SAFETY DATA SHEET

Insulin Glargine Formulation

SECTION 1. IDENTIFICATION

Product name: Insulin Glargine Formulation

Manufacturer or supplier's details
Company name of supplier: Merck & Co., Inc
Address: 126 E. Lincoln Avenue
Rahway, New Jersey U.S.A. 07065
Telephone: 908-740-4000
Emergency telephone: 1-908-423-6000
E-mail address: EHSDATASTEWARD@merck.com

Recommended use of the chemical and restrictions on use
Recommended use: Pharmaceutical
Restrictions on use: Not applicable

SECTION 2. HAZARDS IDENTIFICATION

GHS classification in accordance with the OSHA Hazard Communication Standard (29 CFR 1910.1200)
Combustible dust

Skin irritation: Category 2

Serious eye damage: Category 1

Specific target organ toxicity - repeated exposure (Oral): Category 2 (Blood, Nervous system)

GHS label elements
Hazard pictograms: 

Signal Word: Danger

Hazard Statements:
If small particles are generated during further processing, handling or by other means, may form combustible dust concentrations in air.
H315 Causes skin irritation.
H318 Causes serious eye damage.
H373 May cause damage to organs (Blood, Nervous system) through prolonged or repeated exposure if swallowed.

Precautionary Statements:
Prevention:
P260 Do not breathe dust.
P264 Wash skin thoroughly after handling.
P280 Wear protective gloves, eye protection and face protection.
Response:
P302 + P352 IF ON SKIN: Wash with plenty of soap and water.
P305 + P351 + P338 + P310 IF IN EYES: Rinse cautiously with water for several minutes. Remove contact lenses, if present and easy to do. Continue rinsing. Immediately call a POISON CENTER.
P314 Get medical attention if you feel unwell.
P332 + P313 If skin irritation occurs: Get medical attention.
P362 + P364 Take off contaminated clothing and wash it before reuse.

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

Other hazards
None known.

SECTION 3. COMPOSITION/INFORMATION ON INGREDIENTS

Substance / Mixture : Mixture

Components

<table>
<thead>
<tr>
<th>Chemical name</th>
<th>CAS-No.</th>
<th>Concentration (% w/w)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Insulin Glargine</td>
<td>160337-95-1</td>
<td>&gt;= 90 - &lt;= 100</td>
</tr>
<tr>
<td>m-Cresol</td>
<td>108-39-4</td>
<td>&gt;= 1 - &lt; 5</td>
</tr>
</tbody>
</table>

Actual concentration is withheld as a trade secret

SECTION 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 if symptoms occur.

In case of skin contact : In case of contact, immediately flush skin with plenty of water for at least 15 minutes while removing contaminated clothing and shoes.
Get medical attention.
Wash clothing before reuse.
Thoroughly clean shoes before reuse.

In case of eye contact : In case of contact, immediately flush eyes with plenty of water for at least 15 minutes.
If easy to do, remove contact lens, if worn.
Get medical attention immediately.

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

Most important symptoms and effects, both acute and delayed : Causes skin irritation.
Causes serious eye damage.
May cause damage to organs through prolonged or repeated
SECTION 5. FIRE-FIGHTING MEASURES

Suitable extinguishing media: Water spray
Alcohol-resistant foam
Carbon dioxide (CO2)
Dry chemical

Unsuitable extinguishing media: None known.

Specific hazards during firefighting: Avoid generating dust; fine dust dispersed in air in sufficient concentrations, and in the presence of an ignition source is a potential dust explosion hazard. Exposure to combustion products may be a hazard to health.

Hazardous combustion products: Carbon oxides

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 fire-fighters: In the event of fire, wear self-contained breathing apparatus.
Use personal protective equipment.

SECTION 6. ACCIDENTAL RELEASE MEASURES

Personal precautions, protective equipment and emergency procedures: Use personal protective equipment.
Follow safe handling advice (see section 7) and personal protective equipment recommendations (see section 8).

Environmental precautions: Avoid release to the environment.
Prevent further leakage or spillage if safe to do so.
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: Sweep up or vacuum up spillage and collect in suitable container for disposal.
Avoid dispersal of dust in the air (i.e., clearing dust surfaces with compressed air).
Dust deposits should not be allowed to accumulate on surfaces, as these may form an explosive mixture if they are released into the atmosphere in sufficient concentration.
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.

SECTION 7. HANDLING AND STORAGE

Technical measures: Static electricity may accumulate and ignite suspended dust causing an explosion. Provide adequate precautions, such as electrical grounding and bonding, or inert atmospheres.

Local/Total ventilation: Use only with adequate ventilation.

Advice on safe handling:
- Do not get on skin or clothing.
- Do not breathe dust.
- Do not swallow.
- Do not get in eyes.
- Wash skin thoroughly after handling.
- Handle in accordance with good industrial hygiene and safety practice, based on the results of the workplace exposure assessment
- Keep container tightly closed.
- Minimize dust generation and accumulation.
- Keep container closed when not in use.
- Keep away from heat and sources of ignition.
- Take precautionary measures against static discharges.
- Take care to prevent spills, waste and minimize release to the environment.

Conditions for safe storage:
- Keep in properly labeled containers.
- 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

SECTION 8. EXPOSURE CONTROLS/PERSONAL PROTECTION

Ingredients with workplace control parameters

<table>
<thead>
<tr>
<th>Inert or nuisance dust</th>
<th>50 Million particles per cubic foot</th>
</tr>
</thead>
<tbody>
<tr>
<td>Value type (Form of exposure): TWA (total dust)</td>
<td></td>
</tr>
<tr>
<td>Basis: OSHA Z-3</td>
<td></td>
</tr>
<tr>
<td>15 mg/m³</td>
<td></td>
</tr>
<tr>
<td>Value type (Form of exposure): TWA (total dust)</td>
<td></td>
</tr>
<tr>
<td>Basis: OSHA Z-3</td>
<td></td>
</tr>
<tr>
<td>5 mg/m³</td>
<td></td>
</tr>
<tr>
<td>Value type (Form of exposure): TWA (respirable fraction)</td>
<td></td>
</tr>
<tr>
<td>Basis: OSHA Z-3</td>
<td></td>
</tr>
<tr>
<td>15 Million particles per cubic foot</td>
<td></td>
</tr>
<tr>
<td>Value type (Form of exposure): TWA (respirable fraction)</td>
<td></td>
</tr>
<tr>
<td>Basis: OSHA Z-3</td>
<td></td>
</tr>
<tr>
<td>Dust, nuisance dust and particulates</td>
<td>10 mg/m³</td>
</tr>
<tr>
<td>Value type (Form of exposure): PEL (Total dust)</td>
<td></td>
</tr>
<tr>
<td>Basis: CAL PEL</td>
<td></td>
</tr>
</tbody>
</table>
5 mg/m³
Value type (Form of exposure): PEL (respirable dust fraction)
Basis: CAL PEL

<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>Insulin Glargine</td>
<td>160337-95-1</td>
<td>TWA</td>
<td>3 µg/m³ (OEB 4)</td>
<td>Internal</td>
</tr>
<tr>
<td>m-Cresol</td>
<td>108-39-4</td>
<td>TWA</td>
<td>2.3 ppm</td>
<td>NIOSH REL</td>
</tr>
<tr>
<td></td>
<td></td>
<td>TWA</td>
<td>5 ppm</td>
<td>OSHA Z-1</td>
</tr>
</tbody>
</table>

Engineering measures:
- Ensure adequate ventilation, especially in confined areas.
- Minimize workplace exposure concentrations.
- Apply measures to prevent dust explosions.
- Ensure that dust-handling systems (such as exhaust ducts, dust collectors, vessels, and processing equipment) are designed in a manner to prevent the escape of dust into the work area (i.e., there is no leakage from the equipment).

Personal protective equipment:
Respiratory protection:
- General and local exhaust ventilation is recommended to maintain vapor exposures below recommended limits. Where concentrations are above recommended limits or are unknown, appropriate respiratory protection should be worn. Follow OSHA respirator regulations (29 CFR 1910.134) and use NIOSH/MSHA approved respirators. Protection provided by air purifying respirators against exposure to any hazardous chemical is limited. Use a positive pressure air supplied respirator if there is any potential for uncontrolled release, exposure levels are unknown, or any other circumstance where air purifying respirators may not provide adequate protection.

Hand protection:
- Material: Chemical-resistant gloves
- Remarks: Choose gloves to protect hands against chemicals depending on the concentration specific to place of work. Breakthrough time is not determined for the product. Change gloves often! For special applications, we recommend clarifying the resistance to chemicals of the aforementioned protective gloves with the glove manufacturer. Wash hands before breaks and at the end of workday.

Eye protection:
- Wear the following personal protective equipment: Chemical resistant goggles must be worn. If splashes are likely to occur, wear: Face-shield

Skin and body protection:
- Select appropriate protective clothing based on chemical resistance data and an assessment of the local exposure.
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.

SECTION 9. PHYSICAL AND CHEMICAL PROPERTIES

Appearance: Crystalline powder
Color: white
Odor: No data available
Odor Threshold: No data available
pH: No data available
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): May form explosive dust-air mixture during processing, handling or other means.
Flammability (liquids): No data available
Upper explosion limit / Upper flammability limit: No data available
Lower explosion limit / Lower flammability limit: No data available
Vapor pressure: No data available
Relative vapor density: No data available
Density: No data available
Solubility(ies)
   Water solubility: No data available
Partition coefficient: n-octanol/water: No data available
Autoignition temperature: No data available
Decomposition temperature: No data available
SECTION 10. STABILITY AND REACTIVITY

Reactivity : Not classified as a reactivity hazard.
Chemical stability : Stable under normal conditions.
Possibility of hazardous reactions : May form explosive dust-air mixture during processing, handling or other means. Can react with strong oxidizing agents.

Conditions to avoid : Heat, flames and sparks. Avoid dust formation.
Incompatible materials : Oxidizing agents
Hazardous decomposition products : No hazardous decomposition products are known.

SECTION 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: 3,025 mg/kg
Method: Calculation method

Acute dermal toxicity : Acute toxicity estimate: > 5,000 mg/kg
Method: Calculation method

Components:
Insulin Glargine:
Acute oral toxicity : Remarks: No data available
Acute inhalation toxicity : Remarks: No data available
Acute dermal toxicity : Remarks: No data available
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**

Causes skin irritation.

**Components:**

- **Insulin Glargine**:
  - Remarks: No data available

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

**Serious eye damage/eye irritation**

Causes serious eye damage.

**Components:**

- **Insulin Glargine**:
  - Remarks: No data available

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

**Respiratory or skin sensitization**

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

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

**Components:**

- **Insulin Glargine**:
  - Remarks: No data available

**Germ cell mutagenicity**

Not classified based on available information.

**Components:**

- **Insulin Glargine**:
**Genotoxicity in vitro**
- Test Type: Bacterial reverse mutation assay (AMES)
  - Result: negative
  - Remarks: Based on data from similar materials
- Test Type: In vitro mammalian cell gene mutation test
  - Result: negative
  - Remarks: Based on data from similar materials
- Test Type: Chromosome aberration test in vitro
  - Result: negative
  - Remarks: Based on data from similar materials

**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

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

**Components:**

**Insulin Glargine:**
- Species: Rat
- Exposure time: 2 Years
- NOAEL: 0.455 mg/kg body weight
- Result: negative

**Species:**
- Species: Mouse
- Exposure time: 2 Years
- NOAEL: 0.455 mg/kg body weight
- Result: negative

**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

IARC: No ingredient of this product present at levels greater than or equal to 0.1% is identified as probable, possible or confirmed human carcinogen by IARC.

OSHA: No component of this product present at levels greater than or equal to 0.1% is on OSHA’s list of regulated carcinogens.

NTP: No ingredient of this product present at levels greater than or equal to 0.1% is identified as a known or anticipated carcinogen by NTP.

Reproductive toxicity
Not classified based on available information.

Components:

Insulin Glargine:

Effects on fertility: Test Type: Fertility/early embryonic development
Species: Rat
Application Route: Subcutaneous
Fertility: NOAEL: 0.36 mg/kg body weight
Result: No effects on fertility.

Species: Rabbit
Application Route: Subcutaneous
Fertility: NOAEL: 0.072 mg/kg body weight
Result: No effects on fertility.

Effects on fetal development: Test Type: Embryo-fetal development
Species: Rat
Application Route: Subcutaneous
Developmental Toxicity: NOAEL: 0.36 mg/kg body weight
Result: No effects on fetal development.

Species: Rabbit
Application Route: Subcutaneous
Developmental Toxicity: LOAEL: 0.072 mg/kg body weight
Result: Fetotoxicity.
Remarks: The mechanism or mode of action may not be relevant in humans.

m-Cresol:

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

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

**STOT-single exposure**
Not classified based on available information.

**STOT-repeated exposure**
May cause damage to organs (Blood, Nervous system) through prolonged or repeated exposure if swallowed.

**Components:**

**Insulin Glargine:**
- Routes of exposure: Ingestion
- Target Organs: Blood, Nervous system
- Assessment: May cause damage to organs through prolonged or repeated exposure.

**Repeated dose toxicity**

**Components:**

**Insulin Glargine:**
- Species: Rat
- NOAEL: 0.5 mg/kg
- LOAEL: 1.5 mg/kg
- Application Route: Subcutaneous
- Exposure time: 30 d
- Target Organs: Blood, Nervous system

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

**Aspiration toxicity**
Not classified based on available information.

**Experience with human exposure**

**Components:**

**Insulin Glargine:**
- Inhalation: Target Organs: Blood
  Symptoms: Hypoglycemia, Headache, Sweating, Tremors, Nausea
SECTION 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

Other adverse effects
No data available

SECTION 13. DISPOSAL CONSIDERATIONS

Disposal methods

Waste from residues: Dispose of in accordance with local regulations.
Do not dispose of waste into sewer.

Contaminated packaging: Empty containers should be taken to an approved waste
SECTION 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.

Domestic regulation

49 CFR
UN/ID/NA number: UN 3077
Proper shipping name: Environmentally hazardous substance, solid, n.o.s.
(m-Cresol)
Class: 9
Packing group: III
Labels: CLASS 9
ERG Code: 171
Marine pollutant: no
Remarks: THE ABOVE INFORMATION ONLY APPLIES TO PACKAGE SIZES WHERE THE HAZARDOUS SUBSTANCE MEETS THE REPORTABLE QUANTITY.

Special precautions for user
The transport classification(s) provided herein are for informational purposes only, and solely based upon the properties of the unpackaged material as it is described within this Safety Data Sheet. Transportation classifications may vary by mode of transportation, package sizes, and variations in regional or country regulations.

SECTION 15. REGULATORY INFORMATION

CERCLA Reportable Quantity

<table>
<thead>
<tr>
<th>Components</th>
<th>CAS-No.</th>
<th>Component RQ (lbs)</th>
<th>Calculated product RQ (lbs)</th>
</tr>
</thead>
<tbody>
<tr>
<td>m-Cresol</td>
<td>108-39-4</td>
<td>100</td>
<td>2500</td>
</tr>
</tbody>
</table>

SARA 304 Extremely Hazardous Substances Reportable Quantity
This material does not contain any components with a section 304 EHS RQ.

SARA 302 Extremely Hazardous Substances Threshold Planning Quantity
This material does not contain any components with a section 302 EHS TPQ.

SARA 311/312 Hazards:
- Combustible dust
- Specific target organ toxicity (single or repeated exposure)
- Skin corrosion or irritation
- Serious eye damage or eye irritation
SARA 313: The following components are subject to reporting levels established by SARA Title III, Section 313:

- m-Cresol 108-39-4 >= 1 - < 5 %

US State Regulations

Pennsylvania Right To Know

Insulin Glargine 160337-95-1
m-Cresol 108-39-4

California List of Hazardous Substances

m-Cresol 108-39-4

California Permissible Exposure Limits for Chemical Contaminants

m-Cresol 108-39-4

The ingredients of this product are reported in the following inventories:

- AICS: not determined
- DSL: not determined
- IECSC: not determined

SECTION 16. OTHER INFORMATION

Further information

NFPA 704:

Flammability

Health

3

Special hazard

Instability

0

USA. ACGIH Threshold Limit Values (TLV)

CAL PEL: California permissible exposure limits for chemical contami-
Insulin Glargine Formulation

Sources of key data used to compile the Material Safety Data Sheet:

Revision Date: 04/04/2023

Items where changes have been made to the previous version are highlighted in the body of this document by two vertical lines.
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.

US / Z8