1. IDENTIFICATION OF THE SUBSTANCE/MIXTURE AND THE COMPANY/UNDERTAKING

Product Identifier

Material Name: Sirolimus Oral Solution
Trade Name: RAPAMUNE
Chemical Family: Macrocyclic lactone

Relevant Identified Uses of the Substance or Mixture and Uses Advised Against

Intended Use: Pharmaceutical product used as immunosuppressive agent

Details of the Supplier of the Safety Data Sheet

Pfizer Inc
Pfizer Pharmaceuticals Group
235 East 42nd Street
New York, New York 10017
1-800-879-3477

Emergency telephone number:
CHEMTREC (24 hours): 1-800-424-9300

Contact E-Mail: pfizer-MSDS@pfizer.com

Pfizer Ltd
Ramsgate Road
Sandwich, Kent
CT13 9NJ
United Kingdom
+00 44 (0)1304 616161

Emergency telephone number:
International CHEMTREC (24 hours): +1-703-527-3887

2. HAZARDS IDENTIFICATION

Classification of the Substance or Mixture

GHS - Classification
Reproductive Toxicity: Category 1B
Acute aquatic toxicity: Category 1
Chronic aquatic toxicity: Category 1

Label Elements

Signal Word: Danger
Hazard Statements:
H360FD - May damage fertility. May damage the unborn child.
H400 - Very toxic to aquatic life
H410 - Very toxic to aquatic life with long lasting effects

Precautionary Statements:
P201 - Obtain special instructions before use
P281 - Use personal protective equipment as required
P308 + P313 - IF exposed or concerned: Get medical attention/advice
P405 - Store locked up
P273 - Avoid release to the environment
P391 - Collect spillage
P501 - Dispose of contents/container in accordance with all local and national regulations
SAFETY DATA SHEET

Material Name: Sirolimus Oral Solution
Revision date: 21-Mar-2018

Other Hazards
An Occupational Exposure Value has been established for one or more of the ingredients (see Section 8).

Note:
This document has been prepared in accordance with standards for workplace safety, which requires the inclusion of all known hazards of the product or its ingredients regardless of the potential risk. The precautionary statements and warning included may not apply in all cases. Your needs may vary depending upon the potential for exposure in your workplace.

3. COMPOSITION / INFORMATION ON INGREDIENTS

<table>
<thead>
<tr>
<th>Ingredient</th>
<th>CAS Number</th>
<th>EU EINECS/ELINCS List</th>
<th>GHS Classification</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ethanol</td>
<td>64-17-5</td>
<td>200-578-6</td>
<td>Flam. Liq. 2 (H225)</td>
<td>1.5-2.5</td>
</tr>
<tr>
<td>Sirolimus</td>
<td>53123-88-9</td>
<td>Not Listed</td>
<td>Repr.1B (H360FD)</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Aquatic Acute 1 (H400)</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Aquatic Chronic 1 (H410)</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Ingredient</th>
<th>CAS Number</th>
<th>EU EINECS/ELINCS List</th>
<th>GHS Classification</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Soy fatty acids</td>
<td>68308-53-2</td>
<td>269-657-0</td>
<td>Not Listed</td>
<td>*</td>
</tr>
<tr>
<td>Glycerides, unsatd. mono- and di-</td>
<td>67701-32-0</td>
<td>266-951-0</td>
<td>Not Listed</td>
<td>*</td>
</tr>
<tr>
<td>Lecithin</td>
<td>8002-43-5</td>
<td>232-307-2</td>
<td>Not Listed</td>
<td>*</td>
</tr>
<tr>
<td>Polysorbate 80</td>
<td>9005-65-6</td>
<td>Not Listed</td>
<td>Not Listed</td>
<td>*</td>
</tr>
<tr>
<td>Ascorbyl palmitate</td>
<td>137-66-6</td>
<td>205-305-4</td>
<td>Not Listed</td>
<td>*</td>
</tr>
</tbody>
</table>

Additional Information: * Proprietary Ingredient(s) indicated as hazardous have been assessed under standards for workplace safety.

In accordance with 29 CFR 1910.1200, the exact percentage composition of this mixture has been withheld as a trade secret.

For the full text of the CLP/GHS abbreviations mentioned in this Section, see Section 16

4. FIRST AID MEASURES

Description of First Aid Measures

Eye Contact: Flush with water while holding eyelids open for at least 15 minutes. Seek medical attention immediately.

Skin Contact: Remove contaminated clothing. Flush area with large amounts of water. Use soap. Seek medical attention.

Ingestion: Never give anything by mouth to an unconscious person. Wash out mouth with water. Do not induce vomiting unless directed by medical personnel. Seek medical attention immediately.
Inhalation: Remove to fresh air and keep patient at rest. Seek medical attention immediately.

Most Important Symptoms and Effects, Both Acute and Delayed
Symptoms and Effects of Exposure: For information on potential signs and symptoms of exposure, See Section 2 - Hazards Identification and/or Section 11 - Toxicological Information.
Medical Conditions Aggravated by Exposure: None known

Indication of the Immediate Medical Attention and Special Treatment Needed
Notes to Physician: None

5. FIRE FIGHTING MEASURES

Extinguishing Media: Extinguish fires with CO2, extinguishing powder, foam, or water.

Special Hazards Arising from the Substance or Mixture
Hazardous Combustion Products: Formation of toxic gases is possible during heating or fire.
Fire / Explosion Hazards: Fine particles (such as dust and mists) may fuel fires/explosions.

Advice for Fire-Fighters
During all firefighting activities, wear appropriate protective equipment, including self-contained breathing apparatus.

6. ACCIDENTAL RELEASE MEASURES

Personal Precautions, Protective Equipment and Emergency Procedures
Personnel involved in clean-up should wear appropriate personal protective equipment (see Section 8). Minimize exposure.

Environmental Precautions
Place waste in an appropriately labeled, sealed container for disposal. Care should be taken to avoid environmental release.

Methods and Material for Containment and Cleaning Up
Measures for Cleaning /
Collecting: Contain the source of the spill or leak. Absorb spills with non-combustible absorbent material and transfer into a labeled container for disposal. Clean spill area thoroughly. Prevent discharge to
Additional Consideration for
Large Spills: Non-essential personnel should be evacuated from affected area. Report emergency situations immediately. Cleanup operations should only be undertaken by trained personnel.

7. HANDLING AND STORAGE

Precautions for Safe Handling
Restrict access to work area. Avoid breathing vapor or mist. Avoid contact with eyes, skin and clothing. When handling, use appropriate personal protective equipment (see Section 8). Wash thoroughly after handling. Releases to the environment should be avoided. Refer to Section 12 - Ecological Information, for information on potential effects on the environment. Review and implement appropriate technical and procedural waste water and waste disposal measures to prevent occupational exposure or environmental releases. Potential points of process emissions of this material to the atmosphere should be controlled with dust collectors, HEPA filtration systems or other equivalent controls. It is recommended that all operations be fully enclosed and no air recirculated.

Conditions for Safe Storage, Including any Incompatibilities
Storage Conditions: Store as directed by product packaging.
Specific end use(s): No data available
### 8. EXPOSURE CONTROLS / PERSONAL PROTECTION

**Control Parameters**

Refer to available public information for specific member state Occupational Exposure Limits.

**Ethanol**

<table>
<thead>
<tr>
<th>Source</th>
<th>Limit Value (STEL)</th>
</tr>
</thead>
<tbody>
<tr>
<td>ACGIH TWA</td>
<td>1000 ppm</td>
</tr>
<tr>
<td>Australia TWA</td>
<td>1000 ppm</td>
</tr>
<tr>
<td></td>
<td>1880 mg/m³</td>
</tr>
<tr>
<td>Austria OEL - MAKs</td>
<td>1000 ppm</td>
</tr>
<tr>
<td></td>
<td>1900 mg/m³</td>
</tr>
<tr>
<td>Belgium OEL - TWA</td>
<td>1000 ppm</td>
</tr>
<tr>
<td></td>
<td>1907 mg/m³</td>
</tr>
<tr>
<td>Bulgaria OEL - TWA</td>
<td>1000 mg/m³</td>
</tr>
<tr>
<td>Czech Republic OEL - TWA</td>
<td>1000 mg/m³</td>
</tr>
<tr>
<td>Denmark OEL - TWA</td>
<td>1000 ppm</td>
</tr>
<tr>
<td></td>
<td>1900 mg/m³</td>
</tr>
<tr>
<td>Estonia OEL - TWA</td>
<td>500 ppm</td>
</tr>
<tr>
<td></td>
<td>1000 mg/m³</td>
</tr>
<tr>
<td>Finland OEL - TWA</td>
<td>1000 ppm</td>
</tr>
<tr>
<td></td>
<td>1900 mg/m³</td>
</tr>
<tr>
<td>France OEL - TWA</td>
<td>1000 ppm</td>
</tr>
<tr>
<td></td>
<td>1900 mg/m³</td>
</tr>
<tr>
<td>Germany - TRGS 900 - TWAs</td>
<td>500 ppm</td>
</tr>
<tr>
<td></td>
<td>960 mg/m³</td>
</tr>
<tr>
<td>Germany (DFG) - MAK</td>
<td>500 ppm</td>
</tr>
<tr>
<td></td>
<td>960 mg/m³</td>
</tr>
<tr>
<td>Greece OEL - TWA</td>
<td>1000 ppm</td>
</tr>
<tr>
<td></td>
<td>1900 mg/m³</td>
</tr>
<tr>
<td>Hungary OEL - TWA</td>
<td>1900 mg/m³</td>
</tr>
<tr>
<td>Latvia OEL - TWA</td>
<td>1000 mg/m³</td>
</tr>
<tr>
<td>Lithuania OEL - TWA</td>
<td>500 ppm</td>
</tr>
<tr>
<td></td>
<td>1000 mg/m³</td>
</tr>
<tr>
<td>Netherlands OEL - TWA</td>
<td>260 mg/m³</td>
</tr>
<tr>
<td>OSHA - Final PELS - TWAs:</td>
<td>1000 ppm</td>
</tr>
<tr>
<td></td>
<td>1900 mg/m³</td>
</tr>
<tr>
<td>Poland OEL - TWA</td>
<td>1900 mg/m³</td>
</tr>
<tr>
<td>Portugal OEL - TWA</td>
<td>1000 ppm</td>
</tr>
<tr>
<td>Romania OEL - TWA</td>
<td>1000 ppm</td>
</tr>
<tr>
<td></td>
<td>1900 mg/m³</td>
</tr>
<tr>
<td>Russia OEL - TWA</td>
<td>1000 mg/m³</td>
</tr>
<tr>
<td>Slovakia OEL - TWA</td>
<td>500 ppm</td>
</tr>
<tr>
<td></td>
<td>960 mg/m³</td>
</tr>
<tr>
<td>Slovenia OEL - TWA</td>
<td>1000 ppm</td>
</tr>
<tr>
<td></td>
<td>1900 mg/m³</td>
</tr>
<tr>
<td>Sweden OEL - TWAs</td>
<td>500 ppm</td>
</tr>
<tr>
<td></td>
<td>1000 mg/m³</td>
</tr>
<tr>
<td>Switzerland OEL -TWAs</td>
<td>500 ppm</td>
</tr>
<tr>
<td></td>
<td>960 mg/m³</td>
</tr>
<tr>
<td>Vietnam OEL - TWAs</td>
<td>1000 mg/m³</td>
</tr>
</tbody>
</table>

**Sirolimus**

<table>
<thead>
<tr>
<th>Source</th>
<th>Limit Value (STEL)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pfizer OEL TWA-8 Hr:</td>
<td>0.2 µg/m³</td>
</tr>
</tbody>
</table>
8. EXPOSURE CONTROLS / PERSONAL PROTECTION

The purpose of the Occupational Exposure Band (OEB) classification system is to separate substances into different Hazard categories when the available data are sufficient to do so, but inadequate to establish an Occupational Exposure Limit (OEL). The OEB given is based upon an analysis of all currently available data; as such, this value may be subject to revision when new information becomes available.

Exposure Controls

Engineering Controls: Engineering controls should be used as the primary means to control exposures. General room ventilation is adequate unless the process generates dust, mist or fumes. Keep airborne contamination levels below the exposure limits listed above in this section.

Personal Protective Equipment:

Refer to applicable national standards and regulations in the selection and use of personal protective equipment (PPE). Contact your safety and health professional or safety equipment supplier for assistance in selecting the correct protective clothing/equipment based on an assessment of the workplace conditions, other chemicals used or present in the workplace and specific operational processes.

Hands: Impervious disposable gloves (e.g. Nitrile, etc.) (double recommended) if skin contact with drug product is possible and for bulk processing operations. (Protective gloves must meet the standards in accordance with EN374, ASTM F1001 or international equivalent.)

Eyes: Wear safety glasses or goggles if eye contact is possible. (Eye protection must meet the standards in accordance with EN166, ANSI Z87.1 or international equivalent.)

Skin: Impervious disposable protective clothing is recommended if skin contact with drug product is possible and for bulk processing operations. (Protective clothing must meet the standards in accordance with EN13982, ANSI 103 or international equivalent.)

Respiratory protection: Under normal conditions of use, if the applicable Occupational Exposure Limit (OEL) is exceeded, wear an appropriate respirator with a protection factor sufficient to control exposures to below the OEL (e.g. particulate respirator with a full mask, P3 filter). (Respirators must meet the standards in accordance with EN136, EN143, ASTM F2704-10 or international equivalent.)

9. PHYSICAL AND CHEMICAL PROPERTIES

<table>
<thead>
<tr>
<th>Physical State:</th>
<th>Liquid</th>
<th>Color:</th>
<th>Yellow</th>
</tr>
</thead>
<tbody>
<tr>
<td>Odor:</td>
<td>No data available</td>
<td>Odor Threshold:</td>
<td>No data available</td>
</tr>
<tr>
<td>Molecular Formula:</td>
<td>Mixture</td>
<td>Molecular Weight:</td>
<td>Mixture</td>
</tr>
</tbody>
</table>

| Solvent Solubility: | No data available |
| Water Solubility:   | No data available |
| pH:                 | No data available |
| Melting/Freezing Point (°C): | No data available |
| Boiling Point (°C): | No data available |
| Partition Coefficient: (Method, pH, Endpoint, Value) | |

Sirolimus

Measured Log P >4.63

Propylene glycol
No data available

Ascorbyl palmitate
No data available

Lecithin
No data available

Glycerides, unsatd. mono- and di-
No data available

Ethanol
No data available
9. PHYSICAL AND CHEMICAL PROPERTIES

Polysorbate 80

No data available

Decomposition Temperature (°C): No data available.

Evaporation Rate (Gram/s): No data available

Vapor Pressure (kPa): No data available

Vapor Density (g/ml): No data available

Relative Density: No data available

Viscosity: No data available

Flammability:

Autoignition Temperature (Solid) (°C): No data available

Flammability (Solids): No data available

Flash Point (Liquid) (°C): No data available

Upper Explosive Limits (Liquid) (% by Vol.): No data available

Lower Explosive Limits (Liquid) (% by Vol.): No data available

10. STABILITY AND REACTIVITY

Reactivity: No data available

Chemical Stability: Stable under normal conditions of use.

Possibility of Hazardous Reactions

Oxidizing Properties: No data available

Conditions to Avoid: Fine particles (such as dust and mists) may fuel fires/explosions.

Incompatible Materials: As a precautionary measure, keep away from strong oxidizers

Hazardous Decomposition Products: No data available

11. TOXICOLOGICAL INFORMATION

Information on Toxicological Effects

General Information: The information included in this section describes the potential hazards of the individual ingredients.

Known Clinical Effects: Adverse effects associated with therapeutic use include hypersensitivity reactions, nausea, weakness, skin rash, weight loss, inflammation of the mouth (stomatitis), itching sensation (pruritus), decreased red blood cell count (anemia), decreased white blood cells (leukopenia).

Acute Toxicity: (Species, Route, End Point, Dose)

Sirolimus

Mouse Oral LD50 > 2500 mg/kg
Rat Oral LD50 > 800 mg/kg

Propylene glycol

Rat Oral LD50 22,000 mg/kg
Mouse Oral LD50 24,900 mg/kg
Rabbit Dermal LD50 20,800 mg/kg

Lecithin

Rat Oral LD50 > 8 ml/kg

Ethanol
11. TOXICOLOGICAL INFORMATION

Material Name: Sirolimus Oral Solution

Reproductive & Fertility
- Rat, Oral, LD50 0.1 mg/kg/day
  - NOAEL: Embryotoxicity, Fetotoxicity

Skin Irritation
- Rabbit, Mild

Eye Irritation
- Rabbit, Mild

Ethanol
- Rabbit, Severe

Repeated Dose Toxicity: (Duration, Species, Route, Dose, End Point, Target Organ)

Sirolimus
- Monkey, No route specified, 0.05 mg/kg/day, NOAEL: Lymphoid tissue, Spleen, Thymus, Gastrointestinal System

Propylene glycol
- Skin Irritation, Rabbit, Mild
- Eye Irritation, Rabbit, Mild

Eye Irritation: (Study Type, Species, Severity)
- Rabbit, Severe

In Vitro
- Bacterial Mutagenicity (Ames) for Salmonella, E. coli: Negative
- Chromosome Aberration for Chinese Hamster Ovary (CHO) cells: Negative
- Forward Mutation Assay for Mouse Lymphoma: Negative
- Micronucleus for Bone Marrow: Negative

Reproduction & Development Toxicity: (Duration, Species, Route, Dose, End Point, Effect(s))

Sirolimus
- Reproductive & Fertility, Rat, No route specified, 0.1 mg/kg/day, NOAEL: Embryotoxicity, Fetotoxicity

Genetic Toxicity: (Study Type, Cell Type/Organism, Result)

Sirolimus
- In Vitro Mutagenicity (Ames) for Salmonella, E. coli: Negative
- In Vitro Chromosome Aberration for Chinese Hamster Ovary (CHO) cells: Negative
- In Vitro Forward Mutation Assay for Mouse Lymphoma: Negative
- In Vivo Micronucleus for Bone Marrow: Negative

Carcinogenicity: (Duration, Species, Route, Dose, End Point, Effect(s))

Sirolimus
- 86 Week(s), Mouse, No route specified, 6 mg/kg/day, LOAEL: Tumors, Lymphatic system
- 104 Week(s), Rat, No route specified, 0.2 mg/kg/day, LOAEL: Male reproductive system, Tumors

Carcinogen Status: Carcinogenicity of the mixture has not been determined. Alcohol is listed as a carcinogen by IARC. The IARC monograph examining the carcinogenic potential of ethanol examined only alcoholic beverages. No other components are listed as carcinogens by IARC, US OSHA or NTP.

Ethanol
- IARC: Group 1 (Carcinogenic to Humans)
11. TOXICOLOGICAL INFORMATION

12. ECOLOGICAL INFORMATION

Environmental Overview: See aquatic toxicity data, below:

Toxicity:
Aquatic Toxicity: (Species, Method, End Point, Duration, Result)

Sirolimus
_Pseudokirchneriella subcapitata_ (Green Alga) OECD EC50 72 Hours 0.063 mg/L

Ethanol
Fingerling Trout NPDES LC50 24 Hours 11,200 mg/L
_Oncorhynchus mykiss_ (Rainbow Trout) NPDES LC50 96 Hours 12,900 mg/L
_Pimephales promelas_ (Fathead Minnow) NPDES LC50 96 Hours 14,200 mg/L

Persistence and Degradability: No data available

Bio-accumulative Potential:
Partition Coefficient: (Method, pH, Endpoint, Value)

Sirolimus
Measured Log P > 4.63

Mobility in Soil: No data available

13. DISPOSAL CONSIDERATIONS

Waste Treatment Methods: Dispose of waste in accordance with all applicable laws and regulations. Member State specific and Community specific provisions must be considered. Considering the relevant known environmental and human health hazards of the material, review and implement appropriate technical and procedural waste water and waste disposal measures to prevent occupational exposure and environmental release. It is recommended that waste minimization be practiced. The best available technology should be utilized to prevent environmental releases. This may include destructive techniques for waste and wastewater.

14. TRANSPORT INFORMATION

The following refers to all modes of transportation unless specified below.

Not regulated for transport under USDOT, EUADR, IATA, or IMDG regulations.

15. REGULATORY INFORMATION

Safety, Health and Environmental Regulations/Legislation Specific for the Substance or Mixture
15. REGULATORY INFORMATION

<table>
<thead>
<tr>
<th>Material</th>
<th>CERCLA/SARA 313 Emission reporting</th>
<th>California Proposition 65</th>
<th>Inventory - United States TSCA - Sect. 8(b)</th>
<th>Australia (AICS)</th>
<th>EU EINECS/ELINCS List</th>
</tr>
</thead>
<tbody>
<tr>
<td>Soy fatty acids</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Not Listed</td>
<td>Not Listed</td>
<td>Present</td>
<td></td>
<td>269-657-0</td>
</tr>
<tr>
<td>Ethanol</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Not Listed</td>
<td></td>
<td>carcionogen 4/29/2011 in alcoholic beverages</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>developmental toxicity 10/1/1987 in alcoholic beverages</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sirolimus</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Not Listed</td>
<td>Not Listed</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Glycerides, unsatd. mono- and di-</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Not Listed</td>
<td>Not Listed</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lecithin</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Not Listed</td>
<td>Not Listed</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Polysorbate 80</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ascorbyl palmitate</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Version: 2.1
15. REGULATORY INFORMATION

| Inventory - United States TSCA - Sect. 8(b) | Present |
| Australia (AICS):                        | Present |
| EU EINECS/ELINCS List                    | 205-305-4 |

16. OTHER INFORMATION

Text of CLP/GHS Classification abbreviations mentioned in Section 3

- Reproductive toxicity-Cat.1B; H360FD - May damage fertility. May damage the unborn child.
- Hazardous to the aquatic environment, acute toxicity-Cat.1; H400 - Very toxic to aquatic life
- Hazardous to the aquatic environment, chronic toxicity-Cat.1; H410 - Very toxic to aquatic life with long lasting effects

Data Sources: Pfizer proprietary drug development information. Publicly available toxicity information.

Reasons for Revision: Updated Section 2 - Hazard Identification. Updated Section 8 - Exposure Controls / Personal Protection.

Revision date: 21-Mar-2018


Pfizer Inc believes that the information contained in this Material Safety Data Sheet is accurate, and while it is provided in good faith, it is without warranty of any kind, expressed or implied. If data for a hazard are not included in this document there is no known information at this time.

End of Safety Data Sheet