SAFETY DATA SHEET

Cyclosporine Formulation

Section 1: Identification

Product name : Cyclosporine Formulation

Manufacturer or supplier’s details

Company      : MSD
Address      : 33 Whakatiki Street - Private Bag 908
              Upper Hutt - New Zealand
Telephone    : 908-740-4000
Emergency telephone number : 1-908-423-6000
E-mail address : EHSDATASTEWARD@msd.com
Telefax      : 908-735-1496

Recommended use of the chemical and restrictions on use

Recommended use : Veterinary product

Section 2: Hazard identification

GHS Classification

Carcinogenicity : Carc.1B

GHS label elements

Hazard pictograms :

Signal word : Danger
Hazard statements : H350 May cause cancer.
Precautionary statements :

Prevention:
P201 Obtain special instructions before use.
P202 Do not handle until all safety precautions have been read and understood.
P281 Use personal protective equipment as required.

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
disposal plant.

**Other hazards which do not result in classification**
None known.

### Section 3: Composition/information on ingredients

<table>
<thead>
<tr>
<th>Substance / Mixture</th>
<th>Components</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Chemical name</td>
</tr>
<tr>
<td></td>
<td>Petrolatum</td>
</tr>
<tr>
<td></td>
<td>Cyclosporine</td>
</tr>
</tbody>
</table>

### 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.

- **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 firefighting**: Exposure to combustion products may be a hazard to health.

- **Hazardous combustion products**: Carbon oxides
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 dyeing or other appropriate containment to keep material from spreading. If dyed 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 vapours 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.

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.

Conditions for safe storage:
- Keep in properly labelled 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

Section 8: Exposure controls/personal protection

Components 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>WES-TWA (Mist)</td>
<td>5 mg/m³</td>
<td>NZ OEL</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Further information: Sampled by a method that does not collect vapour.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>WES-STE (Mist)</td>
<td>10 mg/m³</td>
<td>NZ 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>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:
- 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.

### Section 9: Physical and chemical properties

- **Appearance**: viscous liquid
- **Colour**: colourless, to, light yellow
- **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)**: 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
- **Vapour pressure**: No data available
- **Relative vapour 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
- **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.

### 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 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

#### Exposure routes
- 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

**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 sensitisation

Skin sensitisation
Not classified based on available information.

Respiratory sensitisation
Not classified based on available information.
## Components:

### Petrolatum:

<table>
<thead>
<tr>
<th>Test Type</th>
<th>Buehler Test</th>
</tr>
</thead>
<tbody>
<tr>
<td>Exposure routes</td>
<td>Skin contact</td>
</tr>
<tr>
<td>Species</td>
<td>Guinea pig</td>
</tr>
<tr>
<td>Result</td>
<td>negative</td>
</tr>
<tr>
<td>Remarks</td>
<td>Based on data from similar materials</td>
</tr>
</tbody>
</table>

### Cyclosporine:

- **Remarks**: May cause sensitisation of susceptible persons.

## Chronic toxicity

### Germ cell mutagenicity

Not classified based on available information.

## Components:

### Petrolatum:

<table>
<thead>
<tr>
<th>Genotoxicity in vitro</th>
<th>Test Type: Chromosome aberration test in vitro</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Result: negative</td>
</tr>
<tr>
<td></td>
<td>Remarks: Based on data from similar materials</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Genotoxicity in vivo</th>
<th>Test Type: Mammalian erythrocyte micronucleus test (in vivo cytogenetic assay)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Species: Mouse</td>
</tr>
<tr>
<td></td>
<td>Application Route: Intraperitoneal injection</td>
</tr>
<tr>
<td></td>
<td>Method: OECD Test Guideline 474</td>
</tr>
<tr>
<td></td>
<td>Result: negative</td>
</tr>
<tr>
<td></td>
<td>Remarks: Based on data from similar materials</td>
</tr>
</tbody>
</table>

### 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

- **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
Not classified based on available information.

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 foetal development: Test Type: Embryo-foetal development
Species: Rat
Application Route: Skin contact
Result: negative
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

Effects on foetal development:
- Test Type: Embryo-foetal 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 foetal weight, foetal mortality, Retardations, Teratogenic effects

- Test Type: Embryo-foetal 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 foetal weight, foetal 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 yr

- **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
SAFETY DATA SHEET

Cyclosporine Formulation

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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

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

Bioaccumulative potential
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.

National Regulations

- NZS 5433: Not regulated as a dangerous good

Section 15: Regulatory information

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

HSNO Approval Number
HSR100759 Veterinary Medicines Non dispersive Open System Application Group Standard 2017

HSW Controls
Certified handler certificate not required.
Tracking hazardous substance not required.
Refer to the Health and Safety at Work (Hazardous Substances) Regulations 2017, for further information.

The components of this product are reported in the following inventories:

- AICS: not determined
- DSL: not determined
- IECSC: not determined
Section 16: Other information

Further information

Date format: dd.mm.yyyy

Full text of other abbreviations
ACGIH: USA. ACGIH Threshold Limit Values (TLV)
NZ OEL: New Zealand. Workplace Exposure Standards for Atmospheric Contaminants

ACGIH / TWA: 8-hour, time-weighted average
NZ OEL / WES-TWA: Workplace Exposure Standard - Time Weighted average
NZ OEL / WES-STEL: Workplace Exposure Standard - Short-Term Exposure Limit

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; IC50 - 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 Standardization; KECI - 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, Authorisation and Restriction of Chemicals; SADT - Self-Accelerating Decomposition Temperature; SDS - Safety Data Sheet; TCSI - Taiwan Chemical Substance Inventory; TDG - Transportation of Dangerous Goods; TSCA - Toxic Substances Control Act (United States); UN - United Nations; UNRTDG - United Nations Recommendations on the Transport of Dangerous Goods; vPvB - Very Persistent and Very Bioaccumulative; WHMIS - Workplace Hazardous Materials Information System

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 mate-
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.

NZ / EN