area. When reported releases to public freshwater bodies in fiscal 2010 according to the PRTR Law were divided by the ordinary water discharge of the national river channel structure database, estimating the concentration in rivers while taking only dilution into consideration gave a maximum value of 7.0 μg/L. Using this estimated concentration for rivers to calculate oral exposure gave 0.28 μg/kg/day.

The predicted environmental concentration (PEC), which indicates exposure to aquatic organisms, is

reportedly less than 0.0015 μg/L for both public freshwater bodies and seawater. However, for a limited survey area, maximum values of around 0.055 μg/L for public freshwater bodies (filtrate) and 0.028 μg/L for seawater (filtrate) have been reported. The maximum river concentration was estimated to be 7.0 μg/L from reported releases to public freshwater bodies under the PRTR Law.

3.Initial assessment of health risk

This substance may cause irritation to eyes and respiratory tract. Inhalation exposure to the substance may cause coughing, shortness of breath and sore throat, while oral exposure may cause nausea and vomiting. Contact of the substance with eyes may cause redness and pain. In addition, indium chloride may cause corrosion to eyes, skin and respiratory tract. Symptoms of poisoning by its inhalation include coughing, sore throat, burning sensation, labored breathing and shortness of breath, possibly leading to pulmonary edema, while those by its ingestion include burning sensation, abdominal pain, nausea, vomiting, and even shock or collapse. Contact of the substance with skin may cause redness, pain, blisters and skin burns, while its contact with eyes may cause redness, pain and severe eye burns.

As for carcinogenic potential of the substance, an initial assessment was conducted solely on the basis of its non-carcinogenic effects. Although its carcinogenic effects on animals had been observed in animal experiments, its carcinogenicity to human could not be identified as oxidative stress was among factors contributing to the development of cancer. A threshold has been reported.

With regard to oral exposure to the substance, a LOAEL of 50 mg/kg/day for indium trichloride (for suppressed weight increase during gestation; 26 mg/kg/day as indium) obtained from its reproductive and developmental toxicity tests on mice was divided by a factor of 10 for the use of a LOAEL. 2.6 mg/kg/day was identified to be the reliable lowest dose of indium as its ‘non-toxic level*’. With regard to inhalation exposure to indium tin oxide, a LOAEL of 0.01 mg/m^3 (for bronchial/pulmonary alveolar hyperplasia in rats; pulmonary alveolar proteiosis in mice, etc.) from its mid-term and long-term toxicity tests on rats and mice was adjusted for their durations to provide 0.0018 mg/ m^3 (0.0013 mg/m^3 as indium) for its intermittent to continuous exposure, and this was divided by a factor of 10 for the use of a LOAEL. 0.00013 mg/m^3 was identified to be the reliable lowest dose of indium as its ‘non-toxic level*’.

As for oral exposure to the substance, its maximum exposure concentration was predicted to be below 0.00006 μg/kg/day, when its intakes through freshwater from public water bodies were assumed. The MOE (Margin of Exposure) would be above 430,000 when calculated from the substance’s ‘non-toxic level*’ of 2.6 mg/kg/day and the predicted maximum exposure level calculated from animal experiments and divided by a factor of 10 to convert animal data to human, and further divided by a factor of 10 to extrapolate animal data to human carcinogenic hazard. In addition, the maximum exposure concentration would be approximately 0.0022 μg/kg/day, when the intakes of freshwater from public water bodies reported for some areas were assumed. The MOE would be 12,000 when calculated from this value as its reference. The maximum exposure concentration of the substance was calculated to be 0.28 μg/kg/day from its releases into public freshwater bodies reported in FY 2010 under the PRTR Law. The MOE would be 93 when calculated from this value as its reference. Also, as levels of exposure to the substance in the environment through food intakes are unknown, their contributions to its oral exposure are also unknown. Therefore, collection of information would be required to assess health risk from its exposure though food intakes.

With regard to inhalation exposure to the substance, the maximum exposure concentration in the ambient air was predicted to be approximately 0.00035 μg/m^3. The MOE would be 4 when calculated from the substance’s ‘non-toxic level*’ of 0.00013 mg/m^3 and the maximum exposure concentration predicted from animal experiments and divided by a factor of 10 to convert animal data to human, and further divided by a factor of 10

to extrapolate animal data to human carcinogenic hazard. The maximum (annual mean) concentration in the ambient air near the operators discharging high concentrations of the substance was calculated to be 0.059 μg/m^3 from its emissions reported in FY 2010 under the PRTR Law. The MOE would be 0.02 when calculated from this value as its reference. Therefore, the substance would be subject to further research to identify health risk from its inhalation in the 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 doseand concentration				
Oral	'Non-toxic level*' 2.6 mg/kg/day	Mouse	Suppressed weight increase during gestation	Drinking water	— μg/kg/day	MOE	—	×	(▲)
				Freshwater	< 0.00006 μg/kg/day	MOE	> 430,000	○	
Inhalation	'Non-toxic level*' 0.00013 mg/m^3	Rat Mouse	Bronchial/pulmonary alveolar hyperplasia in rats; pulmonary alveolar proteiosis in mice, etc.	Ambient air	0.00035 μg/m^3	MOE	4	■	■
				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 48-h EC_{50} of 26,400 μgIn/L for swimming inhibition in the crustacean *Daphnia magna*, a 96-h LC_{50} of 35,300 μgIn/L for the fish species *Oryzias latipes* (medaka), and a 24-h LC_{50} of 24,420 μgIn/L for the euryhaline rotifer *Brachionus plicatilis*. Accordingly, based on these acute toxicity values and an assessment factor of 1000, a predicted no effect concentration (PNEC) of 26 μgIn/L was obtained.

The value of 26 μgIn/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 0.00006 for both freshwater bodies and seawater. However, the maximum river concentration was estimated to be 7.0 μg/L from reported releases under the PRTR Law. There may be locations with concentrations higher than the PEC or the 0.055 μg/L for public freshwater bodies (filtrate) and 0.028 μg/L for public seawater bodies (filtrate) found in an environmental survey of a limited area.

Accordingly, efforts to collect data on this substance are needed, as are measurements, upon taking PRTR data into consideration, of environmental concentrations based on forms that exist in the environment. Furthermore, there is a need to consider the augmentation of toxicity data by taking into account the findings of these environmental concentration measurements.

Hazard assessment (basis for PNEC)			Assessment factor	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)			
Crustacean *Daphnia magna*	Acute	EC_{50} immobilization	1,000	26	Freshwater	<0.0015	<0.00006	○	▲
					Seawater	<0.0015	<0.00006		

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5. Conclusions

	Conclusions		Judgment
Health risk	Oral exposure	Collection of further information would be required.	(▲)
	Inhalation exposure	Candidates for further work	■
Ecological risk	Requiring information collection.		▲

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

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

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hough a risk characterization cannot be determined, there would be little necessity of collecting information.

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