SECTION 1: Identification of the substance/mixture and of the company/undertaking

1.1 Product identifier
   Trade name : Insulin Glargine Formulation

1.2 Relevant identified uses of the substance or mixture and uses advised against
   Use of the Substance/Mixture : Pharmaceutical

1.3 Details of the supplier of the safety data sheet
   Company : MSD
             117 16th Road
             07033 Halfway house, Midrand, South Africa
   Telephone : +27 11 655 3000
   Telefax : 908-735-1496
   E-mail address of person responsible for the SDS : EHSDATASTEWARD@msd.com

1.4 Emergency telephone number
   1-908-423-6000

SECTION 2: Hazards identification

2.1 Classification of the substance or mixture
   Classification (REGULATION (EC) No 1272/2008)
   Skin irritation, Category 2 : H315: Causes skin irritation.
   Serious eye damage, Category 1 : H318: Causes serious eye damage.
   Specific target organ toxicity - repeated exposure, Category 2 : H373: May cause damage to organs through prolonged or repeated exposure.

2.2 Label elements
   Labelling (REGULATION (EC) No 1272/2008)
   Hazard pictograms : 
   Signal word : Danger
   Hazard statements : H315 Causes skin irritation.
                      H318 Causes serious eye damage.
                      H373 May cause damage to organs through prolonged or repeated exposure.
   Precautionary statements : Prevention:
Hazardous components which must be listed on the label:
Insulin Glargine
m-Cresol

2.3 Other hazards
May form explosive dust-air mixture during processing, handling or other means.

SECTION 3: Composition/information on ingredients

3.2 Mixtures

<table>
<thead>
<tr>
<th>Components</th>
<th>CAS-No.</th>
<th>EC-No.</th>
<th>Index-No.</th>
<th>Classification</th>
<th>Concentration (% w/w)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Insulin Glargine</td>
<td>160337-95-1</td>
<td></td>
<td></td>
<td>STOT RE2; H373</td>
<td>&gt;= 90 - &lt;= 100</td>
</tr>
<tr>
<td>m-Cresol</td>
<td>108-39-4 203-577-9 604-004-00-9</td>
<td></td>
<td></td>
<td>Acute Tox.3; H301 Acute Tox.3; H311 Skin Corr.1B; H314 Eye Dam.1; H318 Aquatic Chronic3; H412</td>
<td>&gt;= 3 - &lt; 5</td>
</tr>
</tbody>
</table>

For explanation of abbreviations see section 16.

SECTION 4: First aid measures

4.1 Description of 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.

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).

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.

4.2 Most important symptoms and effects, both acute and delayed
Risks: Causes skin irritation.
Causes serious eye damage.
May cause damage to organs through prolonged or repeated exposure.

4.3 Indication of any immediate medical attention and special treatment needed
Treatment: Treat symptomatically and supportively.

SECTION 5: Firefighting measures

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

Unsuitable extinguishing media: None known.

5.2 Special hazards arising from the substance or mixture
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

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

SECTION 6: Accidental release measures

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

6.2 Environmental precautions
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.

6.3 Methods and material for containment and cleaning up
Methods for 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.

6.4 Reference to other sections
See sections: 7, 8, 11, 12 and 13.

SECTION 7: Handling and storage

7.1 Precautions for safe handling
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.

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.

7.2 Conditions for safe storage, including any incompatibilities
Requirements for storage areas and containers: Keep in properly labelled containers. Keep tightly closed. Store in accordance with the particular national regulations.
Advice on common storage: Do not store with the following product types: Strong oxidizing agents

7.3 Specific end use(s)
Specific use(s): No data available

SECTION 8: Exposure controls/personal protection

8.1 Control parameters

Occupational Exposure Limits

<table>
<thead>
<tr>
<th>Components</th>
<th>CAS-No.</th>
<th>Value type (Form of exposure)</th>
<th>Control parameters</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>m-Cresol</td>
<td>108-39-4</td>
<td>TWA OEL-RL</td>
<td>5 ppm, 22 mg/m³</td>
<td>ZA OEL</td>
</tr>
</tbody>
</table>

Further information: Absorption through the skin, Recommended Limit

Derived No Effect Level (DNEL) according to Regulation (EC) No. 1907/2006:

<table>
<thead>
<tr>
<th>Substance name</th>
<th>End Use</th>
<th>Exposure routes</th>
<th>Potential health effects</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>m-Cresol</td>
<td>Workers</td>
<td>Inhalation</td>
<td>Long-term systemic effects</td>
<td>3,5 mg/m³</td>
</tr>
<tr>
<td></td>
<td>Workers</td>
<td>Inhalation</td>
<td>Acute systemic effects</td>
<td>343 mg/m³</td>
</tr>
<tr>
<td></td>
<td>Workers</td>
<td>Skin contact</td>
<td>Long-term systemic effects</td>
<td>0,5 mg/kg bw/day</td>
</tr>
<tr>
<td></td>
<td>Workers</td>
<td>Skin contact</td>
<td>Acute systemic effects</td>
<td>1,47 mg/kg bw/day</td>
</tr>
<tr>
<td></td>
<td>Consumers</td>
<td>Inhalation</td>
<td>Long-term systemic effects</td>
<td>0,75 mg/m³</td>
</tr>
</tbody>
</table>
Consumers | Inhalation | Acute systemic effects | 222 mg/m³
---|---|---|---
Consumers | Skin contact | Long-term systemic effects | 0,25 mg/kg bw/day
Consumers | Skin contact | Acute systemic effects | 0,74 mg/kg bw/day
Consumers | Ingestion | Long-term systemic effects | 0,25 mg/kg bw/day
Consumers | Ingestion | Acute systemic effects | 0,74 mg/kg bw/day

**Predicted No Effect Concentration (PNEC) according to Regulation (EC) No. 1907/2006:**

<table>
<thead>
<tr>
<th>Substance name</th>
<th>Environmental Compartment</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>m-Cresol</td>
<td>Fresh water</td>
<td>0,1 mg/l</td>
</tr>
<tr>
<td></td>
<td>Marine water</td>
<td>0,01 mg/l</td>
</tr>
<tr>
<td></td>
<td>Intermittent use/release</td>
<td>0,076 mg/l</td>
</tr>
<tr>
<td></td>
<td>Sewage treatment plant</td>
<td>1,14 mg/l</td>
</tr>
<tr>
<td></td>
<td>Fresh water sediment</td>
<td>0,71 mg/kg</td>
</tr>
<tr>
<td></td>
<td>Marine sediment</td>
<td>0,071 mg/kg</td>
</tr>
<tr>
<td></td>
<td>Soil</td>
<td>0,0831 mg/kg</td>
</tr>
</tbody>
</table>

**8.2 Exposure controls**

**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**

**Eye protection**

Wear the following personal protective equipment:

Chemical resistant goggles must be worn.

If splashes are likely to occur, wear:

Face-shield

**Hand protection**

Material: Chemical-resistant gloves

**Remarks**

Choose gloves to protect hands against chemicals depending on the concentration and quantity of the hazardous substance and 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.

**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).

**Respiratory protection**

If adequate local exhaust ventilation is not available or exposure assessment demonstrates exposures outside the rec-
**SAFETY DATA SHEET**

**Insulin Glargine Formulation**

<table>
<thead>
<tr>
<th>Version</th>
<th>Revision Date:</th>
<th>SDS Number:</th>
<th>Date of last issue:</th>
<th>Date of first issue:</th>
</tr>
</thead>
<tbody>
<tr>
<td>3.2</td>
<td>09/13/2019</td>
<td>42896-00016</td>
<td>24.04.2019</td>
<td>07.01.2015</td>
</tr>
</tbody>
</table>

**Filter type**
- Recommended guidelines, use respiratory protection.
  - Filter type: Combined particulates and organic vapour type (A-P)

### SECTION 9: Physical and chemical properties

#### 9.1 Information on basic physical and chemical properties

- **Appearance**: Crystalline powder
- **Colour**: white
- **Odour**: No data available
- **Odour 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.
- **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
- **Density**: No data available
- **Solubility(ies)**:
  - **Water solubility**: No data available
  - **Partition coefficient: n-octanol/water**: No data available
  - **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.

#### 9.2 Other information

- **Flammability (liquids)**: No data available
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Molecular weight: No data available
Particle size: No data available

SECTION 10: Stability and reactivity

10.1 Reactivity
Not classified as a reactivity hazard.

10.2 Chemical stability
Stable under normal conditions.

10.3 Possibility of hazardous reactions
May form explosive dust-air mixture during processing, handling or other means.
Can react with strong oxidizing agents.

10.4 Conditions to avoid
Heat, flames and sparks. Avoid dust formation.

10.5 Incompatible materials
Oxidizing agents

10.6 Hazardous decomposition products
No hazardous decomposition products are known.

SECTION 11: Toxicological information

11.1 Information on toxicological effects
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:
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 sensitisation

### Skin sensitisation
Not classified based on available information.

### Respiratory sensitisation
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 foetal development:
- Test Type: Embryo-foetal development
  - Species: Rat
  - Application Route: Subcutaneous
  - Developmental Toxicity: NOAEL: 0.36 mg/kg body weight
  - Result: No effects on foetal 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 foetal 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 through prolonged or repeated exposure.

Components:
Insulin Glargine:
Exposure routes : 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

12.1 Toxicity

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: 1,35 mg/l
Exposure time: 32 d
Species: Pimephales promelas (fathead minnow)
Remarks: Based on data from similar materials

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

12.2 Persistence and degradability

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

12.3 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

12.4 Mobility in soil
No data available

12.5 Results of PBT and vPvB assessment
Not relevant

12.6 Other adverse effects
No data available

SECTION 13: Disposal considerations

13.1 Waste treatment methods
Product: Dispose of in accordance with local regulations.
According to the European Waste Catalogue, Waste Codes are not product specific, but application specific.
Waste codes should be assigned by the user, preferably in discussion with the waste disposal authorities.

Contaminated packaging: Empty containers should be taken to an approved waste handling site for recycling or disposal.
SECTION 14: Transport information

14.1 UN number
Not regulated as a dangerous good

14.2 UN proper shipping name
Not regulated as a dangerous good

14.3 Transport hazard class(es)
Not regulated as a dangerous good

14.4 Packing group
Not regulated as a dangerous good

14.5 Environmental hazards
Not regulated as a dangerous good

14.6 Special precautions for user
Not applicable

14.7 Transport in bulk according to Annex II of Marpol and the IBC Code
Remarks : Not applicable for product as supplied.

SECTION 15: Regulatory information

15.1 Safety, health and environmental regulations/legislation specific for the substance or mixture

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

15.2 Chemical safety assessment
A Chemical Safety Assessment has not been carried out.

SECTION 16: Other information

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

Full text of H-Statements

H301 : Toxic if swallowed.
H311 : Toxic in contact with skin.
H314 : Causes severe skin burns and eye damage.
H318 : Causes serious eye damage.
H373 : May cause damage to organs through prolonged or repeated exposure if swallowed.
H412 : Harmful to aquatic life with long lasting effects.
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Full text of other abbreviations

Acute Tox. : Acute toxicity
Aquatic Chronic : Long-term (chronic) aquatic hazard
Eye Dam. : Serious eye damage
Skin Corr. : Skin corrosion
STOT RE : Specific target organ toxicity - repeated exposure
ZA OEL : South Africa. Hazardous Chemical Substances Regulations, Occupational Exposure Limits
ZA OEL / TWA OEL-RL : Long term occupational exposure limits - recommended limit

Further information

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


Classification of the mixture:

<table>
<thead>
<tr>
<th>Class</th>
<th>Code</th>
</tr>
</thead>
<tbody>
<tr>
<td>Skin Irrit. 2</td>
<td>H315</td>
</tr>
<tr>
<td>Eye Dam. 1</td>
<td>H318</td>
</tr>
<tr>
<td>STOT RE 2</td>
<td>H373</td>
</tr>
</tbody>
</table>

Classification procedure:

- Calculation method
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.