Safety Data Sheet

1. Identification of the Substance/Mixture and the Supplier

Supplier: National Institute of Advanced Industrial Science and Technology (AIST)
Address: 1-3-1, Kasumigaseki, Chiyoda, Tokyo, Japan
Office in Charge: Reference Materials Office, Center for Quality Management of Metrology, National Metrology Institute of Japan
Person in Charge: Certified Reference Material Staff
Telephone No.: +81-29-861-4059
Fax No.: +81-29-861-4009

Identity of Substance/Mixture: Certified reference material: NMIJ CRM 4057-a
Recommended Use: This reference material can be used for calibration of analysis equipment as well as quality control of analysis and validation of analysis method/equipment. Do not use this reference material for other purposes than testing/research.

2. Hazards Identification

GHS Classification:
- Flammable liquid: Hazard Category 2
- Acute toxicity (Inhalation: Vapor): Hazard Category 4
- Skin corrosion/irritation: Hazard Category 2
- Serious eye damage/ Eye irritation: Hazard Category 2A
- Carcinogenicity: Hazard Category 2
- Specific target organ toxicity/Systemic toxicity (Single exposure): Hazard Category 1 (Central nervous system)
- Specific target organ toxicity/Systemic toxicity (Repeated exposure): Hazard Category 1 (Kidneys, Liver, Central nervous system)
- Hazard Category 2 (Respiratory organ)

GHS Label Element:

Signal Word: Danger
Hazards Statement:
Highly flammable liquid and vapor
Skin irritation
Strong eye irritation
Harmful if inhaled
Suspected of causing cancer
Cause damage to central nervous system
Cause damage to kidneys, liver and central nervous system through prolonged or repeated exposure
May cause damage to respiratory organ through prolonged or repeated exposure

Precautionary Statement:
Keep away from ignition source such as heat/sparks/open flames/hot surfaces. – No smoking.
Keep container tightly closed.
Ground container if electrostatically sensitive material is for reloading.
Use explosion-proof electrical/ventilating/lighting equipment.
Use only non-sparking tools.
Take precautionary measures against static discharge.
Wear appropriate protective gloves/eye protector/face protection.
Use only outdoors or in a well-ventilated area.
Wash hands thoroughly after handling.
Obtain special instruction before use.
Do not handle until all safety precautions have been read and understood.
Do not breathe mist/vapors/spray.
Do not eat, drink or smoke when using this reference material.

[Action]
In case of fire, use appropriate extinguishing method.
If inhaled: Remove victim to fresh air and keep at rest in a position comfortable for breathing. Call a doctor/physician when feeling unwell.
If on skin (or hair): Wash with soap and plenty of water.
If skin irritation occurs: Get medical advice/attention.
Remove/Take off contaminated clothing and wash before reuse.
If in eyes: Rinse cautiously with clean water for several minutes. Remove contact lenses, if present and easy to do. Continue rinsing.
If eye irritation persists: Get medical advice/attention.
If exposed or concerned: Get medical advice/attention.
If exposed: Call a doctor/physician.
If feeling unwell: Get medical advice/attention.

[Storage]
Store in a well-ventilated place. Store in a cool place. Keep container tightly closed. Store locked up.

[Disposal]
Comply with applicable legislation and local government ordinance.
Entrust disposal of this reference material to a professional waste disposal company licensed by prefectural governor.

The other hazards than the above do not result in classification or are not classifiable.

### 3. Composition/Information on Ingredients

<table>
<thead>
<tr>
<th>Substance or Mixture</th>
<th>Substance</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chemical Identity</td>
<td>1,4-Dioxane</td>
</tr>
<tr>
<td>Synonym</td>
<td>p-Dioxane, 1,4-Diethylene dioxide, 1,4-Dioxacyclohexane</td>
</tr>
<tr>
<td>Content</td>
<td>99 % or more</td>
</tr>
<tr>
<td>Chemical Formula or Structural Formula</td>
<td>C₄H₈O₂</td>
</tr>
<tr>
<td>Molecular Weight</td>
<td>88.11</td>
</tr>
<tr>
<td>Reference Number in Gazetted List in Japan</td>
<td>Act on the Evaluation of Chemical Substances and Regulation of Their Manufacture, etc. : (5) – 839</td>
</tr>
<tr>
<td>CAS Number</td>
<td>123-91-1</td>
</tr>
<tr>
<td>Hazardous Ingredient</td>
<td>1,4-Dioxane</td>
</tr>
</tbody>
</table>

### 4. First-aid Measures

- **If in eyes**: Rinse cautiously with water for several minutes. Remove contact lenses, if present and easy to do. Continue rinsing. If eye irritation persists: Get medical advice/attention.

- **If on skin**: Remove/Take off immediately all contaminated clothing. Rinse skin with running water/shower. Wash with soap and plenty of water. If skin irritation occurs: Get medical advice/attention.

- **If inhaled**: Remove victim to fresh air and keep at rest in a position comfortable for breathing. Call a doctor/physician when feeling unwell.

- **If swallowed**: Immediately rinse mouth/gargle. Give plenty of water and induce vomiting. Do not induce vomiting if convulsion or consciousness clouding occur or if in a stupor. Do not give anything by mouth to an unconscious person. If vomit occurs spontaneously, tilt victim’s body to prevent aspiration. Keep victim’s body warm. Get medical advice/attention immediately.

**Expected Acute and Delayed Symptom**

- If inhaled: Cough, Sore throat, Nausea, Dizziness, Headache, Lethargy, Vomiting, Unconsciousness, Stomachache
- If on skin: May be absorbed through skin. Flare
- If in eyes: Flare, Pain, Watery eyes
- If ingested: Cough, Sore throat, Nausea, Dizziness, Headache, Lethargy, Vomiting, Unconsciousness, Stomachache
- Delayed symptoms: May induce lung congestion/lung edema

**Most Critical**: Alcoholic beverages will intensify harmful effects.
Characteristic and Symptom
Protection of First-Aid Responder: First-aid responder must wear personal protective equipment such as gas mask for organic solvents as necessary.

5. Fire-fighting Measures

Extinguishing Media: For initial firefighting, use such extinguishing media as water spray (water fog), carbon dioxide, foam, dry chemical extinguisher and sand.

Unsuitable Extinguishing Media: Direct water jets

Fire-Specific Hazards: Extremely flammable. In case of fire, may emit irritating or toxic fume (or gas). Heating may cause explosion of container.

Specific Fire-Fighting Method: Eliminate ignition sources at the origin of a fire and put out fire by using extinguishing media. Remove movable containers promptly to a safe place. In the case of immovable containers, cool their surroundings with sprayed water.

Protection of Fire-Fighters: Carry out fire-fighting from the windward in order to avoid breathing hazardous gas. Use personal protective equipment such as fireproof clothing, heat-resistant clothing, protective clothing, compressed air open-circuit self-contained breathing apparatus, compressed oxygen closed-circuit self-contained breathing apparatus, rubber gloves and rubber boots.

6. Accidental Release Measures

Personal Precaution: Remove potential ignition sources from the vicinity promptly. Get fire-fighting kit ready to be prepared for ignition.

Personal Protective Equipment and Emergency Procedures: Ventilate the affected areas thoroughly, if it is in an indoor environment, until the clean-up operation is completed. Use appropriate personal protective equipment during the operation to avoid skin contact of splash etc. and inhalation of dust and gas.

Environmental Precautions: Take precautions to prevent spillage from draining into rivers etc. to adversely impact the environment. Make it sure to appropriately treat contaminated wastewater in order to prevent untreated wastewater from being released into the surrounding environment.

Recovery and Neutralization: Collect spillage in empty containers by getting it adsorbed to wiping cloth, rag or earth and sand, etc. Rinse away the remains with plenty of water.

Prevention of Secondary Disaster: Mark the restricted area with rope etc. to keep out unauthorized people. Carry out the clean-up operation from the windward and make people on the leeward side evacuate.
7. Handling and Storage

Handling

Engineering Precautions: Strict ban on fire.
Precautions: Keep away from hot surfaces/sparks. Avoid contact with strong oxidizers.
Local and General Ventilation Precautions: Keep container tightly closed and use local ventilation system if vapor/mist is generated.
Precautions for Safe Handling: Avoid rough handling such as turning over, dropping, giving a shock to or dragging containers.
Prevent spill, overflow and scattering, and avoid vapor generation.
Keep container tightly closed after use.
Wash hands, face etc. thoroughly and gargle after handling this reference material.
Restrict drinking, eating and smoking to a designated area.
Do not bring gloves and other contaminated personal protective equipment into staff room.
Make a place handling this reference material a restricted area to keep out unauthorized people.
Use appropriate personal protective equipment to avoid inhalation and contact with eyes, skin and clothing.
Use local ventilation system in indoor handling area.

Storage

Appropriate Storage Conditions: Protect from sunlight. Store in tightly-closed container in a well-ventilated and cool place.
Safe Container Packaging Material: Glass
Incompatible Materials: Strong oxidizers

8. Exposure Controls/Personal Protection

Threshold Limit Value

Working Environment Evaluation Criteria 10 ppm

Permissible Concentration

- ACGIH TLV-TWA: 20 ppm (Skin)
- Value recommended by Japan Society for Occupational Health: 10 ppm (36 mg/m³)
- OSHA PEL TWA: No data available

Engineering Controls

Ventilation/Exhaust: Local ventilation system or General ventilation system
Safety Control/ Gas Detection: Measuring equipment, Detecting tube
Storage Precaution: Ventilated along floor surface. Tightly closed. Keep away from combustible substances, reducing substances and...
strong oxidizers.

Personal Protective Equipment (PPE)

Respiratory System: Gas mask for organic gases, Compressed air open-circuit self-contained breathing apparatus

Hands: Impervious protective gloves

Eyes: Eye protector with side plates (or Goggle type)

Skin and Body: Protective clothing with long sleeves, Protective boots

Hygiene Controls

Handle this reference material in accordance with industrial health and safety standards.

9. Physical and Chemical Properties

- Appearance, etc.: Liquid
- Color: Clear and colorless
- Odor: Characteristic odor
- pH: No data
- Melting point: 12 °C
- Boiling point: 102 °C
- Flashing point: 12 °C
- Explosive range: No data
- Vapor pressure: 38.7 kPa (25 °C)
- Relative vapor density (Air=1): 3.03
- Specific gravity or bulk specific gravity: 1.030 g/ml to 1.035 g/ml (20 °C)
- Solubility: Highly soluble in water and ethanol
- \( n \)-Octanol/water partition coefficient (Log Po/w): -0.42
- Auto-ignition temperature: 180 °C

10. Stability and Reactivity

◇ Stability
  - Produce peroxides if exposed to oxygen in air. Hygroscopic.

◇ Reactivity
  - May react, in contact with strong oxidizers.

◇ Conditions to Avoid
  - Sunlight, Heat, Contact with oxidizers

◇ Hazardous Decomposition Products
  - Carbon monoxide, Carbon dioxide

11. Toxicological Information

Acute Toxicity

Oral Rat LD50 = 4200 mg/kg
Dermal Rat LD50 = 7600 µg/kg
Inhalation Rat LC50 = 46 g/m³

Skin Corrosion/

In the skin irritation test (the open Draiz test) using rabbits,
Irritation  “moderate irritation” was reported, and in the skin irritation test using rats and mice, mild irritation was reported. Classified Hazard Category 2, based on these results.

Serious Eye Damage/ Eye Irritation Though the data of environmental effects on humans indicate clear positive reaction, its degree is not described as corrosive. In the eye irritation test using rabbits, “severe chemosis, mild corneal opacity and conjunctiva flare (cornea flare partially remained eight days after)” were reported. Classified Hazard Category 2A, based on these results. Classified R36/37 in EU Classification.

Respiratory Sensitization No data available

Skin Sensitization In the skin sensitization test using guinea pigs, no sensitization was reported. In the human patch test, however, positive results were obtained. Not classifiable, based on these results.

Germ Cell Mutagenicity In the forced oral administration micronucleus test using mice, both positive and negative results were reported. No germ cell mutagenicity classification by ATSDR, CERI · NITE Hazard Assessment Report and NICNAS No.7, based on the professional judgment on reliability of the test. Meanwhile in the DNA damage test, DNA synthesis test and DNA repair test using rat liver, positive results were reported, while in the Ames test, mouse lymphoma assay and chromosome abnormality test, negative results were reported.

Carcinogenicity NPA: R
ACGIH: A3
Japan Society for Occupational Health: Group 2B
IARC: 2B
EU: 3
NTP: R
EPA: B2
Classified Hazard Category 2, based on the above.
Confirmed carcinogen in the carcinogenicity test with administration in drinking water: for male rats, incidence rate of nasal cavity malignant tumor (mainly squamous cell carcinoma), hepatocellular carcinoma, hepatocellular adenoma and abdominal cavity mesothelioma increased, and for female rats, incidence rate of nasal cavity malignancy (mainly squamous cell carcinoma), hepatocellular adenoma and hepatocellular cancer increased to indicate oncogenicity. Health, Labor and Welfare Ministry published a guideline for prevention of health hazards, based on these results.

Reproductive Toxicity In the test in which this reference material was administered orally or by inhalation to rats during their organogenesis period, weight loss and ossification delay were only observed in some rat fetuses, but no adverse effects on fetus development were
Specific Target Organ Toxicity/Systemic Toxicity (Single Exposure)  
- Classified Hazard Category 1 based on the symptoms observed when humans inhaled this reference material: dizziness, drowsiness and loss of consciousness.
- Classified Hazard Category 3 (Narcotic effects) based on the fact that narcotic effects were reported when rats were exposed to this reference material of 155 mg/l by inhalation and when this reference material of 6600 mg/kg was administered orally to rabbits.
- Classified Hazard Category 3 (Airway irritation) based on 1) the multiple reports on nose and throat irritation when humans were exposed to this reference material and 2) the reports on airway mucous membrane irritation when rats were exposed to this reference material by inhalation.

With regard to central nervous system, although the supporting data were available on symptoms indicating toxicity to humans and animals, all of the symptoms were considered mild and temporary. It has been concluded, therefore, that the symptoms were a part of narcotic effects and not classified as toxicity to central nervous system.

For liver and kidneys, no evidences based on actual test data were available.

Specific Target Organ Toxicity/Systemic Toxicity (Repeated Exposure)  
- For five workers who had handled this reference material and died, bleeding in and necrosis of the kidneys and necrosis of the liver were reported. It was also reported that one worker exposed to this reference material for one week in a closed room with no ventilation system had developed hypermyotonia, neurological symptoms, renal failure, necrosis of kidney cortex, severe centrilobular necrosis of liver, demyelination in brain and partial loss of nerve fiber. Classified Hazard Category 1 (kidney, liver, central nervous system) based on these reports.
- Classified Hazard Category 2 (respiratory organ) based on the two-year oral administration test using rats in which degeneration of airway epithelium was observed when this reference material of 16 mg/kg/day (equivalent of Hazard Category 2) was administered.

Aspiration Toxicity to Respiratory Organ  
- No data available

Toxicity to Aquatic Life (Acute)  
- No classification, based on the test results: Fish (Oryzias latipes) 96 hours LC50 >100 mg/l (Environmental Ministry “Ecotoxicity Test Report”)

Toxicity to Aquatic Life (Chronic)  
- No classification, as this reference material is not hardly-soluble (solubility in water = 1.00 ×10⁶ mg/L (PHYSPROP Database)) and features low acute toxicity.
12. Ecological Information
Persistence and Degradability
  · No data available
Bioaccumulative Potential
  · No data available
Ecotoxicity
  · No data available
Hazard to Ozone Layer
  · No data available

13. Disposal Considerations
Residual Waste : Dispose in accordance with applicable regional, national and local laws and regulations.
Contaminated Container and Package : Dispose in accordance with applicable regional, national and local laws and regulations.

14. Transport Information
UN Number : 1165
UN Classification : Class 3
Shipping Name : Dioxane
Packing Group : PG III
ICAO/IATA : Class 3 Grade II
Marine Pollutant : Hazardous liquid substance (Type Y)
Precautions : Transport this reference material carefully while keeping it away from direct sunlight and fire and preventing accidental release due to falling, overturning, etc.

15. Regulatory Information
◇ Fire Service Act
  · Type 4 Hazardous Substance, Class 1 Petroleum, Danger Rating II, Water-soluble
◇ Industrial Safety and Health Law
  · Article 57-2 (Enforcement Order: Article 18) Hazardous substance whose name, etc. must be labeled.
  · Article 57-2 (Enforcement Order: Article 18-2) Hazardous substance whose name, etc. must be notified No. 227
  · Class 2 Organic Solvent
  · Substances listed in the published guideline for prevention of health hazards (Carcinogenic substance)
  · Working Environment Evaluation Criteria (Article 65-2-1)
16. Other Information

Others

The information in this document is not intended to be exhaustive and is based on currently available information and data. The measures given in this document are applicable only to normal handling conditions. When handling this reference material under special conditions etc., it is recommended to take safety measures appropriate to each specific application and context of use. This document is intended to provide information and not intended to guarantee anything in handling this reference material.