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

1.1 Product identifier
   Trade name : Cyclosporine Formulation

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

1.3 Details of the supplier of the safety data sheet
   Company : MSD
              Kilsheean
              Clonmel Tipperary, IE
   Telephone : 353-51-601000
   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)
   Carcinogenicity, Category 1B
   H350: May cause cancer.

2.2 Label elements
   Labelling (REGULATION (EC) No 1272/2008)
   Hazard pictograms :

   Signal word : Danger
   Hazard statements : H350 May cause cancer.
   Precautionary statements :
      Prevention:
      P201 Obtain special instructions before use.
      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.

Hazardous components which must be listed on the label:
Cyclosporine

2.3 Other hazards
This substance/mixture contains no components considered to be either persistent, bioaccumulative and toxic (PBT), or very persistent and very bioaccumulative (vPvB) at levels of 0.1% or higher.

Ecological information: The substance/mixture does not contain components considered to have endocrine disrupting properties according to REACH Article 57(f) or Commission Delegated regulation (EU) 2017/2100 or Commission Regulation (EU) 2018/605 at levels of 0.1% or higher.

Toxicological information: The substance/mixture does not contain components considered to have endocrine disrupting properties according to REACH Article 57(f) or Commission Delegated regulation (EU) 2017/2100 or Commission Regulation (EU) 2018/605 at levels of 0.1% or higher.

SECTION 3: Composition/information on ingredients

3.2 Mixtures

<table>
<thead>
<tr>
<th>Components</th>
<th>CAS-No.</th>
<th>EC-No.</th>
<th>Index-No.</th>
<th>Registration number</th>
<th>Classification</th>
<th>Concentration (% w/w)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cyclosporine</td>
<td>59865-13-3</td>
<td></td>
<td></td>
<td></td>
<td>Acute Tox. 4; H302 Carc. 1B; H350 Repr. 1B; H360Df STOT RE 1; H372 (Kidney, Liver, Immune system)</td>
<td>&gt;= 0.1 - &lt; 0.3</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).
SAFETY DATA SHEET
according to Regulation (EC) No. 1907/2006

Cyclosporine Formulation

Version 2.4
Revision Date: 12.10.2021
SDS Number: 610644-00012
Date of last issue: 23.03.2020
Date of first issue: 08.04.2016

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.

4.2 Most important symptoms and effects, both acute and delayed
Risks: May cause cancer.

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: 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
SECTION 6: Accidental release measures

6.1 Personal precautions, protective equipment and emergency procedures

Personal precautions : Use personal protective equipment.
Follow safe handling advice (see section 7) and personal protective equipment recommendations (see section 8).

6.2 Environmental precautions

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 spillages cannot be contained.

6.3 Methods and material for containment and cleaning up

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

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 : 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.
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.

7.2 Conditions for safe storage, including any incompatibilities

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

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

SECTION 8: Exposure controls/personal protection

8.1 Control parameters

<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>Petrolatum</td>
<td>8009-03-8</td>
<td>TWA (Vapour)</td>
<td>50 mg/m³</td>
<td>FOR-2011-12-06-1358</td>
</tr>
<tr>
<td></td>
<td></td>
<td>TWA (Mist and particles)</td>
<td>1 mg/m³</td>
<td>FOR-2011-12-06-1358</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>

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>Petrolatum</td>
<td>Oral (Secondary Poisoning)</td>
<td>9.33 mg/kg food</td>
</tr>
</tbody>
</table>

8.2 Exposure controls

Engineering measures
- Use appropriate engineering controls and manufacturing technologies to control airborne concentrations (e.g., drip-less 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**

**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.
- Equipment should conform to NS EN 143
- Filter type: Particulates type (P)

### SECTION 9: Physical and chemical properties

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

- **Physical state**: Viscous liquid
- **Colour**: Colourless, to, light yellow
- **Odour**: No data available
- **Odour Threshold**: No data available
- **Melting point/freezing point**: No data available
- **Initial boiling point and boiling range**: 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
- **Flash point**: No data available
SAFETY DATA SHEET  
according to Regulation (EC) No. 1907/2006

Cyclosporine Formulation

Auto-ignition temperature  :  No data available
Decomposition temperature :  No data available
pH  :  No data available
Viscosity
Viscosity, kinematic  :  No data available
Solubility(ies)
Water solubility  :  No data available
Partition coefficient: n-octanol/water
Vapour pressure  :  No data available
Relative density  :  No data available
Density  :  No data available
Relative vapour density  :  No data available
Particle characteristics
Particle size  :  Not applicable

9.2 Other information
Explosives  :  Not explosive
Oxidizing properties  :  The substance or mixture is not classified as oxidizing.
Evaporation rate  :  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  :  Can react with strong oxidizing agents.

10.4 Conditions to avoid
Conditions to avoid  :  None known.

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 hazard classes as defined in Regulation (EC) No 1272/2008

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

Acute toxicity
Not classified based on available information.

Components:

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:

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

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

Components:

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

Respiratory or skin sensitisation

Skin sensitisation
Not classified based on available information.
Cyclosporine Formulation

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

**Components:**

**Cyclosporine:**

Remarks: May cause sensitisation of susceptible persons.

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

**Components:**

**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:**

**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
Cyclosporine Formulation

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:

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 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
### Cyclosporine Formulation

#### 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**

<table>
<thead>
<tr>
<th>Target Organs</th>
<th>Kidney, Liver, Immune system</th>
</tr>
</thead>
<tbody>
<tr>
<td>Assessment</td>
<td>Causes damage to organs through prolonged or repeated exposure.</td>
</tr>
</tbody>
</table>

#### Repeated dose toxicity

**Components:**

**Cyclosporine**

<table>
<thead>
<tr>
<th>Species</th>
<th>Rat</th>
</tr>
</thead>
<tbody>
<tr>
<td>NOAEL</td>
<td>14 mg/kg</td>
</tr>
<tr>
<td>LOAEL</td>
<td>45 mg/kg</td>
</tr>
<tr>
<td>Application Route</td>
<td>Oral</td>
</tr>
<tr>
<td>Exposure time</td>
<td>90 Days</td>
</tr>
<tr>
<td>Target Organs</td>
<td>Kidney, Liver, Immune system</td>
</tr>
<tr>
<td>Symptoms</td>
<td>hair loss</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Species</th>
<th>Monkey</th>
</tr>
</thead>
<tbody>
<tr>
<td>NOAEL</td>
<td>20 mg/kg</td>
</tr>
<tr>
<td>LOAEL</td>
<td>60 mg/kg</td>
</tr>
<tr>
<td>Application Route</td>
<td>Oral</td>
</tr>
<tr>
<td>Exposure time</td>
<td>90 Days</td>
</tr>
<tr>
<td>Target Organs</td>
<td>Immune system</td>
</tr>
<tr>
<td>Symptoms</td>
<td>Gastrointestinal disturbance, Liver disorders, Kidney disorders</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Species</th>
<th>Dog</th>
</tr>
</thead>
<tbody>
<tr>
<td>LOAEL</td>
<td>15 mg/kg</td>
</tr>
<tr>
<td>Application Route</td>
<td>Oral</td>
</tr>
<tr>
<td>Exposure time</td>
<td>12 Months</td>
</tr>
<tr>
<td>Target Organs</td>
<td>Immune system</td>
</tr>
<tr>
<td>Symptoms</td>
<td>Changes in the blood count, Kidney disorders, Skin disorders, hair loss</td>
</tr>
</tbody>
</table>

**Aspiration toxicity**

Not classified based on available information.
11.2 Information on other hazards

Endocrine disrupting properties

Product:
Assessment : The substance/mixture does not contain components considered to have endocrine disrupting properties according to REACH Article 57(f) or Commission Delegated regulation (EU) 2017/2100 or Commission Regulation (EU) 2018/605 at levels of 0.1% or higher.

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

12.1 Toxicity
No data available

12.2 Persistence and degradability
No data available

12.3 Bioaccumulative potential
No data available

12.4 Mobility in soil
No data available

12.5 Results of PBT and vPvB assessment

Product:
Assessment : This substance/mixture contains no components considered to be either persistent, bioaccumulative and toxic (PBT), or very persistent and very bioaccumulative (vPvB) at levels of 0.1% or higher.

12.6 Endocrine disrupting properties

Product:
Assessment : The substance/mixture does not contain components considered to have endocrine disrupting properties according to REACH Article 57(f) or Commission Delegated regulation (EU) 2017/2100 or Commission Regulation (EU) 2018/605 at levels of 0.1% or higher.
12.7 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 or ID 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 Maritime transport in bulk according to IMO instruments
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) : Conditions of restriction for the following entries should be considered: Number on list 3
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 (EU) 2019/1021 on persistent organic pollu-
tants (recast)
Regulation (EC) No 649/2012 of the European Parliament and the Council concerning the export and import of dangerous chemicals

Not applicable

Other regulations:
Take note of Directive 92/85/EEC regarding maternity protection or stricter national regulations, where applicable.
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

Full text of H-Statements
H302 : Harmful if swallowed.
H350 : May cause cancer.
H360Df : May damage the unborn child. Suspected of damaging fertility.
H372 : Causes damage to organs through prolonged or repeated exposure.

Full text of other abbreviations
Acute Tox. : Acute toxicity
Carc. : Carcinogenicity
Repr. : Reproductive toxicity
STOT RE : Specific target organ toxicity - repeated exposure
FOR-2011-12-06-1358 : Norway. Occupational Exposure limits
FOR-2011-12-06-1358 / : Long term exposure limit
TWA

ADN - European Agreement concerning the International Carriage of Dangerous Goods by Inland Waterways; ADR - European Agreement concerning the International Carriage of Dangerous Goods by Road; AIIC - Australian Inventory of Industrial Chemicals; ASTM - American Society for the Testing of Materials; bw - Body weight; CMR - Classification Labelling Packaging Regulation; Regulation (EC) No 1272/2008; DIN - Standard of the German Institute for Standardisation; DSL - Domestic Substances List (Canada);
Cyclosporine Formulation

Version | Revision Date | SDS Number | Date of last issue | Date of first issue
2.4     | 12.10.2021   | 610644-00012 | 23.03.2020        | 08.04.2016

Further information

Classification of the mixture:
| Carc. 1B | H350 |

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