SECTION 1. IDENTIFICATION

Product name : Insulin Glargine Formulation
Other means of identification : No data available

Manufacturer or supplier’s details
Company name of supplier : Merck & Co., Inc
Address : 2000 Galloping Hill Road
          Kenilworth - New Jersey - U.S.A. 07033
Telephone : 908-740-4000
Telefax : 908-735-1496
Emergency telephone : 1-908-423-6000
E-mail address : EHSDATASTEWARD@merck.com

Recommended use of the chemical and restrictions on use
Recommended use : Pharmaceutical

SECTION 2. HAZARDS IDENTIFICATION

GHS classification in accordance with the Hazardous Products Regulations
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 : 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/ fume/ gas/ mist/ vapors/ spray.
P264 Wash skin thoroughly after handling.
P280 Wear protective gloves/ eye protection/ face protection.
Response:
P302 + P352 IF ON SKIN: Wash with plenty of 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/doctor.
P314 Get medical advice/ attention if you feel unwell.
Other hazards
May form explosive dust-air mixture during processing, handling or other means.

SECTION 3. COMPOSITION/INFORMATION ON INGREDIENTS

<table>
<thead>
<tr>
<th>Substance / Mixture</th>
<th>Components</th>
</tr>
</thead>
<tbody>
<tr>
<td>Insulin Glargine</td>
<td>Chemical name</td>
</tr>
<tr>
<td></td>
<td>Insulin Glargine</td>
</tr>
<tr>
<td></td>
<td>m-Cresol</td>
</tr>
</tbody>
</table>

Actual concentration or concentration range 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 exposure if swallowed.

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

Unsuitable extinguishing media: None known.

Specific hazards during fire fighting: 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.

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.

Hazardous combustion products: Carbon oxides

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 and personal protective equipment recommendations.

Environmental precautions: Discharge into the environment must be avoided. 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.
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>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>50 µg/m³</td>
<td>Internal</td>
</tr>
<tr>
<td></td>
<td>TWA</td>
<td>TWA</td>
<td>50 µg/m³ (OEB 3)</td>
<td>Internal</td>
</tr>
<tr>
<td>m-Cresol</td>
<td>108-39-4</td>
<td>TWA</td>
<td>5 ppm 22 mg/m³</td>
<td>CA AB OEL</td>
</tr>
<tr>
<td></td>
<td></td>
<td>TWA</td>
<td>5 ppm 22 mg/m³</td>
<td>CA BC OEL</td>
</tr>
<tr>
<td></td>
<td></td>
<td>TWA (Inhalable fraction and vapor)</td>
<td>20 mg/m³</td>
<td>ACGIH</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:
- If adequate local exhaust ventilation is not available or exposure assessment demonstrates exposures outside the recommended guidelines, use respiratory protection.

Filter type:
- Combined particulates and organic vapor type
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 potential.
Skin contact must be avoided by using impervious protective clothing (gloves, aprons, boots, etc).

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
SAFETY DATA SHEET

Insulin Glargine Formulation

Version 3.2  Revision Date: 09/13/2019  SDS Number: 42877-00016  Date of last issue: 04/24/2019
Date of first issue: 01/07/2015

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
Viscosity
  Viscosity, kinematic: No data available
Explosive properties: Not explosive
Oxidizing properties: The substance or mixture is not classified as oxidizing.
Molecular weight: No data available
Particle size: 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: 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

**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.

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

Effects on 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 rele-
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.
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.

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
TDG
Not regulated as a dangerous good

SECTION 15. REGULATORY INFORMATION

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

SECTION 16. OTHER INFORMATION

Full text of other abbreviations
ACGIH : USA. ACGIH Threshold Limit Values (TLV)
CA BC OEL : Canada. British Columbia OEL
CA QC OEL : Québec. Regulation respecting occupational health and safety, Schedule 1, Part 1: Permissible exposure values for airborne contaminants
ACGIH / TWA : 8-hour, time-weighted average
CA AB OEL / TWA : 8-hour Occupational exposure limit
Sources of key data used to compile the Material Safety Data Sheet: