| 2 | CAS No.: 149-57-5 | Substance: 2-Ethylhexanoic acid |
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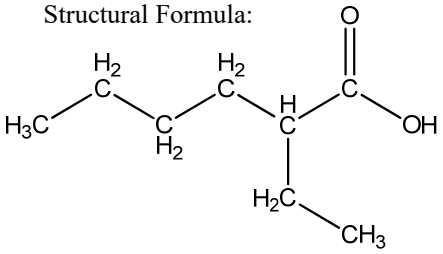
Chemical Substances Control Law Reference No.: 2-608 (Alkanoic acid (C=4–30))

PRTR Law Cabinet Order No.: 1-51

Molecular Formula: $C_8H_{16}O_2$

Molecular Weight: 144.21

Structural Formula:




**1.General information**

The aqueous solubility of this substance is $2\times10^3$ mg/L (20°C), the partition coefficient (1-octanol/water) (log $K_{ow}$) is 2.64, and the vapor pressure is 0.03 mmHg (=4 Pa) (20°C). The biodegradability (aerobic degradation) is characterized by a BOD degradation rate (lead (II)=bis (2-ethylhexanoate) degradation rate of 99% and biodegradability is judged to be good (judgment based on degradability of a similar chemical). In addition, this substance does not possess any hydrolyzable groups.

This substance is classified as a Class 1 Designated Chemical Substance under the PRTR Law.

The main uses of this substance are as a raw material for metallic soaps, synthetic lubricants, specialty plasticizers, rust prevention additives, and alkyd resin modifiers. The production and import quantity of alkanoic acid (C=4–30) in fiscal 2018 was 100,000 t. The production and import category under the PRTR Law is more than 100 t.

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**2. Exposure assessment**

Total release to the environment in fiscal 2018 under the PRTR Law was approximately 18 t, of which approximately 0.44 t or 2% of overall releases were reported. The majority of reported releases were to the atmosphere. In addition, approximately 71 t was transferred to waste materials and approximately 8.9 t was transferred to sewage. The chemical and electrical machinery manufacturing industries reported releases to the atmosphere, while the chemical industry reported releases to public water bodies.

A multi-media model used to predict the proportions distributed to individual media in the environment indicated that in regions where the largest quantities were estimated to have been released to the environment or public water bodies, the predicted proportion distributed to water bodies was 98.4%. Where the largest quantities were estimated to have been released to the atmosphere, the predicted proportion distributed to water bodies was 93.8%.

The maximum expected concentration of exposure to humans via inhalation, based on ambient atmospheric data, was around less than 0.39 μg/$m^3$. Further, the mean annual value for atmospheric concentration in fiscal 2018 was calculated by use of a plume-puff model on the basis of releases to the atmosphere reported under the PRTR Law; this model predicts a maximum level of 0.031 μg/$m^3$.

Data for potable water, ground water, food, and soil to assess oral exposure could not be obtained. Thus, assuming intake solely from public freshwater bodies, a maximum expected concentration of exposure of around 0.014 μg/kg/day was obtained. However, when releases to public freshwater bodies in fiscal 2018 reported under the PRTR Law 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 0.089 μg/L. Using this estimated concentration for rivers to calculate oral exposure gives 0.0035 μg/kg/day. In addition, when releases to public freshwater bodies estimated from the transfers to sewage 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 0.15 μg/L. Calculating oral exposure based on this gives 0.0060 μg/kg/day. The risk of exposure to this substance by intake from an environmental medium via food is considered slight, given the low bioaccumulation of the substance expected on the basis of its physicochemical properties.

The predicted environmental concentration (PEC), which indicates exposure to aquatic organisms, was reported to be around 0.35 μg/L for public freshwater bodies and around less than 0.16 μg/L for seawater. When releases to public freshwater bodies in fiscal 2018 reported under the PRTR Law 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 0.089 μg/L. In addition, when releases to public freshwater bodies estimated from the transfers to sewage 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 0.15 μg/L.

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**3. Initial assessment of health risk**

This substance irritates the respiratory tract, and inhalation will cause a cough. Ingestion will cause abdominal pain, burning sensation and diarrhea. This substance irritates the skin and eyes as well. Contact to the skin will cause redness. Contact to the eyes will cause redness and pain.

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

The NOAEL of 61 mg/kg/day for oral exposure (based on increase in the relative weight of liver and hepatocyte hypertrophy), determined from toxicity tests in rats, was divided by a factor of 10 to account for extrapolation to chronic exposure. The calculated value of 6.1 mg/kg/day was deemed to be the lowest reliable dose and was identified as the 'non-toxic level' of the substance for oral exposure. The 'non-toxic level' for inhalation exposure could not be identified.

Regarding the oral exposure, assuming that the substance is absorbed via public freshwater bodies, the predicted maximum exposure level would be 0.014 μg/kg/day, approximately. The MOE (Margin of Exposure) would be 44,000, when calculated from the predicted maximum exposure level and the 'non-toxic level' of 6.1 mg/kg/day, and subsequently divided by a factor of 10 to account for extrapolation from animals to the humans. This would lead to the health risk judgment that no further work would be required at present. In addition, the MOE for reference would be 170,000, when calculated from the estimated maximum exposure level of 0.0035 μg/kg/day. This maximum exposure level was estimated according to the concentration in effluents from the high discharging plants derived from the releases to public freshwater bodies reported in FY 2018 under the PRTR Law. When considering the transfers to the sewage system, the maximum exposure level would be 0.0060 μg/kg/day, giving an MOE of 100,000. Since exposure to the substance in environmental media via food is presumed to be limited despite the lack of exposure level via food, including it in the calculation would not change the MOE significantly. Therefore, as a comprehensive judgment, no further work would be required at present.

Regarding the inhalation exposure, due to the lack of identified 'non-toxic level', the health risk could not be assessed. However, the tentative 'non-toxic level' for inhalation exposure, derived from the conversion of the 'non-toxic level' for oral exposure would be 20 mg /$m^3$, assuming that 100% of the inhaled substance is absorbed. The MOE for reference would exceed 5,100, when calculated from the tentative 'non-toxic level' for inhalation exposure and the predicted maximum exposure concentration in ambient air of less than 0.39 μg/$m^3$, approximately, and subsequently divided by a factor of 10 to account for extrapolation from animals to the humans. In addition, the MOE would be 65,000, when calculated from the concentration in ambient air of 0.031μg/$m^3$. This concentration was estimated as the maximum concentration (annual mean) in ambient air, near the operators that are releasing large amount of the substance, based on the releases to air reported in FY 2018 under the PRTR Law. Therefore, as a comprehensive judgment, collection of further information would not be required to assess the health risk of this substance via inhalation in ambient air.

| Toxicity | | | | Exposure assessment | | MOE | | Comprehensive judgment |
|---|---|---|---|---|---|---|---|---|
| Exposure Path | Criteria for risk assessment | Animal | Criteria for diagnoses (endpoint) | Exposure medium | Predicted maximum exposure dose and concentration | | | |
| Oral | 'Non-toxic level' 6.1 mg/kg/day | Rats | Increase in the relative weight of liver and hepatocyte hypertrophy | Drinking water | - μg/kg/day | MOE | - | ○ |
| | | | | Public Freshwater bodies | 0.014 μg/kg/day | MOE | 44,000 | |
| Inhalation | 'Non-toxic level' - mg/$m^3$ | - | - | Ambient air | <0.39 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 of 2-ethylhexanoic acid, the following reliable data were obtained: a 72-h $EC_{50}$ of 430,000 μg/L for growth inhibition in the alga *Raphidocelis subcapitata*, a 48-h $EC_{50}$ of 792,000 μg/L for swimming inhibition in the crustacean *Daphnia magna*, a 96-h $LC_{50}$ exceeding 86,000 μg/L for the fish species *Oryzias latipes* (medaka), and a 96-h $LC_{50}$ of 645,500 μg/L for the African clawed frog *Xenopus laevis*. Accordingly, based on these acute toxicity values and an assessment factor of 100, a predicted no effect concentration (PNEC) of 4,300 μg/L was obtained

With regard to chronic toxicity of 2-ethylhexanoic acid, the following reliable data were obtained: a 72-h NOEC of 113,000 μg/L for growth inhibition in the alga *R. subcapitata* and a 21-d NOEC of 15,600 μg/L for reproductive inhibition in the crustacean *D. magna*. Accordingly, based on this chronic toxicity value and an assessment factor of 100, a PNEC of 156 μg/L was obtained

The value of 156 μg/L obtained from the chronic toxicity to the crustacean was used as the PNEC for this substance.

The PEC/PNEC ratio is 0.002 for freshwater bodies and less than 0.001 for seawater; accordingly, further work to determine the ecological risk is considered unnecessary at this time.

When releases to public freshwater bodies in fiscal 2018 reported under the PRTR Law 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 0.089 μg/L. The ratio of this value to the PNEC is 0.0006. In addition, when releases to public freshwater bodies estimated from the transfers to sewage 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 0.15 μg/L. The ratio of this value to the PNEC is 0.001. Accordingly, based on a comprehensive review of the above findings, there is little need to collect new data regarding this substance.

| Hazard assessment (basis for PNEC) | | | Assessment coefficient | Predicted no effect concentration PNEC (μg/L) | Exposure assessment | | PEC/ PNEC ratio | Comprehensive judgment |
|---|---|---|---|---|---|---|---|---|
| Species | Acute/ chronic | Endpoint | | | Water body | Predicted environmental concentration PEC (μg/L) | | |
| Crustacean *Daphnia magna* | Chronic | NOEC Reproductive inhibition | 100 | 156 | Freshwater | 0.35 | 0.002 | ○ |
| | | | | | Seawater | <0.16 | <0.001 | |

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**5. Conclusions**

| | Conclusions | | Judgment |
|---|---|---|---|
| Health risk | Oral exposure | No need for further work. | ○ |
| | Inhalation exposure | No need for further work. | ○ |
| Ecological risk | No need for further work. | | ○ |

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

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