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 6211-a
Recommended Use : 4-Hydroxy-clomifene Standard Solution
Restriction on Use : Do not use this reference material for other purposes than testing/research.

2. Hazards Identification

GHS Classification :
- Flammable liquid : Hazard Category 2
- Acute Toxicity (oral) : Hazard Category 4
- Serious Eye Damage/ Eye Irritation : Hazard Category 2
- Reproductive toxicity : Hazard Category 1B
- Specific Target Organ Toxicity/Systemic Toxicity (Single Exposure) : Hazard Category 1 (central nervous system, visual organ, systemic toxicity)
- Specific Target Organ Toxicity/Systemic Toxicity (Repeated Exposure) : Hazard Category 3 (anesthetic action, respiratory tract irritation)

GHS Label Element:
- Signal Word : Danger
- Hazards Statement: Flammable liquid and vapor
  May be harmful if swallowed.
  Eye irritation
May cause adverse effects on fertility or the unborn child.
Causes damage to organs (visual organ and nerve system)

Systemic Toxicity
May cause respiratory irritation
May cause drowsiness or dizziness
Causes damage to organs (visual organ and nerve system) through prolonged or repeated exposure

Precautionary Statement:

[Safety Precaution]
Get the instruction manual before use.
Do not handle until all safety precautions have been read and understood.
Use personal protective equipment if necessary.
Do not eat, drink or smoke when using this product.
Keep away from heat/sparks/open flames/hot surfaces. No smoking.
Wash hands thoroughly after use.
Seal tightly after use.
Use explosion-proof electrical/ventilating/lighting equipment.
Use only non-sparking tools.
Ground and fix container and receiving equipment.
Take precautions against electrostatic discharge.
Avoid breathing dust/fume/gas/mist/vapors/spray.
Use only outdoors or in a well-ventilated area.

[First-aid Action]

If there is an exposure or a concern on an exposure, consult a doctor.
Get medical advice/attention if you feel unwell.
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 on skin or hair: Remove/Take off all contaminated clothing and adhered materials. Rinse skin or hair with running water.

In case of fire, use a powder, CO$_2$ or foam fire extinguisher.

[Storage]
Store this reference material in a light-shielded clean environment at –30 °C to –15 °C.

[Disposal]
Dispose of this reference material in accordance 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

Substance/Mixture: Mixture
Chemical name : 4-Hydroxy-clomiphene Standard Solution
Ingredient 1 : Methanol (Methyl alcohol)
Synonym : Methyl alcohol, Wood alcohol
Chemical Formula or Structural Formula : CH₃OH
Molecular Weight : 32.04
CAS Number : 67-56-1
Content : Ca. 99 %
Reference Number in Gazetted List in Japan : Act on the Evaluation of Chemical Substances and Regulation of Their Manufacture, etc. : (2)-201
Industrial Safety and Health Act : Published

Ingredient 2 : 4-hydroxy-clomiphene
Synonym : 4-[2-Chloro-1-[4-[2-(diethylamino)ethoxy]phenyl]-2-phenylethenyl]phenol
Chemical Formula or Structural Formula : C₂₆H₂₈ClNO₂
Molecular Weight : 421.97
CAS Number : 79838-51-0
Content : 254 µg/g, 200 µg/mL
Reference Number in Gazetted List in Japan : Act on the Evaluation of Chemical Substances and Regulation of Their Manufacture, etc. :
Industrial Safety and Health Act :
Hazardous Ingredient : Methanol

4-hydroxy-clomiphene is a mixture of the following two chemical components :

<table>
<thead>
<tr>
<th>Name</th>
<th>CAS Number</th>
<th>Content</th>
</tr>
</thead>
<tbody>
<tr>
<td>(E)-4-hydroxy-clomiphene</td>
<td>104575-08-8</td>
<td>176 µg/g</td>
</tr>
<tr>
<td>(Z)-4-hydroxy-clomiphene</td>
<td>104575-09-9</td>
<td>78 µg/g</td>
</tr>
</tbody>
</table>

### 4. First-aid Measures

If inhaled : Remove victim to fresh air and keep at rest and warm. Get medical advice/attention.

If on Skin : Rinse away thoroughly with clean water. Take off/Remove contaminated clothing, shoes, etc. If skin irritation or rash occurs get medical advice/attention.

If in Eyes : Rinse away thoroughly with clean water. Get medical advice/attention.

If swallowed : Rinse mouth thoroughly with water. Get medical advice/attention immediately.

Protection for first aid provider : Use appropriate protective equipment to avoid inhalation.

### 5. Fire-fighting Measures

Extinguishing media : Powder, foam, carbon dioxide, dry sand, water spray.

Fire-Specific Hazards : In case of fire, may emit irritating or toxic fume (or gas).
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.

Protecting fire-fighting personnel: Extinguish from windward, avoid inhaling toxic gases. Use personal protective equipment such as fire-resistant clothing, self-contained compressed air breathing apparatus, closed circuit breathing apparatus, rubber grooves, rubber boots, etc.

6. Accidental Release Measures

Personal Precaution: Remove ignition source in the vicinity immediately. Prepare fire-fighting equipment for the possibility of fires.

Protective and emergency equipment: 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: Adsorb spillage with waste clothes or wiping clothes or dry sand, and collect in empty containers. 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.

Local and General Ventilation Precautions for Safe Handling: Keep away from hot surfaces and sparks. Do not allow contact with strong oxidizer.

Precautions: When vapor or mist is generated, seal the source, and provide local exhaust ventilation or central ventilation.

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: This CRM should be stored at a temperature between −30 °C to −15 °C in a clean place and protected from light.

Safe Container Packaging Material: Glass

※Refer to the reference material certificate for the precaution statement regarding the appropriate condition of the storage and usage of the reference material.

8. Exposure Controls/Personal Protection (Methanol)

Threshold Limit Value

Not specified

Permissible Concentration

- ACGIH TLV-TWA : 200 ppm (260 mg/m³)
- Value recommended by Japan Society for Occupational Health : 200 ppm (260 mg/m³)
- OSHA PEL TWA : 200 ppm

Engineering Controls

Ventilation/Exhaust : Local ventilation system or General ventilation system

Safety Control/ Gas Detection : Measuring equipment, Detecting tube

Storage Precaution : Ventilate along floor surface. Seal. Keep away from flammable substances, reducing agents and strong oxidizers.

Personal Protective Equipment (PPE)

Respiratory System : Protective gas mask for organic vapors, Self-contained compressed air breathing apparatus as required.

Hands : Protective gloves

Eyes : Eye protector (Goggle type as necessary)

Skin and Body : Protective clothing, Protective face mask

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 : −98 °C (methanol)

Boiling point : 64 °C (methanol)
<table>
<thead>
<tr>
<th>Property</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Flashing point</td>
<td>11 °C (methanol)</td>
</tr>
<tr>
<td>Explosive range</td>
<td>From 6.0 v/v% to 36.5 v/v% (methanol)</td>
</tr>
<tr>
<td>Vapor pressure</td>
<td>12.3 kPa (methanol)</td>
</tr>
<tr>
<td>Relative vapor density (Air=1)</td>
<td>1.1 (methanol)</td>
</tr>
<tr>
<td>Specific gravity or bulk specific gravity</td>
<td></td>
</tr>
<tr>
<td>Solubility</td>
<td>Easily soluble in water, diethyl ether and ethanol.</td>
</tr>
<tr>
<td>Octanol/water partition coefficient (Log Po/w)</td>
<td>−0.74 (methanol)</td>
</tr>
<tr>
<td>Auto-ignition temperature</td>
<td>464 °C (methanol)</td>
</tr>
<tr>
<td>Decomposition temperature</td>
<td>No data</td>
</tr>
<tr>
<td>Flammability</td>
<td>No data</td>
</tr>
</tbody>
</table>

### 10. Stability and Reactivity

- **Stability**: Stable under recommended storage conditions
- **Reactivity**: Contact with strong oxidizer may cause fire or explosion.
- **Conditions to Avoid**: Direct sunlight, heat, open flame, high temperature material, spark, static electrical charge, and other fire sources. Contact with oxidizers.
- **Incompatible materials**: Contact with strong oxidizer.
- **Hazardous Decomposition Products**: Carbon monoxide, carbon dioxide

### 11. Toxicological Information (Methanol)

- **Acute Toxicity**
  - Oral Rat, LD₅₀ = 6200 mg/kg
  - Dermal Rabbit, LD₅₀ = 15800 mg/kg
- **Serious Eye Damage/Eye Irritation**
  - In the Draize test using rabbits, the mean score for conjunctivitis after 24, 48, and 72 hours was 2.1 (greater than 2.0), and conjunctive edema was observed for 4 hours (score 2.00), but it was noticeably improved after 72 hours (score 0.50). However, it is unknown whether the symptoms recovered within 7 days.
- **Carcinogenicity**: Not classifiable
- **Reproductive Toxicity**
  - In a test of pregnant mice exposed by inhalation during the period of organogenesis, fetal resorption and exencephaly were observed. In separate inhalation and oral exposure tests, similar results were obtained, including cleft palate.
  - As for the effect of methanol on reproduction, there is sufficient evidence to provide a strong presumption on the basis of sound scientific judgment that exposure to methanol may result in health impairment. Although the available data on humans are limited, there is clear evidence for effects on animals, and it is concluded that sufficient human exposure to methanol may result in adverse effects on human development. It is
accordingly assumed that it causes developmental toxicity to humans.

Specific Target Organ/Systemic Toxicity (Single Exposure)

Symptoms of acute intoxication in humans include central nervous system depression and metabolic acidosis resulting from formic acid accumulation in the blood. Symptoms such as vision disorders, blindness, headache, dizziness, nausea, vomiting, tachypnea, and coma can occur, in addition to death. Disorders in the central nervous system, specifically tremor and extrapyramidal paralysis, as well as cerebral white matter necrosis, have been reported. The visual organs are the primary target organs: eye disorders are distinctive clinical features of metabolic acidosis, in addition to headache, nausea, vomiting, tachypnea, and coma. Anesthesia is produced by inhalation exposure in mice, rats, and humans as a result of central nervous system depression.

Specific Target Organ/Systemic Toxicity (Repeated Exposure)

In humans, long-term exposure to low-concentration methanol causes eye damage: blindness is a toxic effect of chronic occupational methanol exposure. Chronic toxic symptoms caused by repeated exposure to methanol vapor include headache, dizziness, insomnia, and stomach disorders have been reported. Although changes in liver weight and hepatocyte hypertrophy have been reported in rats following oral administration, such changes are considered to be adaptive changes to methanol exposure.

Other

* For the toxicity information, due to no information as a mixture, it is originated from the information about raw materials.

The present product is stable under the normal condition, and there is no hazard such as eluting any harmful additive agent ingredients: however, in case of special handling such as its use under higher temperature, sufficient measures for safety should be taken.

12. Ecological Information

<table>
<thead>
<tr>
<th>Ecotoxicity</th>
<th>No data</th>
</tr>
</thead>
<tbody>
<tr>
<td>Persistence and Degradability</td>
<td>Easily degradable by microorganisms.</td>
</tr>
<tr>
<td>Bioaccumulative Potential</td>
<td>No data</td>
</tr>
<tr>
<td>Mobility in soil</td>
<td>No data</td>
</tr>
<tr>
<td>Influence to the ozone layer</td>
<td>No data</td>
</tr>
</tbody>
</table>

13. Disposal Considerations

Residual Waste : Incineration method

Incinerate in an incinerator equipped with scrubber.
Dispose in accordance with applicable legislation and local
government ordinance.
When the above-mentioned treatments are not possible, entrust disposal of this reference material to a professional waste disposal company licensed by local or national authority.

Contaminated Container and Package

Dispose of containers after thoroughly removing their contents.

14. Transport Information

| UN Number | 1230 |
| UN Classification | Class 3 |
| Shipping Name | METHANOL |
| Packing Group | PG II |
| ICAO/IATA | Class 8, grade II |
| Marine Pollutant | Hazardous Liquid Substance (Class Y Substance) |
| Precautions | Avoid direct sunlight and fire sources and transfer with care not to spill/leak by dropping or falling, etc. |

15. Regulatory Information

◇ Fire Service Act
   • Hazardous materials Category IV Alcohols Hazard Class II Water soluble
◇ Industrial Safety and Health Act
   • Article 57 (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. 560
   • Type 2 Organic Solvents (Order of Enforcement Appended Table 6-2 Ordinance on Prevention of Organic Solvent Poisoning Article 1 Section 1 Paragraph 4
   • Dangerous goods and flammable substances (Order of Enforcement Appended Table 1 Paragraph 4)
   • Criteria for assessment of the working environment (Article 65-2, Paragraph 1 of the Act)
◇ Regulations for the Carriage and Storage of Dangerous Goods in Ships
   • Flammable liquid (Dangerous Goods Regulations Article 3 Notification of Dangerous Goods Appended Table 1)
◇ Civil Aeronautics Act
   • Flammable liquid (Regulations for Enforcement Article 194 Notification of Dangerous Goods Appended Table 1)
◇ Act for the Prevention of Marine Pollution and Maritime Disasters
   • Order for Enforcement Appended Table 1 Noxious Liquid Substances Category Y Substance

◎ This SDS is originally prepared for the use of the material in Japan, thus the stated laws and regulations are stipulated and carried out in Japan. The use of the material in other countries should be referred to and by application of the relevant laws and regulations of the country in which the material will be used.
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.