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: 2000 Galloping Hill Road
Kenilworth - New Jersey - U.S.A. 07033
Telephone: 908-740-4000
Telex: 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: Veterinary product

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.
H360/Df 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/ face protection.

Response:
P308 + P313 IF exposed or concerned: Get medical advice/ attention.

Storage:
P405 Store locked up.

Disposal:
P501 Dispose of contents/ container to an approved waste dis-
SAFETY DATA SHEET

Cyclosporine Formulation

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>Petrolatum</td>
<td>8009-03-8</td>
<td>&gt;= 30 - &lt; 60</td>
</tr>
<tr>
<td>Corn oil</td>
<td>8001-30-7</td>
<td>&gt;= 30 - &lt; 60</td>
</tr>
<tr>
<td>Cyclosporine</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
Carbon dioxide (CO2)
Dry chemical

Unsuitable extinguishing media : None known.

Specific hazards during fire fighting : 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 and personal protective equipment recommendations.

Environmental precautions:
- Discharge into the environment must be avoided.
- 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 spillages 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 with local exhaust ventilation.

Advice on safe handling:
- Do not get on skin or clothing.
- Do not breathe vapors or spray mist.
- 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
  - 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>TWAEV (Mist)</td>
<td>5 mg/m³</td>
<td>CA QC OEL</td>
</tr>
<tr>
<td></td>
<td></td>
<td>STEV (Mist)</td>
<td>10 mg/m³</td>
<td>CA QC 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>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
  - Hand protection
    - Particulates type

Material:
- 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
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
SAFETY DATA SHEET

Cyclosporine Formulation

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

SECTION 10. STABILITY AND REACTIVITY

Reactivity : Not classified as a reactivity hazard.
Chemical stability : Stable under normal conditions.
Possibility of hazardous reac-
tions : 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): > 5,000 mg/kg

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  
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
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

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

Cyclosporine:
Genotoxicity in vitro: Test Type: Bacterial reverse mutation assay (AMES)
Result: negative

Test Type: In vitro mammalian cell gene mutation test
Test system: Chinese hamster cells
Result: negative

Test Type: sister chromatid exchange assay
Result: positive
SAFETY DATA SHEET

Cyclosporine Formulation

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
- 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
- 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.

**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

**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  
- **LOAEL:** 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:
  - LC0 (Danio rerio (zebra fish)): > 100 mg/l
  - Exposure time: 96 h
  - Remarks: Based on data from similar materials

- Toxicity to daphnia and other aquatic invertebrates:
  - EC0 (Daphnia magna (Water flea)): > 100 mg/l
  - Exposure time: 48 h
  - Remarks: Based on data from similar materials

- Toxicity to algae/aquatic plants:
  - EL50 (Desmodesmus subspicatus (green algae)): > 100 mg/l
  - Exposure time: 72 h
  - 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:** Remarks: No data available
- **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**
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 / TWAEV: Time-weighted average exposure value
CA QC OEL / STEV: Short-term exposure value

AICS - Australian Inventory of Chemical Substances; 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 Standardisation; DSL - Domestic Substances List (Canada); ECx - Concentration associated with x% response; ELx - Loading rate associated with x% response; EmS - Emergency Schedule; ENCS - Existing and New Chemical Substances (Japan); ErCx - Concentration associated with x% growth rate response; ERG - Emergency Response Guide; GHS - Globally Harmonized System; GLP - Good Laboratory Practice; IARC - International Agency for Research on Cancer; IATA - International Air Transport Association; IBC - International Code for the Construction and Equipment of Ships carrying Dangerous Chemicals in Bulk; ICSO - Half maximal inhibitory concentration; ICAO - International Civil Aviation Organization; IECSC - Inventory of Existing Chemical Substances in China; IMDG - International Maritime Dangerous Goods; IMO - International Maritime Organization; ISHL - Industrial Safety and Health Law (Japan); ISO - International Organisation for Standardisation; KECP - Korea Existing Chemicals Inventory; LC50 - Lethal Concentration to 50% of a test population; LD50 - Lethal Dose to 50% of a test population (Median Lethal Dose); MARPOL - International Convention for the Prevention of Pollution from Ships; n.o.s. - Not Otherwise Specified; Nch - Chilean Norm; NO(A)EC - No Observed (Adverse) Effect Concentration; NO(A)EL - No Observed (Adverse) Effect Level; NOELR - No Observable Effect Loading Rate; NOM - Official Mexican Norm; NTP - National Toxicology Program; NZIoC - New Zealand Inventory of Chemicals; OECD - Organization for Economic Co-operation and Development; OPPTS - Office of Chemical Safety and Pollution Prevention; PBT - Persistent, Bioaccumulative and Toxic substance; PICCS - Philippines Inventory of Chemicals and Chemical Substances; (Q)SAR - (Quantitative) Structure Activity Relationship; REACH - Regulation (EC) No 1907/2006 of the European Parliament and of the Council concerning the Registration, Evaluation,
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.

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