

**1. IDENTIFICATION OF THE SUBSTANCE/PREPARATION AND THE COMPANY/UNDERTAKING****Product Identifier****Material Name:** Sirolimus Oral Solution (Greenstone LLC)**Trade Name:** Not applicable**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**Greenstone LLC  
100 Route 206 North  
Peapack, NJ 07977  
800-435-7095**Emergency telephone number:**  
CHEMTREC (24 hours): 1-800-424-9300**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**Other Hazards**

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

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**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

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

Ingredient	CAS Number	EU EINECS/ELINCS List	GHS Classification	%
Soy fatty acids	68308-53-2	269-657-0	Not Listed	*
Propylene glycol	57-55-6	200-338-0	Not Listed	*
Glycerides, unsatd. mono- and di-	67701-32-0	266-951-0	Not Listed	*
Lecithin	8002-43-5	232-307-2	Not Listed	*
Polysorbate 80	9005-65-6	Not Listed	Not Listed	*
Ascorbyl palmitate	137-66-6	205-305-4	Not Listed	*

**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

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### 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

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### 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/m <sup>3</sup>
Austria OEL - MAKs	1000 ppm
	1900 mg/m <sup>3</sup>
Belgium OEL - TWA	1000 ppm
	1907 mg/m <sup>3</sup>
Bulgaria OEL - TWA	1000 mg/m <sup>3</sup>
Czech Republic OEL - TWA	1000 mg/m <sup>3</sup>
Denmark OEL - TWA	1000 ppm
	1900 mg/m <sup>3</sup>
Estonia OEL - TWA	500 ppm
	1000 mg/m <sup>3</sup>
Finland OEL - TWA	1000 ppm
	1900 mg/m <sup>3</sup>
France OEL - TWA	1000 ppm
	1900 mg/m <sup>3</sup>
Germany - TRGS 900 - TWAs	500 ppm
	960 mg/m <sup>3</sup>
Germany (DFG) - MAK	500 ppm
	960 mg/m <sup>3</sup>
Greece OEL - TWA	1000 ppm
	1900 mg/m <sup>3</sup>
Hungary OEL - TWA	1900 mg/m <sup>3</sup>
Latvia OEL - TWA	1000 mg/m <sup>3</sup>
Lithuania OEL - TWA	500 ppm
	1000 mg/m <sup>3</sup>
Netherlands OEL - TWA	260 mg/m <sup>3</sup>
OSHA - Final PELs - TWAs:	1000 ppm
	1900 mg/m <sup>3</sup>
Poland OEL - TWA	1900 mg/m <sup>3</sup>
Portugal OEL - TWA	1000 ppm
Romania OEL - TWA	1000 ppm
	1900 mg/m <sup>3</sup>
Slovakia OEL - TWA	500 ppm
	960 mg/m <sup>3</sup>
Slovenia OEL - TWA	1000 ppm
	1900 mg/m <sup>3</sup>
Sweden OEL - TWAs	500 ppm
	1000 mg/m <sup>3</sup>

#### Sirolimus

Manufacturer OEL: 0.2ug/m<sup>3</sup>

#### Propylene glycol

Australia TWA  
150 ppm  
474 mg/m<sup>3</sup>  
10 mg/m<sup>3</sup>

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Ireland OEL - TWAs	150 ppm 470 mg/m <sup>3</sup> 10 mg/m <sup>3</sup>
Latvia OEL - TWA	7 mg/m <sup>3</sup>
Lithuania OEL - TWA	7 mg/m <sup>3</sup>

### Manufacturer OEB Statement:

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.

<b>Hands:</b>	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.)
<b>Eyes:</b>	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.)
<b>Skin:</b>	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.)
<b>Respiratory protection:</b>	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

<b>Physical State:</b>	Liquid	<b>Color:</b>	Yellow
<b>Odor:</b>	No data available.	<b>Odor Threshold:</b>	No data available.
<b>Molecular Formula:</b>	Mixture	<b>Molecular Weight:</b>	Mixture

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

### Sirolimus

Measured Log P >4.63

### Propylene glycol

No data available

### Ascorbyl palmitate

No data available

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### 9. PHYSICAL AND CHEMICAL PROPERTIES

#### 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.

**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 > 800mg/kg

##### Propylene glycol

Rat Oral LD 50 22,000 mg/kg

Mouse Oral LD 50 24,900mg/kg

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### 11. TOXICOLOGICAL INFORMATION

Rabbit Dermal LD 50 20,800mg/kg

#### Lecithin

Rat Oral LD50 > 8 ml/kg

#### Ethanol

Mouse Oral LD50 3,450 g/m<sup>3</sup>

Rat Oral LD50 7,060mg/kg

Mouse Inhalation LC50 4h 39g/m<sup>3</sup>

Rat Inhalation LC50 10h 20,000ppm

#### 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 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

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### 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)

### 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.



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### 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

##### **Ethanol**

CERCLA/SARA 313 Emission reporting	Not Listed
California Proposition 65	carcinogen 4/29/2011 in alcoholic beverages developmental toxicity 10/1/1987 in alcoholic beverages
Inventory - United States TSCA - Sect. 8(b)	Present
Australia (AICS):	Present
EU EINECS/ELINCS List	200-578-6

##### **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

##### **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

##### **Glycerides, unsatd. mono- and di-**

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	266-951-0

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### 15. REGULATORY INFORMATION

#### 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

#### 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

#### 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

### 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:** The data contained in this MSDS may have been gathered from confidential internal sources, raw material suppliers, or from the published literature.

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

**Revision date:** 21-Mar-2018  
Product Stewardship Hazard Communication

**Prepared by:** Global Environment, Health, and Safety Operations

It is believed that the information contained in this Material Safety Data Sheet is accurate, and while it is provided in good faith, it is without a 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**