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

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

EU Classification:

EU Indication of danger: Toxic to Reproduction: Category 2
Dangerous for the Environment

EU Risk Phrases:

R60 - May impair fertility.
R61 - May cause harm to the unborn child.
R50/53 - Very toxic to aquatic organisms, may cause long-term adverse effects in the aquatic environment.

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

Other Hazards
Australian Hazard Classification (NOHSC):


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

#### Hazardous

<table>
<thead>
<tr>
<th>Ingredient</th>
<th>CAS Number</th>
<th>EU EINECS/ELINCS List</th>
<th>EU Classification</th>
<th>GHS Classification</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sirolimus</td>
<td>53123-88-9</td>
<td>Not Listed</td>
<td>Repr. Cat.2;R60-61; N;R50/53</td>
<td>Repr. 1B,H360FD; Aquatic Acute 1,H400; Aquatic Chronic 1,H410</td>
<td>1</td>
</tr>
<tr>
<td>Ethanol</td>
<td>64-17-5</td>
<td>200-578-6</td>
<td>F;R11</td>
<td>Flam. Liq. 2 (H225)</td>
<td>1.5-2.5</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Ingredient</th>
<th>CAS Number</th>
<th>EU EINECS/ELINCS List</th>
<th>EU Classification</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>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>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>Not Listed</td>
<td>*</td>
</tr>
<tr>
<td>Propylene glycol</td>
<td>57-55-6</td>
<td>200-338-0</td>
<td>Not Listed</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>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>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  R phrases and 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 fire fighting 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. Clean up operations should only be undertaken by trained personnel.

7. HANDLING AND STORAGE

**Precautions for Safe Handling**
7. HANDLING AND STORAGE
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
ACGIH Threshold Limit Value (STEL) 1000 ppm
Australia TWA 1000 ppm 1880 mg/m³
Austria OEL - MAKs 1000 ppm 1900 mg/m³
Belgium OEL - TWA 1000 ppm 1907 mg/m³
Bulgaria OEL - TWA 1000.0 mg/m³
Czech Republic OEL - TWA 1000 mg/m³
Denmark OEL - TWA 1000 ppm 1900 mg/m³
Estonia OEL - TWA 500 ppm 1000 mg/m³
Finland OEL - TWA 1000 ppm 1900 mg/m³
France OEL - TWA 1000 ppm 1900 mg/m³
Germany - TRGS 900 - TWAs 500 ppm 960 mg/m³
Germany (DFG) - MAK 500 ppm 960 mg/m³
Greece OEL - TWA 1000 ppm 1900 mg/m³
Hungary OEL - TWA 1900 mg/m³
Latvia OEL - TWA 1000 mg/m³
Lithuania OEL - TWA 500 ppm
Netherlands OEL - TWA 260 mg/m³
OSHA - Final PELS - TWAs: 1000 ppm 1900 mg/m³
Poland OEL - TWA 1900 mg/m³
Portugal OEL - TWA 1000 ppm
Romania OEL - TWA 1000 ppm 1900 mg/m³
Russia OEL - TWA 1000 mg/m³
8. EXPOSURE CONTROLS / PERSONAL PROTECTION

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).

Hands: Impervious, disposable gloves (double suggested) are recommended if skin contact with drug product is possible and for bulk processing operations.

Eyes: Wear safety glasses or goggles if eye contact is possible.

Skin: Impervious disposable protective clothing is recommended if skin contact with drug product is possible and for bulk processing operations.

Respiratory protection: If airborne exposures are within or exceed the Occupational Exposure Band (OEB) range, wear an appropriate respirator with a protection factor sufficient to control exposures to the bottom of the OEB range.

9. PHYSICAL AND CHEMICAL PROPERTIES

Physical State: Liquid
Odor: No data available.
Molecular Formula: Mixture
Solvent Solubility: No data available

Color: Yellow
Odor Threshold: No data available.
Molecular Weight: Mixture
## 9. PHYSICAL AND CHEMICAL PROPERTIES

<table>
<thead>
<tr>
<th>Property</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Water Solubility</td>
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</tr>
<tr>
<td>pH</td>
<td>No data available.</td>
</tr>
<tr>
<td>Melting/Freezing Point (°C)</td>
<td>No data available.</td>
</tr>
<tr>
<td>Boiling Point (°C)</td>
<td>No data available.</td>
</tr>
<tr>
<td>Partition Coefficient: (Method, pH, Endpoint, Value)</td>
<td>No data available.</td>
</tr>
<tr>
<td>Decomposition Temperature (°C):</td>
<td>No data available.</td>
</tr>
<tr>
<td>Evaporation Rate (Gram/s)</td>
<td>No data available</td>
</tr>
<tr>
<td>Vapor Pressure (kPa)</td>
<td>No data available</td>
</tr>
<tr>
<td>Vapor Density (g/ml)</td>
<td>No data available</td>
</tr>
<tr>
<td>Relative Density</td>
<td>No data available</td>
</tr>
<tr>
<td>Viscosity</td>
<td>No data available</td>
</tr>
<tr>
<td>Flammability</td>
<td>No data available</td>
</tr>
<tr>
<td>Autoignition Temperature (Solid) (°C):</td>
<td>No data available</td>
</tr>
<tr>
<td>Flammability (Solids):</td>
<td>No data available</td>
</tr>
<tr>
<td>Flash Point (Liquid) (°C):</td>
<td>No data available</td>
</tr>
<tr>
<td>Upper Explosive Limits (Liquid) (% by Vol.):</td>
<td>No data available</td>
</tr>
<tr>
<td>Lower Explosive Limits (Liquid) (% by Vol.):</td>
<td>No data available</td>
</tr>
</tbody>
</table>

### 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

### Polysorbate 80
- No data available

### Decomposition Temperature (°C):
- No data available.

## 10. STABILITY AND REACTIVITY

<table>
<thead>
<tr>
<th>Property</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Reactivity</td>
<td>No data available</td>
</tr>
<tr>
<td>Chemical Stability</td>
<td>Stable under normal conditions of use.</td>
</tr>
<tr>
<td>Possibility of Hazardous Reactions</td>
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</tr>
<tr>
<td>Oxidizing Properties</td>
<td>No data available</td>
</tr>
<tr>
<td>Conditions to Avoid</td>
<td>Fine particles (such as dust and mists) may fuel fires/explosions.</td>
</tr>
<tr>
<td>Incompatible Materials</td>
<td>As a precautionary measure, keep away from strong oxidizers</td>
</tr>
<tr>
<td>Hazardous Decomposition Products</td>
<td>No data available</td>
</tr>
</tbody>
</table>

## 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).
11. TOXICOLOGICAL INFORMATION

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

**Sirolimus**
- Mouse Oral LD50 > 2500 mg/kg
- Rat Oral LD50 > 800 mg/kg

**Lecithin**
- Rat Oral LD50 > 8 ml/kg

**Ethanol**
- Mouse Oral LD50 3,450 g/m³
- Rat Oral LD50 7,060 mg/kg
- Mouse Inhalation LC50 4h 39 g/m³
- Rat Inhalation LC50 10h 20,000 ppm

**Polysorbate 80**
- Rat Oral LD50 25 g/kg

**Acute Toxicity Comments:** A greater than symbol (>) indicates that the toxicity endpoint being tested was not achievable at the highest dose used in the test.

Irritation / Sensitization: (Study Type, Species, Severity)

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

**Ethanol**
- Eye Irritation 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

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

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

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

PZ01855
11. TOXICOLOGICAL INFORMATION

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)
OSHA: Listed

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

Canada - WHMIS: Classifications

WHMIS hazard class:
Class D, Division 2, Subdivision A

Soy fatty acids
CERCLA/SARA 313 Emission reporting: Not Listed
California Proposition 65: Not Listed
Inventory - United States TSCA - Sect. 8(b): Present
Australia (AICS): Present
EU EINECS/ELINCS List: 269-657-0

Sirolimus
CERCLA/SARA 313 Emission reporting: Not Listed
California Proposition 65: Not Listed

Standard for the Uniform Scheduling for Drugs and Poisons: Schedule 4
EU EINECS/ELINCS List: Not Listed

Ethanol
CERCLA/SARA 313 Emission reporting: Not Listed
carcinogen initial date 4/29/11 in alcoholic beverages
developmental toxicity initial date 10/1/87 in alcoholic beverages
California Proposition 65: Present
Inventory - United States TSCA - Sect. 8(b): Present
Australia (AICS): Present
EU EINECS/ELINCS List: 200-578-6

Ascorbyl palmitate
CERCLA/SARA 313 Emission reporting: Not Listed
California Proposition 65: Not Listed
Inventory - United States TSCA - Sect. 8(b): Present
Australia (AICS): Present
EU EINECS/ELINCS List: 205-305-4

Glycerides, unsatd. mono- and di-
CERCLA/SARA 313 Emission reporting: Not Listed
California Proposition 65: Not Listed
15. REGULATORY INFORMATION

Inventory - United States TSCA - Sect. 8(b) Present
Australia (AICS): Present
EU EINECS/ELINCS List 266-951-0

Propylene glycol
CERCLA/SARA 313 Emission reporting Not Listed
California Proposition 65 Not Listed
Inventory - United States TSCA - Sect. 8(b) Present
Australia (AICS): Present
EU EINECS/ELINCS List 200-338-0

Polysorbate 80
CERCLA/SARA 313 Emission reporting Not Listed
California Proposition 65 Not Listed
Inventory - United States TSCA - Sect. 8(b) Present
Australia (AICS): Present
EU EINECS/ELINCS List Not Listed

Lecithin
CERCLA/SARA 313 Emission reporting Not Listed
California Proposition 65 Not Listed
Inventory - United States TSCA - Sect. 8(b) Present
Australia (AICS): Present
REACH - Annex IV - Exemptions from the obligations of Register: Present
EU EINECS/ELINCS List 232-307-2

16. OTHER INFORMATION

Text of R phrases and 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
Toxic to Reproduction: Category 2
N - Dangerous for the environment
R60 - May impair fertility.
R61 - May cause harm to the unborn child.
R50/53 - Very toxic to aquatic organisms, may cause long-term adverse effects in the aquatic environment.

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

Reasons for Revision: Updated Section 2 - Hazard Identification. Updated Section 3 - Composition / Information on Ingredients.

Revision date: 31-Mar-2014
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