Cyclosporine Formulation

SECTION 1. IDENTIFICATION

Product name: Cyclosporine Formulation
Other means of identification: No data available

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: Veterinary product
Restrictions on use: Not applicable

SECTION 2. HAZARDS IDENTIFICATION

GHS classification in accordance with the Hazardous Products Regulations
Carcinogenicity: Category 1B
Reproductive toxicity: Category 1B

GHS label elements
Hazard pictograms:

Signal Word: Danger

Hazard Statements: H350 May cause cancer.
H360Df May damage the unborn child. Suspected of damaging fertility.

Precautionary Statements: Prevention:
P201 Obtain special instructions before use.
P202 Do not handle until all safety precautions have been read and understood.
P280 Wear protective gloves, protective clothing, eye protection and face protection.
Response:
P308 + P313 IF exposed or concerned: Get medical attention.
Storage:
P405 Store locked up.
Disposal:
SAFETY DATA SHEET
according to the Hazardous Products Regulations

Cyclosporine Formulation

Version 2.9  Revision Date: 09/30/2023  SDS Number: 608874-00017  Date of last issue: 04/04/2023
Date of first issue: 04/08/2016

Other hazards
None known.

SECTION 3. COMPOSITION/INFORMATION ON INGREDIENTS

Substance / Mixture: Mixture
Components

<table>
<thead>
<tr>
<th>Chemical name</th>
<th>Common Name/Synonym</th>
<th>CAS-No.</th>
<th>Concentration (% w/w)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Petrolatum</td>
<td>No data available</td>
<td>8009-03-8</td>
<td>&gt;= 30 - &lt; 60 *</td>
</tr>
<tr>
<td>Corn oil</td>
<td>Corn oil</td>
<td>8001-30-7</td>
<td>&gt;= 30 - &lt; 60 *</td>
</tr>
<tr>
<td>Cyclosporine</td>
<td>No data available</td>
<td>59865-13-3</td>
<td>&gt;= 0.1 - &lt; 1 *</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.

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 cause cancer.
May damage the unborn child. Suspected of damaging fertility.

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.

SECTION 5. FIRE-FIGHTING MEASURES

Suitable extinguishing media: Water spray
Alcohol-resistant foam

P501 Dispose of contents and container to an approved waste disposal plant.
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. 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 spills cannot be contained.

Methods and materials for containment and cleaning up: Soak up with inert absorbent material. For large spills, provide diking or other appropriate containment to keep material from spreading. If diked 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.

SECTION 7. HANDLING AND STORAGE

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

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

Advice on safe handling: Do not get on skin or clothing.
Do not breathe vapors.
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.

Conditions for safe storage:
- Keep in properly labeled 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
  - Self-reactive substances and mixtures
  - Organic peroxides
  - Explosives
  - Gases

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>Petrolatum</td>
<td>8009-03-8</td>
<td>TWA (Mist)</td>
<td>5 mg/m³</td>
<td>CA AB OEL</td>
</tr>
<tr>
<td></td>
<td></td>
<td>STEL (Mist)</td>
<td>10 mg/m³</td>
<td>CA AB OEL</td>
</tr>
<tr>
<td></td>
<td></td>
<td>TWA (Mist)</td>
<td>1 mg/m³</td>
<td>CA BC OEL</td>
</tr>
<tr>
<td></td>
<td></td>
<td>TWAEV (Mist - Inhalable dust)</td>
<td>5 mg/m³</td>
<td>CA QC OEL</td>
</tr>
<tr>
<td></td>
<td></td>
<td>TWA (Inhalable particulate matter)</td>
<td>5 mg/m³</td>
<td>ACGIH</td>
</tr>
<tr>
<td>Corn oil</td>
<td>8001-30-7</td>
<td>TWAEV (Mist)</td>
<td>10 mg/m³</td>
<td>CA QC OEL</td>
</tr>
<tr>
<td>Cyclosporine</td>
<td>59865-13-3</td>
<td>TWA</td>
<td>10 µg/m³ (OEB 3)</td>
<td>Internal</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Wipe limit</td>
<td>100 µg/100 cm²</td>
<td>Internal</td>
</tr>
</tbody>
</table>

Engineering measures:
- Use appropriate engineering controls and manufacturing technologies to control airborne concentrations (e.g., dripless quick connections).
- 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**

**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**: 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.

**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.

**SECTION 9. PHYSICAL AND CHEMICAL PROPERTIES**

**Appearance**: Viscous liquid

**Color**: Colorless, to, light yellow

**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
**SAFETY DATA SHEET**

according to the Hazardous Products Regulations

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**Cyclosporine Formulation**

**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

**Vapor pressure**: No data available

**Relative vapor 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

**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.

**Particle size**: Not applicable

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**SECTION 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.
SECTION 11. TOXICOLOGICAL INFORMATION

Information on likely routes of exposure
Inhalation
Skin contact
Ingestion
Eye contact

Acute toxicity
Not classified based on available information.

Components:

Petrolatum:
Acute oral toxicity: LD50 (Rat): > 5,000 mg/kg
Method: OECD Test Guideline 401
Remarks: Based on data from similar materials

Acute dermal toxicity: LD50 (Rat): > 2,000 mg/kg
Method: OECD Test Guideline 402
Assessment: The substance or mixture has no acute dermal toxicity
Remarks: Based on data from similar materials

Corn oil:
Acute oral toxicity: LD50 (Rat): > 2,000 mg/kg
Method: OECD Test Guideline 401
Remarks: Based on data from similar materials

Cyclosporine:
Acute oral toxicity: LD50 (Rat): 1,480 mg/kg
LD50 (Mouse): 2,329 mg/kg

Acute inhalation toxicity: Remarks: No data available

Acute dermal toxicity: Remarks: No data available

Acute toxicity (other routes of administration):
LD50 (Mouse): 107 mg/kg
Application Route: Intravenous
LD50 (Rat): 25.8 mg/kg
Application Route: Intravenous

Skin corrosion/irritation
Not classified based on available information.

Components:

Petrolatum:
Species: Rabbit
Method: OECD Test Guideline 404
Cyclosporine Formulation

Result: No skin irritation
Remarks: Based on data from similar materials

**Corn oil:**
Species: Rabbit
Method: OECD Test Guideline 404
Result: No skin irritation
Remarks: Based on data from similar materials

**Cyclosporine:**
Remarks: No data available
May irritate skin.

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

**Components:**

**Petrolatum:**
Species: Rabbit
Result: No eye irritation
Method: OECD Test Guideline 405
Remarks: Based on data from similar materials

**Corn oil:**
Species: Rabbit
Result: No eye irritation
Method: OECD Test Guideline 405
Remarks: Based on data from similar materials

**Cyclosporine:**
Remarks: No data available
May irritate eyes.

Respiratory or skin sensitization

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

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

**Components:**

**Petrolatum:**
Test Type: Buehler Test
Routes of exposure: Skin contact
Species: Guinea pig
Result: negative
Remarks: Based on data from similar materials
## SAFETY DATA SHEET
according to the Hazardous Products Regulations

### Cyclosporine Formulation

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<tr>
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</tr>
</tbody>
</table>

**Corn oil:**
- **Test Type:** Human repeat insult patch test (HRIPT)
- **Routes of exposure:** Skin contact
- **Result:** negative

**Cyclosporine:**
- **Remarks:** May cause sensitization of susceptible persons.

**Germ cell mutagenicity**
Not classified based on available information.

**Components:**

**Petrolatum:**
- **Genotoxicity in vitro:** Test Type: Chromosome aberration test in vitro
  - Result: negative
  - Remarks: Based on data from similar materials
- **Genotoxicity in vivo:** Test Type: Mammalian erythrocyte micronucleus test (in vivo cytogenetic assay)
  - Species: Mouse
  - Application Route: Intraperitoneal injection
  - Method: OECD Test Guideline 474
  - Result: negative
  - Remarks: Based on data from similar materials

**Corn oil:**
- **Genotoxicity in vitro:** Test Type: Bacterial reverse mutation assay (AMES)
  - Result: negative

**Cyclosporine:**
- **Genotoxicity in vitro:**
  - Test Type: In vitro mammalian cell gene mutation test
    - Test system: Chinese hamster cells
    - Result: negative
  - Test Type: sister chromatid exchange assay
    - Result: positive
- **Genotoxicity in vivo:**
  - Test Type: Micronucleus test
    - Species: Mouse
    - Application Route: Oral
    - Result: negative
  - Test Type: Chromosomal aberration
    - Species: Chinese hamster
    - Cell type: Bone marrow
    - Result: negative
Cyclosporine Formulation

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<td></td>
</tr>
</tbody>
</table>

Test Type: Chromosomal aberration  
Species: Mouse  
Result: negative

### Carcinogenicity
May cause cancer.

### Components:

**Petrolatum:**
- **Species:** Rat  
- **Application Route:** Ingestion  
- **Exposure time:** 2 Years  
- **Result:** negative

**Cyclosporine:**
- **Species:** Mouse  
  - **Application Route:** Oral  
  - **Exposure time:** 78 weeks  
  - **LOAEL:** 4 mg/kg body weight  
  - **Result:** positive  
  - **Target Organs:** Liver, lymphatic system  
- **Species:** Rat  
  - **Application Route:** Oral  
  - **Exposure time:** 2 Years  
  - **LOAEL:** 0.5 mg/kg body weight  
  - **Result:** positive  
  - **Target Organs:** Pancreas  
- **Species:** Humans  
  - **Result:** May cause cancer.  
  - **Target Organs:** Immune system, Skin  
  - **Remarks:** Information taken from reference works and the literature.

Carcinogenicity - Assessment: May cause cancer.

### Reproductive toxicity
May damage the unborn child. Suspected of damaging fertility.

### Components:

**Petrolatum:**
- **Effects on fertility:**  
  - **Test Type:** Reproduction/Developmental toxicity screening test  
  - **Species:** Rat  
  - **Application Route:** Ingestion  
  - **Result:** negative  
  - **Remarks:** Based on data from similar materials

- **Effects on fetal development:**  
  - **Test Type:** Embryo-fetal development  
  - **Species:** Rat  
  - **Application Route:** Skin contact
Cyclosporine Formulation

Result: negative
Remarks: Based on data from similar materials

Cyclosporine:
Effects on fertility : Test Type: One-generation reproduction toxicity study
Species: Rat
Application Route: Oral
General Toxicity F1: LOAEL: 15 mg/kg body weight
Result: No effects on fertility., Effect on reproduction capacity.

Test Type: Fertility
Species: Rat, males
Application Route: Subcutaneous
Fertility: LOAEL: 10 mg/kg body weight
Result: Reduced fertility

Effects on fetal development : Test Type: Embryo-fetal development
Species: Rat
Application Route: Oral
Developmental Toxicity: LOAEL: 30 mg/kg body weight
Result: Embryotoxic effects and adverse effects on the offspring were detected only at high maternally toxic doses, Reduced fetal weight., Fetal mortality., Retardations., Teratogenic effects.

Test Type: Embryo-fetal development
Species: Rabbit
Developmental Toxicity: LOAEL: 100 mg/kg body weight
Result: Embryotoxic effects and adverse effects on the offspring were detected only at high maternally toxic doses, Reduced fetal weight., Fetal mortality., Retardations., Teratogenic effects.

Test Type: Development
Species: Rabbit
Application Route: Subcutaneous
Developmental Toxicity: LOAEL: 10 mg/kg body weight
Target Organs: Kidney
Result: Visceral malformations.

Test Type: Development
Species: Rat
Application Route: Intravenous
Developmental Toxicity: LOAEL: 12 mg/kg body weight
Target Organs: Heart
Result: Visceral malformations.

STOT-single exposure
Not classified based on available information.

STOT-repeated exposure
Not classified based on available information.
Cyclosporine Formulation

Components:

Cyclosporine:
- Target Organs: Kidney, Liver, Immune system
- Assessment: Causes damage to organs through prolonged or repeated exposure.

Repeated dose toxicity

Components:

Petrolatum:
- Species: Rat
- NOAEL: 5,000 mg/kg
- Application Route: Ingestion
- Exposure time: 2 y

Corn oil:
- Species: Rat
- NOAEL: > 300 mg/kg
- Application Route: Ingestion
- Exposure time: 28 Days
- Remarks: Based on data from similar materials

Cyclosporine:
- Species: Rat
- NOAEL: 14 mg/kg
- LOAEL: 45 mg/kg
- Application Route: Oral
- Exposure time: 90 Days
- Target Organs: Kidney, Liver, Immune system
- Symptoms: hair loss

Species: Monkey
- NOAEL: 20 mg/kg
- LOAEL: 60 mg/kg
- Application Route: Oral
- Exposure time: 90 Days
- Target Organs: Immune system
- Symptoms: Gastrointestinal disturbance, Liver disorders, Kidney disorders

Species: Dog
- NOAEL: 15 mg/kg
- Application Route: Oral
- Exposure time: 12 Months
- Target Organs: Immune system
- Symptoms: Changes in the blood count, Kidney disorders, Skin disorders, hair loss

Aspiration toxicity
Not classified based on available information.
Experience with human exposure

**Components:**

**Cyclosporine:**
- **Inhalation:** Remarks: May cause irritation of respiratory tract.
- **Skin contact:** Remarks: May irritate skin.
- **Eye contact:** Symptoms: Eye irritation, eye pain
- **Ingestion:** Symptoms: Kidney disorders, Tremors, hypertension, blood effects, Gastrointestinal disturbance

SECTION 12. ECOLOGICAL INFORMATION

**Ecotoxicity**

**Components:**

**Petrolatum:**
- **Toxicity to fish:**
  - LL50 (Pimephales promelas (fathead minnow)): > 100 mg/l
  - Exposure time: 96 h
  - Test substance: Water Accommodated Fraction
  - Method: OECD Test Guideline 203
  - Remarks: Based on data from similar materials

- **Toxicity to daphnia and other aquatic invertebrates:**
  - EC50 (Daphnia magna (Water flea)): > 10,000 mg/l
  - Exposure time: 48 h
  - Test substance: Water Accommodated Fraction
  - Remarks: Based on data from similar materials

- **Toxicity to algae/aquatic plants:**
  - NOEL (Pseudokirchneriella subcapitata (green algae)): >= 100 mg/l
  - Exposure time: 72 h
  - Test substance: Water Accommodated Fraction
  - Method: OECD Test Guideline 201
  - Remarks: Based on data from similar materials

- **Toxicity to daphnia and other aquatic invertebrates (Chronic toxicity):**
  - NOEC (Daphnia magna (Water flea)): 10 mg/l
  - Exposure time: 21 d
  - Test substance: Water Accommodated Fraction
  - Remarks: Based on data from similar materials

**Corn oil:**
- **Toxicity to fish:**
  - LL50 (Danio rerio (zebra fish)): > 100 mg/l
  - Exposure time: 96 h
  - Method: ISO 7346/1
  - Remarks: Based on data from similar materials

- **Toxicity to daphnia and other aquatic invertebrates:**
  - EL50 (Daphnia magna (Water flea)): > 100 mg/l
  - Exposure time: 48 h
  - Test substance: Water Accommodated Fraction
  - Remarks: Based on data from similar materials
Toxicity to algae/aquatic plants: EL50 (Desmodesmus subspicatus (green algae)): > 100 mg/l
Exposure time: 72 h
Test substance: Water Accommodated Fraction
Remarks: Based on data from similar materials

Toxicity to daphnia and other aquatic invertebrates (Chronic toxicity): NOELR (Daphnia magna (Water flea)): > 1 mg/l
Exposure time: 21 d
Test substance: Water Accommodated Fraction
Method: OECD Test Guideline 211
Remarks: Based on data from similar materials

Persistence and degradability
Components:

Petrolatum:
Biodegradability: Result: Not readily biodegradable.
Biodegradation: 31 %
Exposure time: 28 d
Method: OECD Test Guideline 301F
Remarks: Based on data from similar materials

Corn oil:
Biodegradability: Result: Readily biodegradable.
Remarks: Based on data from similar materials

Bioaccumulative potential
Components:

Corn oil:
Partition coefficient: n-octanol/water: log Pow: > 4
Method: OECD Test Guideline 117

Mobility in soil
No data available

Other adverse effects
No data available

SECTION 13. DISPOSAL CONSIDERATIONS

Disposal methods
Waste from residues: Do not dispose of waste into sewer.
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

Special precautions for user
Not applicable

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
CA AB OEL / STEL : 15-minute occupational exposure limit
CA BC OEL / TWA : 8-hour time weighted average
CA QC OEL / TWA: Time-weighted average exposure value

AIIIC - Australian Inventory of Industrial Chemicals; 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
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