12	CAS No.: 335-67-1 (acid) 3825-26-1 (ammonium salt) 335-95-5 (sodium salt) 2395-00-8 (potassium salt) 335-93-3 (silver salt)	Substance: Perfluorooctanoic Acid and its salts (Perfluorooctanoic Acid: PFOA)

Chemical Substances Control Law Reference No.:

2-2659 (Perfluoroalkyl carboxylic acids [C = 7–13])

2-1182 (Fluoroalkyl [C = 2–10] carboxylic acids)

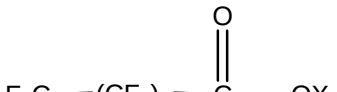
2-1195 (Ammonium perfluorooctanoate)

2-1176 (Fluoroalkyl [C = 5–12] carboxylates [Na, K, Ca])

PRTR Law Cabinet Order No.*: 2-89 (Ammonium Pentadecafluorooctanoate)

Molecular Formula: $C_8F_{15}O_2X$ (X: H, NH_4, etc.) Structural formula:

Molecular Weight: 414.07 (acid)



X=H, NH_4 etc.

*Note: No. in Revised Cabinet Order enacted on October 1, 2009

1. General information

The aqueous solubility of this substance is 9.5×10^3 mg/L (25°C), and the vapor pressure is 0.031 mmHg (=4.2 Pa) (25°C, extrapolated value). Biodegradability (aerobic degradation) is judged to be difficult for acids and ammonium salts, and bioaccumulation is not considered to be high.

PFOA is designated as a Type II Monitoring Chemical Substance under the Law Concerning the Examination and Regulation of Manufacture, etc. of Chemical Substances, while the NH_4 salt is designated as a Type II Monitoring Chemical Substance under the Law Concerning the Examination and Regulation of Manufacture, etc. of Chemical Substances and a Class 2 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). The main uses of PFOA are for export and as intermediates, additives (for resins), and other products (catalysts). Unintentional sources of perfluorooctanoic acid include impurities in perfluorooctanesulfonyl fluoride-based products and byproducts of fluorotelomer-based products. Furthermore, there are reports of fluorotelomer-based products breaking down in the environment to form perfluorocarboxylates such as PFOA. The production and import quantity of NH_4 salts in fiscal 2007 was 363 t, and the production and import category under the PRTR Law was 1 to <100 t. The production (shipments) and import quantity for fluoroalkyl (C＝2–10) carboxylates in fiscal 2007 was 1,000 to <10,000t/y.

---

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 were not attempted because reliable log K_{ow} could not be obtained for this substance.

The predicted maximum exposure to humans via inhalation, based on general environmental atmospheric data, was around 0.0025 μg/m^3.

The predicted maximum oral exposure was estimated to be around 0.0020 μg/kg/day based on calculations from data

for drinking water and food. Furthermore, the predicted maximum oral exposure was estimated to be around 0.0034 μg/kg/day based on calculations from data for food and drinking water for a limited area. Further, oral exposure was calculated for reference based on groundwater and food data. A maximum of 150 μg/L was detected in a well at a factory site and the oral exposure based on this groundwater and food data was 6.0 μg/kg/day, but at a well located a distance of approximately 400 m from the site containing a concentration of 28 μg/L, the oral exposure was 1.1 μg/kg/day.

The predicted environmental concentration (PEC), which indicates exposure to aquatic organisms, was found to be maximum around 0.36 μg/L for public freshwater bodies and around 0.011 μg/L for seawater based on a survey conducted at the national level. However, several environmental studies carried out over limited areas reported higher detected concentrations than around 0.36 μg/L for public freshwater bodies and around 0.011 μg/L for seawater. Among these studies covering limited areas, a 2003–2004 environmental study reported a maximum of 87 μg/L for public freshwater bodies, whereas a 2007 survey of the same river reported markedly lower values and a fiscal 2009 study of the same river reported a maximum value of 3.0 μg/L. In addition, a 2007 study of another river reported a maximum of 31 μg/L but additional studies at the same location have not been conducted since 2007 and the current concentration is unknown. For seawater areas, a 2007 environmental study reported a maximum of 0.57 μg/L in a harbor, while in 2008, a maximum of 0.19 μg/L was reported for coastal areas around the same harbor. Further, business establishments in the vicinity of rivers where concentrations of 3.0 μg/L and 31 μg/L have been obtained and seawater areas where a concentration of 0.57 μg/L has been obtained, have promised measures to completely dispose of these substances, precursor substances that break down and form these substances, and similar substances with carbon numbers higher than these by 2015. In addition, business establishments in the vicinity of rivers where these concentrations were obtained have committed to totally abolish handling of these substances by 2012.

---

3. Initial assessment of health risk

This substance is irritable to the eyes, skin and respiratory tract. Contact with the substance can cause redness and pain in the eyes and blurred vision. Symptoms of poisoning via the inhalation route include cough and sore throat, while those via the oral route include abdominal pain, nausea and vomiting.

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, 0.17 mg/kg/day (for increased liver weight) was derived based on the lower 95% confidence limit on a benchmark dose associated with 5% extra risk, or Benchmark Dose Lower Confidence Limit (BMDL 5) from reproductive/developmental toxicity tests where mice were administered ammonium salt of the substance, or APFO. 0.03 mg/kg/day was obtained after division by 5 due to the short test periods was identified as the ‘non-toxic level*’ of the substance. As for inhalation exposure, a NOAEL of 1 mg/m^3 (for increased liver weight, elevated ALP, and hypertrophy of hepatocytes) was derived for this substance from mid-term and long-term toxicity tests where rats inhaled ammonium salt of the substance, or APFO. This NOAEL was adjusted to 0.18 mg/m^3 according to exposure conditions, and then divided by 5 due to the short test periods. 0.03 mg/m^3 derived was identified as the ‘non-toxic level*’ of the substance.

As to oral exposure to the substance, when intakes through foods and drinks were assumed, the predicted maximum exposure was approximately 0.0020 μg/kg/day. The MOE derived was 1,500 when calculated from the ‘non-toxic level*’ of 0.03 mg/kg/day and the predicted maximum exposure divided by 10 due to the need to convert the ‘non-toxic level*’ obtained from the animal experiments to a human equivalent dose. As for oral exposure, the predicted maximum exposure when intakes of groundwater and food were was approximately 0.0014 μg/kg/day, and the MOE derived was 2,100.

With regard to inhalation exposure to the substance, the maximum exposure concentration was approximately 0.0025

μg/m^3 based on its concentrations in the ambient air. The MOE would be 140 when calculated from its 'non-toxic level*' of 0.03 mg/m^3 and its predicted maximum exposure concentration divided by 10 due to the need to convert the 'non-toxic level*' obtained from the animal experiments to a human equivalent dose.

Toxicokinetics and metabolism of this substance largely depend on animal species and sex. Especially, the half-life of this substance in human serum (3.8 yrs) is much longer than those in laboratory animals. Accordingly, it would be appropriate to assess the health risk of this substance based on the body burden instead of the exposure dose or concentration. The MOE calculated based on the body burden was greatly different from the MOE above, and too little information was available on the toxicity mechanisms of this substance to identify its health risk. Therefore, collection of information would be required to assess health risk from inhalation exposure to this substance in the ambient air.

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 * '	0.03	mg/kg/day	Mice	Increase of liver weight	Drinking water/Food	0.0020	μg/kg/day	MOE	1,500	×	(▲)
						Groundwater/Food	0.0014	μg/kg/day	MOE	2,100	×	
Inhalation	'Non-toxic level * '	0.03	mg/m^3	Rats	Increase of liver weight, increased ALP, hepatic hemosiderosis, etc.	Ambient air	0.0025	μg/m^3	MOE	1,200	×	(▲)
						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.

---

4. Initial assessment of ecological risk

With regard to acute toxicity, the following reliable data were obtained: a 96-h EC_{50} of more than 355,000 μg/L for growth inhibition in the green algae *Pseudokirchneriella subcapitata*, a 48-h EC_{50} of 181,000 μg/L for swimming inhibition in the crustacean *Daphnia magna*, a 48-h LC_{50} of 555,000 μg/L for the fish species *Pimephales promelas* (fathead minnow), and a 96-h LC_{50} of 337,000 μg/L for the flatworm *Dugesia japonica*. Accordingly, based on these acute toxicity values and an assessment coefficient of 100, a predicted no effect concentration (PNEC) of 1,800 μg/L was obtained.

With regard to chronic toxicity, the following reliable data were obtained: a 96-h NOEC of 10,900 μg/L for growth inhibition in the green algae *P. subcapitata*, a 7-d NOEC of 3,125 μg/L for reproductive inhibition in the crustacean *Moina macrocopa*, and an 85-d NOEC of 38,400 μg/L for growth inhibition and mortality in the fish species *Oncorhynchus mykiss* (rainbow trout). Accordingly, based on these chronic toxicity values and an assessment coefficient of 10, a predicted no effect concentration (PNEC) of 310 μg/L was obtained. The value of 310 μg/L obtained from the chronic toxicity to the crustacean was used as the PNEC for this substance.

The PEC/PNEC ratio was 0.001 for freshwater bodies and less than 0.00004 for seawater. Accordingly, further work is thought to be unnecessary at this time. An environmental study of a limited area reported a maximum value of 31 μg/L for public water bodies and freshwater, and the ratio of this concentration and the PNEC is 0.099. Although not adopted for this initial assessment, a lower toxicity value was obtained in a two-generation PFOA test using medaka than that obtained from the reliable early life stage toxicity test in fish. Furthermore, accumulation in marine and terrestrial mammals, and birds is also feared. Accordingly, further collection of data is considered desirable in order to elucidate the transfer of environmental concentrations of this substance, long-term toxicity, and the mechanisms of in vivo uptake and accumulation.

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 *Moina macrocopa*	Chronic	NOEC reproductive inhibition	10	310	Freshwater	0.36	0.001	○	▲
					Seawater	0.011	0.00004		

---

5. Conclusions

	Conclusions		Judgment
Health risk	Oral exposure	Further information collection would be required for risk characterization.	(▲)
	Inhalation exposure	Further information collection would be required for risk characterization.	(▲)
Ecological risk	Further collection of data considered desirable in order to elucidate the transfer of environmental concentrations of this substance, long-term toxicity, and the mechanisms of in vivo uptake and accumulation.		▲

［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.