SAFETY DATA SHEET

Interferon Alfa-2b Liquid Formulation

**1. PRODUCT AND COMPANY IDENTIFICATION**

Product name: Interferon Alfa-2b Liquid Formulation

**Manufacturer or supplier's details**

Company name of supplier: MSD

Address: Kumagaya, Saitama Prefecture, Xicheng 810 MSD Co., Ltd.

Menuma factory

Telephone: 048-588-8411

E-mail address: EHSDATASTEWARD@msd.com

Emergency telephone number: 1-908-423-6000

**Recommended use of the chemical and restrictions on use**

Recommended use: Pharmaceutical

**2. HAZARDS IDENTIFICATION**

**GHS Classification**

Reproductive toxicity: Category 1B

Specific target organ toxicity - repeated exposure: Category 2 (Blood, Bone marrow)

**GHS label elements**

Hazard pictograms:

Signal word: Danger

Hazard statements: H360FD May damage fertility. May damage the unborn child.

H373 May cause damage to organs (Blood, Bone marrow) through prolonged or repeated exposure.

Precautionary statements: Prevention:

P201 Obtain special instructions before use.

P202 Do not handle until all safety precautions have been read and understood.

P260 Do not breathe mist or vapours.

P280 Wear protective gloves/protective clothing/eye protection/face protection.

Response:

P308 + P313 IF exposed or concerned: Get medical advice/attention.
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Version 5.6  Revision Date: 09/13/2019  SDS Number: 42812-00011  Date of last issue: 2019/04/24  Date of first issue: 2015/01/07

Storage:
P405 Store locked up.

Disposal:
P501 Dispose of contents/ container to an approved waste disposal plant.

Other hazards which do not result in classification
None known.

3. COMPOSITION/INFORMATION ON INGREDIENTS

<table>
<thead>
<tr>
<th>Substance / Mixture</th>
<th>Components</th>
<th>Chemical name</th>
<th>CAS-No.</th>
<th>Concentration (% w/w)</th>
<th>ENCS No.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mixture</td>
<td>m-Cresol</td>
<td>108-39-4</td>
<td>&gt;= 0.1 - &lt; 0.25</td>
<td>3-499, 4-57</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Interferon alfa-2b</td>
<td>98530-12-2</td>
<td>&gt;= 0.001 - &lt; 0.1</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

4. FIRST AID MEASURES

General advice:
In the case of accident or if you feel unwell, seek medical advice immediately.
When symptoms persist or in all cases of doubt seek medical advice.

If inhaled:
If inhaled, remove to fresh air.
Get medical attention.

In case of skin contact:
In case of contact, immediately flush skin with soap and plenty of water.
Remove contaminated clothing and shoes.
Get medical attention.
Wash clothing before reuse.
Thoroughly clean shoes before reuse.

In case of eye contact:
Flush eyes with water as a precaution.
Get medical attention if irritation develops and persists.

If swallowed:
If swallowed, DO NOT induce vomiting.
Get medical attention.
Rinse mouth thoroughly with water.

Most important symptoms and effects, both acute and delayed:
May damage fertility. May damage the unborn child.
May cause damage to organs through prolonged or repeated exposure.

Protection of first-aiders:
First Aid responders should pay attention to self-protection, and use the recommended personal protective equipment when the potential for exposure exists (see section 8).

Notes to physician:
Treat symptomatically and supportively.

5. FIREFIGHTING MEASURES

Suitable extinguishing media:
Water spray
Alcohol-resistant foam
Carbon dioxide (CO2)
### 3. DRY CHEMICAL

**Unsuitable extinguishing media:** None known.

**Specific hazards during firefighting:** Exposure to combustion products may be a hazard to health.

**Hazardous combustion products:** No hazardous combustion products are known.

**Specific extinguishing methods:**
- Use extinguishing measures that are appropriate to local circumstances and the surrounding environment.
- Use water spray to cool unopened containers.
- Remove undamaged containers from fire area if it is safe to do so.
- Evacuate area.

**Special protective equipment for firefighters:**
- In the event of fire, wear self-contained breathing apparatus.
- Use personal protective equipment.

### 6. ACCIDENTAL RELEASE MEASURES

**Personal precautions, protective equipment and emergency procedures:**
- Use personal protective equipment.
- Follow safe handling advice and personal protective equipment recommendations.

**Environmental precautions:**
- Discharge into the environment must be avoided.
- Prevent further leakage or spillage if safe to do so.
- Prevent spreading over a wide area (e.g. by containment or oil barriers).
- Retain and dispose of contaminated wash water.
- Local authorities should be advised if significant spillages cannot be contained.

**Methods and materials for containment and cleaning up:**
- Soak up with inert absorbent material.
- For large spills, provide dyking or other appropriate containment to keep material from spreading. If dyked material can be pumped, store recovered material in appropriate container. Clean up remaining materials from spill with suitable absorbent.
- Local or national regulations may apply to releases and disposal of this material, as well as those materials and items employed in the cleanup of releases. You will need to determine which regulations are applicable.
- Sections 13 and 15 of this SDS provide information regarding certain local or national requirements.

### 7. HANDLING AND STORAGE

#### Handling

**Technical measures:**
- See Engineering measures under EXPOSURE CONTROLS/PERSONAL PROTECTION section.

**Local/Total ventilation:**
- If sufficient ventilation is unavailable, use with local exhaust ventilation.

**Advice on safe handling:**
- Do not get on skin or clothing.
- Do not breathe vapours or spray mist.
- Do not swallow.
Avoid contact with eyes.
Handle in accordance with good industrial hygiene and safety practice, based on the results of the workplace exposure assessment
Keep container tightly closed.
Take care to prevent spills, waste and minimize release to the environment.

Avoidance of contact: Oxidizing agents
Hygiene measures: If exposure to chemical is likely during typical use, provide eye flushing systems and safety showers close to the working place.
When using do not eat, drink or smoke.
Wash contaminated clothing before re-use.
The effective operation of a facility should include review of engineering controls, proper personal protective equipment, appropriate degowning and decontamination procedures, industrial hygiene monitoring, medical surveillance and the use of administrative controls.

Storage
Conditions for safe storage: Keep in properly labelled containers.
Store locked up.
Keep tightly closed.
Store in accordance with the particular national regulations.

Materials to avoid: Do not store with the following product types:
Strong oxidizing agents

Packaging material: Unsuitable material: None known.

8. EXPOSURE CONTROLS/PERSONAL PROTECTION

Threshold limit value and permissible exposure limits for each component in the work environment

<table>
<thead>
<tr>
<th>Components</th>
<th>CAS-No.</th>
<th>Value type (Form of exposure)</th>
<th>Control parameters / Permissible concentration</th>
<th>Basis</th>
</tr>
</thead>
<tbody>
<tr>
<td>m-Cresol</td>
<td>108-39-4</td>
<td>ACL</td>
<td>5 ppm</td>
<td>JP OEL ISHL</td>
</tr>
<tr>
<td></td>
<td></td>
<td>OEL-M</td>
<td>5 ppm 22 mg/m³</td>
<td>JP OEL JSOH</td>
</tr>
</tbody>
</table>

Further information: Skin absorption

Interferon alfa-2b 98530-12-2 TWA (Inhalable fraction and vapor) 20 mg/m³ ACGIH

Wipe limit 2 µg/100 cm² Internal

Engineering measures: Use closed processing systems or containment technologies to control at source (e.g., glove boxes/isolators) and to prevent leakage of compounds into the workplace.
All engineering controls should be implemented by facility design and operated in accordance with GMP principles to protect products, workers, and the environment.
No open handling permitted.
Totally enclosed processes and materials transport systems are required. Operations require the use of appropriate containment technology designed to prevent leakage of compounds into the workplace.

**Personal protective equipment**

Respiratory protection: No personal respiratory protective equipment normally required.

Hand protection

- Material: Chemical-resistant gloves

Remarks: Consider double gloving.

Eye protection: Wear safety glasses with side shields or goggles. If the work environment or activity involves dusty conditions, mists or aerosols, wear the appropriate goggles. Wear a faceshield or other full face protection if there is a potential for direct contact to the face with dusts, mists, or aerosols.

Skin and body protection: Work uniform or laboratory coat. Additional body garments should be used based upon the task being performed (e.g., sleevelets, apron, gauntlets, disposable suits) to avoid exposed skin surfaces. Use appropriate degowning techniques to remove potentially contaminated clothing.

### 9. PHYSICAL AND CHEMICAL PROPERTIES

- **Appearance**: liquid
- **Colour**: colourless
- **Odour**: No data available
- **Odour Threshold**: No data available
- **pH**: 6.5 - 8
- **Melting point/freezing point**: No data available
- **Initial boiling point and boiling range**: No data available
- **Flash point**: No data available
- **Evaporation rate**: No data available
- **Flammability (solid, gas)**: Not applicable
- **Flammability (liquids)**: No data available
- **Upper explosion limit / Upper flammability limit**: No data available
Lower explosion limit / Lower flammability limit: No data available
Vapour pressure: No data available
Relative vapour density: No data available
Relative density: No data available
Density: No data available
Solubility(ies)
Water solubility: No data available
Partition coefficient: n-octanol/water: Not applicable
Auto-ignition temperature: No data available
Decomposition temperature: No data available
Viscosity
Viscosity, kinematic: No data available
Explosive properties: Not explosive
Oxidizing properties: The substance or mixture is not classified as oxidizing.
Molecular weight: Not applicable
Particle size: Not applicable

10. STABILITY AND REACTIVITY
Reactivity: Not classified as a reactivity hazard.
Chemical stability: Stable under normal conditions.
Possibility of hazardous reactions: Can react with strong oxidizing agents.
Conditions to avoid: None known.
Incompatible materials: Oxidizing agents
Hazardous decomposition products: No hazardous decomposition products are known.

11. TOXICOLOGICAL INFORMATION
Information on likely routes of exposure:
- Inhalation
- Skin contact
- Ingestion
- Eye contact

Acute toxicity:
Not classified based on available information.

Product:
Acute oral toxicity: Acute toxicity estimate: > 2,000 mg/kg
Method: Calculation method

**Acute dermal toxicity**
- Acute toxicity estimate: > 2,000 mg/kg
- Method: Calculation method

**Components:**

**m-Cresol:**
- Acute oral toxicity: LD50 (Rat): 121 mg/kg
  - Remarks: Based on data from similar materials
- Acute inhalation toxicity: Assessment: Corrosive to the respiratory tract.
- Acute dermal toxicity: LD50 (Rabbit): 301 mg/kg
  - Remarks: Based on data from similar materials

**Skin corrosion/irritation**
- Not classified based on available information.

**Components:**

**m-Cresol:**
- Species: Rabbit
  - Result: Corrosive after 3 minutes to 1 hour of exposure

**Interferon alfa-2b:**
- Species: Rat
  - Result: Skin irritation

**Serious eye damage/eye irritation**
- Not classified based on available information.

**Components:**

**m-Cresol:**
- Species: Rabbit
  - Result: Irreversible effects on the eye

**Interferon alfa-2b:**
- Species: Rabbit
  - Remarks: slight irritation

**Respiratory or skin sensitisation**

**Skin sensitisation**
- Not classified based on available information.

**Respiratory sensitisation**
- Not classified based on available information.

**Germ cell mutagenicity**
- Not classified based on available information.
Components:

**m-Cresol:**
- Genotoxicity in vitro: Test Type: Chromosome aberration test in vitro, Method: OECD Test Guideline 473, Result: positive
- Test Type: Bacterial reverse mutation assay (AMES), Method: OECD Test Guideline 471, Result: negative
- Genotoxicity in vivo: Test Type: Mutagenicity (in vivo mammalian bone-marrow cytogenetic test, chromosomal analysis), Species: Mouse, Application Route: Ingestion, Method: OECD Test Guideline 475, Result: negative

**Interferon alfa-2b:**
- Genotoxicity in vitro: Test Type: Chromosome aberration test in vitro, Result: negative
- Test Type: Bacterial reverse mutation assay (AMES), Result: negative
- Genotoxicity in vivo: Test Type: Micronucleus test, Species: Mouse, Result: negative, Remarks: Based on data from similar materials

**Carcinogenicity**
Not classified based on available information.

Components:

**m-Cresol:**
- Species: Mouse, males
- Application Route: Ingestion
- Exposure time: 105 weeks
- Result: equivocal
- Remarks: Based on data from similar materials
- Species: Mouse, female
- Application Route: Ingestion
- Exposure time: 106 - 107 weeks
- Result: positive
- Remarks: Based on data from similar materials

**Carcinogenicity - Assessment:** Weight of evidence does not support classification as a carcinogen

**Reproductive toxicity**
May damage fertility. May damage the unborn child.
Components:

m-Cresol:
Effects on fertility : Test Type: Two-generation reproduction toxicity study
Species: Rat
Application Route: Ingestion
Result: negative

Effects on foetal development : Test Type: Prenatal development toxicity study (teratogenicity)
Species: Rat
Application Route: Ingestion
Result: negative

Interferon alfa-2b:
Effects on fertility : Test Type: Fertility/early embryonic development
Species: Monkey
Fertility: LOAEL: 3.8 µg/kg
Result: menstrual irregularities
Remarks: Abortion

Effects on foetal development : Test Type: Fertility/early embryonic development
Species: Monkey
Developmental Toxicity: LOAEL: 3.8 µg/kg body weight
Result: Embryolethal effects

Reproductive toxicity - Assessment : May damage fertility. May damage the unborn child.

STOT - single exposure
Not classified based on available information.

STOT - repeated exposure
May cause damage to organs (Blood, Bone marrow) through prolonged or repeated exposure.

Components:

Interferon alfa-2b:
Target Organs : Blood, Bone marrow
Assessment : May cause damage to organs through prolonged or repeated exposure.

Repeated dose toxicity
Components:

m-Cresol:
Species : Rat
NOAEL : 150 mg/kg
Application Route : Ingestion
Exposure time : 13 Weeks
Method : OECD Test Guideline 408

Interferon alfa-2b:
Species : Monkey
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NOAEL : 0.095 mg/kg  Application Route: Intramuscular  Exposure time: 1 Months  Remarks: No significant adverse effects were reported

Species : Rat  NOAEL : 0.38 mg/kg  Application Route: Subcutaneous  Exposure time: 3 Months  Remarks: No significant adverse effects were reported

Species : Mouse  NOAEL : 0.076 mg/kg  Application Route: Intraperitoneal  Exposure time: 9 d  Remarks: No significant adverse effects were reported

Species : Monkey  LOAEL : 0.38 mg/kg  Application Route: Intramuscular  Exposure time: 3 Months  Target Organs: Blood, Bone marrow  Remarks: Significant toxicity observed in testing

Aspiration toxicity
Not classified based on available information.

Experience with human exposure

Components:

Interferon alfa-2b:
Skin contact: Symptoms: The most common side effects are: flu-like symptoms, Fever, chills, Fatigue

12. ECOLOGICAL INFORMATION

Ecotoxicity

Components:

m-Cresol:
Toxicity to fish : LC50 (Oncorhynchus mykiss (rainbow trout)): 8.6 mg/l  Exposure time: 96 h

Toxicity to daphnia and other aquatic invertebrates : EC50 (Daphnia pulex (Water flea)): > 99.5 mg/l  Exposure time: 48 h

Toxicity to fish (Chronic toxicity) : NOEC (Pimephales promelas (fathead minnow)): 1.35 mg/l  Exposure time: 32 d  Remarks: Based on data from similar materials

Toxicity to daphnia and other aquatic invertebrates (Chronic toxicity) : NOEC (Daphnia magna (Water flea)): 1 mg/l  Exposure time: 21 d  Remarks: Based on data from similar materials
Persistence and degradability

Components:
m-Cresol:
Biodegradability: Result: Readily biodegradable.
Biodegradation: 90 %
Exposure time: 28 d
Method: OECD Test Guideline 301D

Bioaccumulative potential

Components:
m-Cresol:
Bioaccumulation: Species: Leuciscus idus (Golden orfe)
Bioconcentration factor (BCF): 17 - 20
Partition coefficient: n-octanol/water: log Pow: 1.96

Mobility in soil: No data available
Hazardous to the ozone layer: Not applicable
Other adverse effects: No data available

13. DISPOSAL CONSIDERATIONS

Disposal methods
Waste from residues: Dispose of in accordance with local regulations.
Contaminated packaging: Empty containers should be taken to an approved waste handling site for recycling or disposal.
If not otherwise specified: Dispose of as unused product.

14. TRANSPORT INFORMATION

International Regulations

UNRTDG: Not regulated as a dangerous good
IATA-DGR: Not regulated as a dangerous good
IMDG-Code: Not regulated as a dangerous good

Transport in bulk according to Annex II of MARPOL 73/78 and the IBC Code: Not applicable for product as supplied.
15. REGULATORY INFORMATION

Related Regulations

Fire Service Law
Not applicable to dangerous materials / designated flammables.

Chemical Substance Control Law
Priority Assessment Chemical Substance

<table>
<thead>
<tr>
<th>Chemical name</th>
<th>Number</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cresol</td>
<td>156</td>
</tr>
</tbody>
</table>

Industrial Safety and Health Law

Harmful Substances Prohibited from Manufacture
Not applicable

Harmful Substances Required Permission for Manufacture
Not applicable

Substances Prevented From Impairment of Health
Not applicable

Circular concerning Information on Chemicals having Mutagenicity - Annex 2: Information on Existing Chemicals having Mutagenicity
Not applicable

Circular concerning Information on Chemicals having Mutagenicity - Annex 1: Information on Notified Substances having Mutagenicity
Not applicable

Substances Subject to be Notified Names

Article 57-2 (Enforcement Order Table 9)

<table>
<thead>
<tr>
<th>Chemical name</th>
<th>Number</th>
<th>Concentration (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cresol</td>
<td>141</td>
<td>&gt;=0.1 - &lt;1</td>
</tr>
</tbody>
</table>

Substances Subject to be Indicated Names
Not applicable

Ordinance on Prevention of Hazards Due to Specified Chemical Substances
Not applicable

Ordinance on Prevention of Lead Poisoning
Not applicable

Ordinance on Prevention of Tetraalkyl Lead Poisoning
Not applicable

Ordinance on Prevention of Organic Solvent Poisoning
Not applicable

Enforcement Order of the Industrial Safety and Health Law - Attached table 1 (Dangerous Substances)
Not applicable
Poisonous and Deleterious Substances Control Law
Not applicable

Act on Confirmation, etc. of Release Amounts of Specific Chemical Substances in the Environment and Promotion of Improvements to the Management Thereof
Not applicable

High Pressure Gas Safety Act
Not applicable

Explosive Control Law
Not applicable

Vessel Safety Law
Not regulated as a dangerous good

Aviation Law
Not regulated as a dangerous good

Marine Pollution and Sea Disaster Prevention etc Law
Bulk transportation : Not classified as noxious liquid substance
Pack transportation : Not classified as marine pollutant

Narcotics and Psychotropics Control Act
Narcotic or Psychotropic Raw Material (Export / Import Permission)
Not applicable

Specific Narcotic or Psychotropic Raw Material (Export / Import permission)
Not applicable

Waste Disposal and Public Cleansing Law
Industrial waste

The components of this product are reported in the following inventories:
AICS : not determined
DSL : not determined
IECSC : not determined

16. OTHER INFORMATION

Further information
Date format : yyyy/mm/dd

Full text of other abbreviations
ACGIH : USA. ACGIH Threshold Limit Values (TLV)
JP OEL ISHL : Japan. Administrative Control Levels
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ACGIH / TWA : 8-hour, time-weighted average
JP OEL ISHL / ACL : Administrative Control level
JP OEL JSOH / OEL-M : Occupational Exposure Limit-Mean

AICS - Australian Inventory of Chemical Substances; ANTT - National Agency for Transport by Land of Brazil; ASTM - American Society for the Testing of Materials; bw - Body weight; CMR - Carcinogen, Mutagen or Reproductive Toxicant; DIN - Standard of the German Institute for Standardisation; DSL - Domestic Substances List (Canada); ECx - Concentration associated with x% response; ELx - Loading rate associated with x% response; EmS - Emergency Schedule; ENCS - Existing and New Chemical Substances (Japan); ErCx - Concentration associated with x% growth rate response; ERG - Emergency Response Guide; GHS - Globally Harmonized System; GLP - Good Laboratory Practice; IARC - International Agency for Research on Cancer; IATA - International Air Transport Association; IBC - International Code for the Construction and Equipment of Ships carrying Dangerous Chemicals in Bulk; IC50 - Half maximal inhibitory concentration; ICAO - International Civil Aviation Organization; IECSC - Inventory of Existing Chemical Substances in China; IMDG - International Maritime Dangerous Goods; IMO - International Maritime Organization; ISHL - Industrial Safety and Health Law (Japan); ISO - International Organisation for Standardization; KECI - Korea Existing Chemicals Inventory; LC50 - Lethal Concentration to 50 % of a test population; LD50 - Lethal Dose to 50% of a test population (Median Lethal Dose); MARPOL - International Convention for the Prevention of Pollution from Ships; n.o.s. - Not Otherwise Specified; Nch - Chilean Norm; NO(A)EC - No Observed (Adverse) Effect Concentration; NO(A)EL - No Observed (Adverse) Effect Level; NOELR - No Observable Effect Loading Rate; NOM - Official Mexican Norm; NTP - National Toxicology Program; NZIoC - New Zealand Inventory of Chemicals; OECD - Organization for Economic Co-operation and Development; OPPTS - Office of Chemical Safety and Pollution Prevention; PBT - Persistent, Bioaccumulative and Toxic substance; PICCS - Philippines Inventory of Chemicals and Chemical Substances; (Q)SAR - (Quantitative) Structure Activity Relationship; REACH - Regulation (EC) No 1907/2006 of the European Parliament and of the Council concerning the Registration, Evaluation, Authorisation and Restriction of Chemicals; SADT - Self-Accelerating Decomposition Temperature; SDS - Safety Data Sheet; TCSI - Taiwan Chemical Substance Inventory; TDG - Transportation of Dangerous Goods; TSCA - Toxic Substances Control Act (United States); UN - United Nations; UNRTDG - United Nations Recommendations on the Transport of Dangerous Goods; vPvB - Very Persistent and Very Bioaccumulative; WHMIS - Workplace Hazardous Materials Information System

The information provided in this Safety Data Sheet is correct to the best of our knowledge, information and belief at the date of its publication. The information is designed only as a guidance for safe handling, use, processing, storage, transportation, disposal and release and shall not be considered a warranty or quality specification of any type. The information provided relates only to the specific material identified at the top of this SDS and may not be valid when the SDS material is used in combination with any other materials or in any process, unless specified in the text. Material users should review the information and recommendations in the specific context of their intended manner of handling, use, processing and storage, including an assessment of the appropriateness of the SDS material in the user’s end product, if applicable.

JP / EN