SAFETY DATA SHEET 
according to Regulation (EC) No. 1907/2006

Simvastatin Formulation

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

1.1 Product identifier

Trade name : Simvastatin 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
Shotton Lane
NE23 3JU Cramlington NU - Great Britain

Telephone : 44 1 670 59 30 00
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 sensitisation, Category 1
Specific target organ toxicity - repeated exposure, Category 2
Long-term (chronic) aquatic hazard, Category 3

H317: May cause an allergic skin reaction.
H373: May cause damage to organs through prolonged or repeated exposure.
H412: Harmful to aquatic life with long lasting effects.

2.2 Label elements

Labelling (REGULATION (EC) No 1272/2008)

Hazard pictograms : 

Signal word : Warning

Hazard statements : H317 May cause an allergic skin reaction.
H373 May cause damage to organs through prolonged or repeated exposure.
H412 Harmful to aquatic life with long lasting effects.
Precautionary statements:

**Prevention:**
- P260 Do not breathe dust.
- P273 Avoid release to the environment.
- P280 Wear protective gloves.

**Response:**
- P314 Get medical advice/attention if you feel unwell.
- P333 + P313 If skin irritation or rash occurs: Get medical advice/attention.
- P362 + P364 Take off contaminated clothing and wash it before reuse.

Hazardous components which must be listed on the label:

**Simvastatin**

2.3 **Other hazards**

Dust contact with the eyes can lead to mechanical irritation.
May form explosive dust-air mixture during processing, handling or other means.

### SECTION 3: Composition/information on ingredients

3.2 **Mixtures**

**Components**

<table>
<thead>
<tr>
<th>Chemical name</th>
<th>CAS-No.</th>
<th>EC-No.</th>
<th>Index-No.</th>
<th>Registration number</th>
<th>Classification</th>
<th>Concentration (% w/w)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Simvastatin</td>
<td>79902-63-9</td>
<td></td>
<td></td>
<td></td>
<td>Skin Irrit.2; H315 Skin Sens.1; H317 STOT RE1; H372 Aquatic Chronic2; H411</td>
<td>&gt;= 2,5 - &lt; 10</td>
</tr>
<tr>
<td>Citric acid monohydrate</td>
<td>5949-29-1</td>
<td></td>
<td></td>
<td></td>
<td>Eye Irrit.2; H319</td>
<td>&gt;= 1 - &lt; 10</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.
In case of skin contact: In case of contact, immediately flush skin with 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: If in eyes, rinse well with water. Get medical attention if irritation develops and persists.

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: May cause an allergic skin reaction. May cause damage to organs through prolonged or repeated exposure.

Dust contact with the eyes can lead to mechanical irritation.

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. Avoid contact with eyes. Handle in accordance with good industrial hygiene and safety
### 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.

### 7.2 Conditions for safe storage, including any incompatibilities

- **Requirements for storage areas and containers**: Keep in properly labelled containers. Store in accordance with the particular national regulations.
- **Advice on common storage**: Do not store with the following product types:
  - Strong oxidizing agents
  - Organic peroxides
  - Explosives
  - Gases

### 7.3 Specific end use(s)

- **Specific use(s)**: No data available

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### 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>Simvastatin</td>
<td>79902-63-9</td>
<td>TWA</td>
<td>25 µg/m³ (OEB 3)</td>
<td>Internal</td>
</tr>
<tr>
<td>Further information</td>
<td>DSEN</td>
<td>Wipe limit</td>
<td>250 µg/100 cm²</td>
<td>Internal</td>
</tr>
</tbody>
</table>

**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>Citric acid monohydrate</td>
<td>Fresh water</td>
<td>0,44 mg/l</td>
</tr>
<tr>
<td></td>
<td>Marine water</td>
<td>0,044 mg/l</td>
</tr>
<tr>
<td></td>
<td>Sewage treatment plant</td>
<td>1000 mg/l</td>
</tr>
<tr>
<td></td>
<td>Fresh water sediment</td>
<td>34,6 mg/kg dry weight (d.w.)</td>
</tr>
<tr>
<td></td>
<td>Marine sediment</td>
<td>3,46 mg/kg dry weight (d.w.)</td>
</tr>
</tbody>
</table>
Simvastatin Formulation

SECTION 9: Physical and chemical properties

9.1 Information on basic physical and chemical properties

<table>
<thead>
<tr>
<th>Property</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Appearance</td>
<td>powder</td>
</tr>
<tr>
<td>Colour</td>
<td>No data available</td>
</tr>
<tr>
<td>Odour</td>
<td>odourless</td>
</tr>
<tr>
<td>Odour Threshold</td>
<td>No data available</td>
</tr>
<tr>
<td>pH</td>
<td>No data available</td>
</tr>
<tr>
<td>Melting point/freezing point</td>
<td>No data available</td>
</tr>
<tr>
<td>Initial boiling point and boiling range</td>
<td>No data available</td>
</tr>
<tr>
<td>Flash point</td>
<td>Not applicable</td>
</tr>
<tr>
<td>Evaporation rate</td>
<td>Not applicable</td>
</tr>
</tbody>
</table>

8.2 Exposure controls

Engineering measures

All engineering controls should be implemented by facility design and operated in accordance with GMP principles to protect products, workers, and the environment.

Containment technologies suitable for controlling compounds are required to control at source and to prevent migration of the compound to uncontrolled areas (e.g., open-face containment devices).

Minimize open handling.

Personal protective equipment

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.

Hand protection

Material: Chemical-resistant gloves

Remarks: Consider double gloving.

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.

Respiratory protection

If adequate local exhaust ventilation is not available or exposure assessment demonstrates exposures outside the recommended guidelines, use respiratory protection.

Filter type: Particulates type (P)
Simvastatin Formulation

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 : Not applicable
Relative vapour density : Not applicable
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 : Not applicable
Explosive properties : Not explosive
Oxidizing properties : The substance or mixture is not classified as oxidizing.

9.2 Other information
Flammability (liquids) : 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
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
Conditions to avoid : Heat, flames and sparks.
Avoid dust formation.

10.5 Incompatible materials
Materials to avoid: Oxidizing agents

10.6 Hazardous decomposition products
No hazardous decomposition products are known.

SECTION 11: Toxicological information

11.1 Information on toxicological effects
Information on likely routes of exposure:
Inhalation
Skin contact
Ingestion
Eye contact

Acute toxicity
Not classified based on available information.

Components:

Simvastatin:
Acute oral toxicity: LD50 (Rat): 5.000 mg/kg
LD50 (Mouse): 3.800 mg/kg

Citric acid monohydrate:
Acute oral toxicity: LD50 (Mouse): 5.400 mg/kg
Acute dermal toxicity: LD50 (Rat): > 2.000 mg/kg
Method: OECD Test Guideline 402
Assessment: The substance or mixture has no acute dermal toxicity

Skin corrosion/irritation
Not classified based on available information.

Components:

Simvastatin:
Species: Rabbit
Remarks: Moderate skin irritation

Citric acid monohydrate:
Species: Rabbit
Result: No skin irritation

Serious eye damage/eye irritation
Not classified based on available information.
Simvastatin Formulation

Components:

Simvastatin:
Species : Rabbit
Remarks : slight irritation

Citric acid monohydrate:
Species : Rabbit
Result : Irritation to eyes, reversing within 21 days

Respiratory or skin sensitisation
Skin sensitisation
May cause an allergic skin reaction.

Respiratory sensitisation
Not classified based on available information.

Components:

Simvastatin:
Assessment : Probability or evidence of skin sensitisation in humans
Result : positive

Germ cell mutagenicity
Not classified based on available information.

Components:

Simvastatin:
Genotoxicity in vitro : Test Type: Bacterial reverse mutation assay (AMES)
Result: negative
Test Type: Alkaline elution assay
Result: negative
Test Type: Chromosomal aberration
Result: negative
Test Type: In vitro mammalian cell gene mutation test
Result: negative
Genotoxicity in vivo : Test Type: Micronucleus test
Species: Mouse
Application Route: Oral
Result: negative

Germ cell mutagenicity- Assessment : Weight of evidence does not support classification as a germ cell mutagen.

Citric acid monohydrate:
Genotoxicity in vitro : Test Type: Bacterial reverse mutation assay (AMES)
Simvastatin Formulation

Result: negative
Test Type: in vitro micronucleus test
Result: positive
Test Type: Bacterial reverse mutation assay (AMES)
Result: negative

Genotoxicity in vivo:
Test Type: Mutagenicity (in vivo mammalian bone-marrow cytogenetic test, chromosomal analysis)
Species: Rat
Application Route: Ingestion
Result: negative

Carcinogenicity
Not classified based on available information.

Components:
Simvastatin:
Species: Mouse
Application Route: Oral
Exposure time: < 92 weeks
Target Organs: Harderian gland
Tumor Type: Liver, Lungs
Remarks: The significance of these findings for humans is not certain.

Species: Rat
Application Route: Oral
Exposure time: 2 Years
Tumor Type: Liver, Thyroid
Remarks: The significance of these findings for humans is not certain.

Reproductive toxicity
Not classified based on available information.

Components:
Simvastatin:
Effects on fertility:
Test Type: Fertility
Species: Rat, male
Application Route: Oral
Fertility: LOAEL: 25 mg/kg body weight

Effects on foetal development:
Test Type: Embryo-foetal development
Species: Rat
Application Route: Oral
Embryo-foetal toxicity: NOAEL: 25 mg/kg body weight
Result: No teratogenic effects, No adverse effects

Test Type: Embryo-foetal development
Species: Rabbit
Application Route: Oral
Embryo-foetal toxicity: NOAEL: 10 mg/kg body weight
Result: No teratogenic effects, No adverse effects

Test Type: Embryo-foetal development
Species: Rat
Application Route: Oral
Embryo-foetal toxicity: LOAEL: 60 mg/kg body weight
Result: Teratogenic potential
Remarks: Based on data from similar materials

Citric acid monohydrate:
Effects on foetal development
Test Type: Embryo-foetal development
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:

Simvastatin:
Target Organs: Liver, muscle, optic nerve, Eye
Assessment: Causes damage to organs through prolonged or repeated exposure.

Repeated dose toxicity

Components:

Simvastatin:
Species: Rat
NOAEL: 5 mg/kg
LOAEL: 30 mg/kg
Application Route: Oral
Exposure time: 14 - 104 Weeks
Target Organs: Liver, Testis, Musculo-skeletal system, Eye

Species: Dog
LOAEL: 10 mg/kg
Application Route: Oral
Exposure time: 14 - 104 Weeks
Target Organs: Liver, Testis, Eye

Species: Rabbit
NOAEL: 30 mg/kg
LOAEL: 50 mg/kg
Application Route: Oral
Target Organs: Liver, Kidney
Citric acid monohydrate:
Species: Rat
NOAEL: 4,000 mg/kg
LOAEL: 8,000 mg/kg
Application Route: Ingestion
Exposure time: 10 Days

Aspiration toxicity
Not classified based on available information.

Experience with human exposure

Components:

Simvastatin:
Skin contact: Remarks: May produce an allergic reaction.
Ingestion: Target Organs: Liver
Symptoms: upper respiratory tract infection, Headache, Abdominal pain, constipation, Nausea
Target Organs: Musculo-skeletal system

SECTION 12: Ecological information

12.1 Toxicity

Components:

Simvastatin:
Toxicity to fish: LC50 (Pimephales promelas (fathead minnow)): 2,91 mg/l
Exposure time: 96 h
Method: OECD Test Guideline 203

Toxicity to daphnia and other aquatic invertebrates: EC50 (Daphnia magna (Water flea)): 3,5 mg/l
Exposure time: 48 h
Method: OECD Test Guideline 202

Toxicity to algae/aquatic plants: EC50 (Pseudokirchneriella subcapitata (green algae)): > 25 mg/l
Exposure time: 96 h

NOEC (Pseudokirchneriella subcapitata (green algae)): 25 mg/l
Exposure time: 96 h

Toxicity to microorganisms: EC50: > 30 mg/l
Exposure time: 3 h
Test Type: Respiration inhibition
Method: OECD Test Guideline 209

NOEC: 21 mg/l
Exposure time: 3 h
Test Type: Respiration inhibition
Method: OECD Test Guideline 209
Simvastatin Formulation

Citric acid monohydrate:
Toxicity to fish: LC50 (Pimephales promelas (fathead minnow)): > 100 mg/l
Exposure time: 96 h

Toxicity to daphnia and other aquatic invertebrates: EC50 (Daphnia magna (Water flea)): 1.535 mg/l
Exposure time: 24 h

12.2 Persistence and degradability

**Components:**

**Simvastatin:**
Biodegradability: Result: rapidly degradable
Stability in water: Hydrolysis: 50 % (3,2 d)

**Citric acid monohydrate:**
Biodegradability: Result: Readily biodegradable.
Biodegradation: 97 %
Exposure time: 28 d
Method: OECD Test Guideline 301B

12.3 Bioaccumulative potential

**Components:**

**Simvastatin:**
Partition coefficient: n-octanol/water: log Pow: > 4,07

**Citric acid monohydrate:**
Partition coefficient: n-octanol/water: log Pow: -1,72

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. If not otherwise specified: Dispose of as unused product.

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

- REACH - Restrictions on the manufacture, placing on the market and use of certain dangerous substances, preparations and articles (Annex XVII) : Not applicable
- REACH - Candidate List of Substances of Very High Concern for Authorisation (Article 59) : Not applicable
- REACH - List of substances subject to authorisation (Annex XIV) : Not applicable
- Regulation (EC) No 1005/2009 on substances that deplete the ozone layer : Not applicable
- Regulation (EC) No 850/2004 on persistent organic pollutants : Not applicable
- Regulation (EC) No 649/2012 of the European Parliament and the Council concerning the export and import of dangerous chemicals : Not applicable

Other regulations:
Young people under the age of 18 are not allowed to use or be exposed to the product professionally. Young people above the age of 15 are, however, except from this rule if the product is a necessary part of their education.
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

H315 : Causes skin irritation.
H317 : May cause an allergic skin reaction.
H319 : Causes serious eye irritation.
H372 : Causes damage to organs through prolonged or repeated exposure.
H411 : Toxic to aquatic life with long lasting effects.

Full text of other abbreviations

Aquatic Chronic : Long-term (chronic) aquatic hazard
Eye Irrit. : Eye irritation
Skin Irrit. : Skin irritation
Skin Sens. : Skin sensitisation
STOT RE : Specific target organ toxicity - repeated exposure
## Simvastatin 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>
</table>

Further information

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

### Classification of the mixture:

<table>
<thead>
<tr>
<th>Skin Sens. 1</th>
<th>STOT RE 2</th>
<th>Aquatic Chronic 3</th>
</tr>
</thead>
<tbody>
<tr>
<td>H317</td>
<td>H373</td>
<td>H412</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.

NO / EN