

Summary of Initial Risk Assessment Report

***N,N*-Dimethylformamide** CAS No : 68-12-2

PRTR No of Japan: 172

This substance is assessed based on Guideline for Initial Risk Assessment Version 1.0

1. General Information

1.1 Physico-chemical properties

| | |
|---|--|
| Appearance | Colorless or pale yellow liquid |
| Melting point | -61 degC |
| Boiling point | 153 degC |
| Water solubility | Miscible |
| Henry's constant | 7.49×10^{-3} Pa*m ³ /mol (7.39×10^{-8} atm*m ³ /mol) (25degC, measured) |
| Octanol/water partition coefficient (log Kow) | -1.01 (measured), -0.93 (estimated) |
| Soil adsorption coefficient | Koc = 7 (estimated) |

1.2 Environmental fate

| | |
|------------------------------|---|
| Bioaccumulation | Exhibits little to no bioaccumulation Bioconcentration factor (BCF) : 0.3-0.8 (20 mg/L), 0.3-1.2 (2 mg/L) (carp) (measured) |
| Biodegradation | Non-biodegradable |
| Stability in the environment | (In air) Reaction with OH radical: Reaction rate constant is 1.75×10^{-11} cm ³ /molecule-sec. (25 degC, estimated) The half-life is 0.5-1 day, given OH radical concentration of 5×10^5 - 1×10^6 molecule/cm ³ . Reaction with ozone: No data Reaction with nitrate radical: No data. As <i>N,N</i> -Dimethylformamide does not absorb light with wavelengths of 290 nm or longer , it is not directly photodegraded (In water) Hydrolysis in the aquatic environment is slow. The hydrolysis half-life is considered to be 1 year or longer. |
| Environmental fate | When released to water, <i>N,N</i> -Dimethylformamide is expected to be removed by biodegradation under specific conditions. Removal from water by volatilization is not considered an important fate process. |

2. Sources of release to the environment

2.1 Annual production, import, export and domestic supply in 2001 (ton/year)

| Production | Import | Export | Domestic supply | Remarks |
|------------|--------|--------|-----------------|---------|
| 57,724 | | -- | -- | |

2.2 Uses

Solvents, catalysts, gas absorbents

2.3 Release from the industries within the scope of PRTR system (in 2001)

| Release sources | | Air (ton) | Waters (ton) | Soil (ton) | Remarks |
|---|------------------------------|-----------|--------------|------------|-------------------------------|
| Listed industries | Reported release | 6,315 | 289 | 0 | Release to rivers: 1,040 tons |
| | Release outside notification | 18,495 | 848 | 0 | |
| Release outside notification from non listed industry | | 140 | 0 | 0 | |
| Households | | < 0.5 | 0 | 0 | |
| Mobile sources | | -- | -- | -- | |
| Total | | 24,951 | 1,137 | 0 | |

2.4 Releases from other sources

No information about the substance is available.

2.5 Main release route

N,N-Dimethylformamide is expected to be released to the environment mainly during use of *N,N*-Dimethylformamide and products containing it.

3. Exposure Assessment

3.1 Measured environmental concentration

| Media | No. of points detected / No. of points measured | No. of samples detected / No. of samples measured | Detection range | 95th percentile | Detection limit | Year of investigation, Institution |
|---------------------------------|--|--|-----------------|-----------------|-----------------|--|
| Air (microg/m ³) | 12/17 | 30/49 | nd-0.62 | 0.50 | 0.0039 - 0.1 | 1997 Ministry of the Environment |
| River water (microg/L) | 25/35 | 25/35 | nd-1.3 | 0.93 | 0.07 | 2001 Chemicals Evaluation and Research Institute, Japan |
| Sea water (microg/L) | 2/12 | 5/36 | nd-0.11 | 0.091 | 0.007-0.009 | 1998 Ministry of the Environment |
| Drinking water | -- | -- | -- | -- | -- | -- |
| Food (microg/g) | 0/9 | 0/45 | nd | -- | 0.1 | 1997 Japan Food Research Laboratories |

nd: Not detected.

For calculation of the 95th percentile, data less than the detection limit are replaced with a value of one-half of the detection limit.

3.2 Estimated environmental concentration

| Media | Estimated concentration | Description |
|------------------------------|-------------------------|--|
| Air (microg/m ³) | 13 | Calculated by mathematical model / Atmospheric Dispersion Model for Exposure and Risk Assessment ver.1.0 (AIST-ADMER) |
| River water (microg/L) | 340 | Calculated by mathematical model / Integrated River Model to predict the distribution of chemical concentration (IRM1) |

3.3 Estimated environmental concentration in water (EEC)

| | |
|---------------|---|
| EEC(microg/L) | 0.93 |
| | The ninety-fifth percentile of measured concentration in river was used for the risk assessment ¹⁾ . |

3.4 Estimated human intake

| Intake route | | Concentration used for estimation of intake | Estimated intake (microg/ person/ day) | Estimated intake (microg/ kg-Bodyweight (BW)/ day) |
|--------------|----------------|--|--|--|
| Inhalation | Air | 0.50 (microg/m ³) | 10 | 0.20 |
| | | The ninety-fifth percentile (0.50 microg/m ³) of measured concentrations was used for the risk assessment. ¹⁾ | | |
| Oral | Drinking water | 0.93 (microg/L) | 1.9 | 0.038 |
| | | -Concentrations in river water were used, since measured concentrations in drinking water were unavailable. -The ninety-fifth percentile (0.93 microg/L) of concentrations surveyed by the Chemicals Evaluation and Research Institute, Japan in 2001 was used for the risk assessment. | | |
| | Food | 0.00011 (microg/g) | 0.013 | 0.00026 |
| | | - <i>N,N</i> -dimethylformamide was not detected in any of the samples from 45 households in a duplicate diet study conducted by Japan Food Research Laboratories. -The detection limit of the survey was high. Using a value equal to 1/2 of the detection limit would have resulted in overestimation of human intake via food. -Therefore, the intake via food was estimated using the concentration in fish. The concentration in fish was calculated as a product of the concentration in seawater and a BCF. $0.091 \text{ (microg/L)} * 1.2 \text{ (L/kg)} = 0.00011 \text{ (microg/g)}$ | | |
| Subtotal | -- | 1.9 | 0.038 | |
| Total route | | -- | 12 | 0.24 |

1) This substance is assessed based on the Guideline for Initial Risk Assessment Version1.0. If adequate measured concentrations are available, they are given priority and used as values for risk assessment. If they are not available, an estimated value calculated using a mathematical model is used.

4. Hazard assessment

4.1 Effects on organisms in the environment

| | Acute or Chronic | Species | Endpoint | Concentration |
|-----------|------------------|--|--|---------------|
| Algae | Chronic | <i>Selenastrum capricornutum</i> | 96 hours NOEC Growth inhibition (chlorophyll a) | 940 (mg/L) |
| Crustacea | Chronic | <i>Daphnia magna</i> | 28 days NOEC Reproduction | 1,100 (mg/L) |
| Fish | Acute | <i>Lepomis macrochirus</i> | 96 hours LC ₅₀ | 7,100 (mg/L) |
| Key study | | The data of algae (<i>Selenastrum capricornutum</i>) was chosen for the key study because effects were observed at the lowest concentration. | | |

4.2 Human health toxicity

| Toxicity | Exposure route | Species | Duration / Dose method | Toxic effects (Key study is underlined) | NOAEL or LOAEL |
|---|---|---------|------------------------|---|--|
| Repeated dose toxicity | Inhalation | Mouse | 18 months | <u>Hepatocellular hypertrophy, hepatocellular single cell necrosis, lipofuscin and hemosiderin accumulation in Kupffer cells</u> , increased absolute and relative weight of liver | LOAEL: 25 ppm (76 mg/m ³) (equivalent to 23 mg/kg/day) |
| | Oral | Rat | 90 days | <u>Increased relative weight of liver, hypercholesterolemia associated with decreased hepatic fat content</u> , reduced body weight gains, anemia, leucocytosis, hepatocellular hypertrophy, increased hepatocellular mitosis | NOAEL: 200 ppm (equivalent to 17.2 mg/kg/day) |
| | Dermal | -- | -- | -- | -- |
| Reproductive and developmental toxicity | Inhalation | Rat | GD 6-15 | F ₀ : Reduced body weight F ₁ : Reduced birth weight, increased skeletal deformity | NOAEL: 32 ppm (97 mg/m ³) (equivalent to 18 mg/kg/day) |
| | Oral | Rat | GD 6-20 Gavage | F ₀ : Reduced body weight gain and decreased feed intake F ₁ : Reduced birth weight | NOAEL: 50 mg/kg/day |
| Carcinogenicity | Evaluation by IARC : Group 3 (not classifiable as to its carcinogenicity to humans) | | | | |
| Genotoxicity | Not considered to be genotoxic. | | | | |

5. Risk Assessment

5.1 Environmental organisms

| Risk characterization | EEC (microg/L) | NOEC * (mg/L) | MOE (NOEC * /EEC) | Product of uncertainty factors | Conclusion |
|--|-------------------|------------------|----------------------|--------------------------------|----------------------|
| | 0.93 | NOEC: 940 | 1,000,000 | 50 | No immediate concern |
| Product of uncertainty factors (UF): Extrapolation from laboratory test (10) * Toxicity data on two nutritional stages (5) = 50 | | | | | |
| Recommendation : | | | | | |
| The substance is considered to be of no immediate concern for the moment, and a low priority for further work. | | | | | |

NOEC* means NOEC, LOEC, EC₅₀, etc.

5.2 Human health

5.2.1 Repeated dose toxicity

| Exposure route | Intake (microg/kgBW/day) | NOAEL (mg/kgBW/day) | Risk characterization | | |
|----------------|-----------------------------|------------------------|-----------------------|--------------------------------|----------------------|
| | | | MOE | Product of uncertainty factors | Conclusion |
| Inhalation | 0.20 | LOAEL: 23 | 120,000 | 1,000 | No immediate concern |
| Oral | 0.038 | 17.2 | 450,000 | 500 | No immediate concern |
| Total | 0.24 | 17.2 (Oral) | 72,000 | 500 | No immediate concern |

Product of uncertainty factors (UF):
 Inhalation: Interspecies (10) * Intraspecies (10) * Using of LOAEL (10) = 1,000
 Oral/Total: Interspecies (10) * Intraspecies (10) * Duration of test (5) = 500

5.2.2 Reproductive and developmental toxicity

As NOAEL of developmental toxicity is larger than NOAEL of repeated toxicity, the risk characterization of developmental toxicity of the substance was not carried out.

5.2.3 Carcinogenicity

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5.2.4. Recommendation for Human Health

The substance is considered to be of no immediate concern for the moment, and a low priority for further work.

6. Supplement

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