

**1. IDENTIFICATION OF THE SUBSTANCE/PREPARATION AND THE COMPANY/UNDERTAKING**

Greenstone LLC  
100 Route 206 North  
Peapack, NJ 07977  
800-435-7095

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

**Material Name: Sirolimus Tablets (Greenstone LLC)**

Trade Name:	Not applicable
Synonyms:	Sirolimus tablets
Chemical Family:	Macrocyclic lactone
Intended Use:	Pharmaceutical product used as, immunosuppressive agent

**2. HAZARDS IDENTIFICATION**

Appearance: Tan, White, or Yellow to Beige tablets  
Signal Word: DANGER

Statement of Hazard: May damage fertility or the unborn child.

Additional Hazard Information:  
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)

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

EU Hazard Symbols:



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.

Australian Hazard Classification (NOHSC): Hazardous Substance. Dangerous Goods.

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

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### 3. COMPOSITION/INFORMATION ON INGREDIENTS

#### Hazardous

Ingredient	CAS Number	EU EINECS/ELINCS List	EU Classification	%
Microcrystalline cellulose	9004-34-6	232-674-9	Not Listed	*
Sirolimus	53123-88-9	Not Listed	Repr. Cat.2;R60-61; N,R50/53	10
Lactose NF, monohydrate	64044-51-5	Not Listed	Not Listed	*
Sodium lauryl sulfate	151-21-3	205-788-1	Not Listed	*
Talc (non-asbestiform)	14807-96-6	238-877-9	Not Listed	*
Titanium dioxide	13463-67-7	236-675-5	Not Listed	<1.0
Triethyl Citrate	77-93-0	201-070-7	Not Listed	*

Ingredient	CAS Number	EU EINECS/ELINCS List	EU Classification	%
Hydroxypropyl cellulose	9004-64-2	Not Listed	Not Listed	*
Polysorbate 80	9005-65-6	Not Listed	Not Listed	*
Disodium Hydrogen Phosphate, Dihydrate	Not Available	Not Listed	Not Listed	*
Water, purified	7732-18-5	231-791-2	Not Listed	*
Glyceryl monostearate	31566-31-1	250-705-4	Not Listed	*
Mannitol	69-65-8	200-711-8	Not Listed	*

#### Additional Information:

\* Proprietary

Ingredient(s) indicated as hazardous have been assessed under standards for workplace safety.

For the full text of the R phrases mentioned in this Section, see Section 16

### 4. FIRST AID MEASURES

<b>Eye Contact:</b>	Flush with water while holding eyelids open for at least 15 minutes. Seek medical attention immediately.
<b>Skin Contact:</b>	Remove contaminated clothing. Flush area with large amounts of water. Use soap. Seek medical attention.
<b>Ingestion:</b>	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.
<b>Inhalation:</b>	Remove to fresh air and keep patient at rest. Seek medical attention immediately.
<b>Symptoms and Effects of Exposure:</b>	For information on potential signs and symptoms of exposure, See Section 2 - Hazards Identification and/or Section 11 - Toxicological Information.

### 5. FIRE FIGHTING MEASURES

<b>Extinguishing Media:</b>	Use carbon dioxide, dry chemical, or water spray.
<b>Hazardous Combustion Products:</b>	Formation of toxic gases is possible during heating or fire.
<b>Fire Fighting Procedures:</b>	During all fire fighting activities, wear appropriate protective equipment, including self-contained breathing apparatus.
<b>Fire / Explosion Hazards:</b>	Fine particles (such as dust and mists) may fuel fires/explosions.

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### 6. ACCIDENTAL RELEASE MEASURES

- Health and Safety Precautions:** Personnel involved in clean-up should wear appropriate personal protective equipment (see Section 8). Minimize exposure.
- Measures for Cleaning / Collecting:** Contain the source of spill if it is safe to do so. Collect spilled material by a method that controls dust generation. A damp cloth or a filtered vacuum should be used to clean spills of dry solids. Clean spill area thoroughly.
- Measures for Environmental Protections:** Place waste in an appropriately labeled, sealed container for disposal. Care should be taken to avoid environmental release.
- 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

- General Handling:** Minimize dust generation and accumulation. If tablets or capsules are crushed and/or broken, avoid breathing dust and avoid contact with eyes, skin, and clothing. When handling, use appropriate personal protective equipment (see Section 8). Wash thoroughly after handling. Refer to Section 12 - Ecological Information, for information on potential effects on the environment. Releases to the environment should be avoided. 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.
- Storage Conditions:** Store as directed by product packaging.

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### 8. EXPOSURE CONTROLS / PERSONAL PROTECTION

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

#### Microcrystalline cellulose

ACGIH Threshold Limit Value (TWA)	10 mg/m <sup>3</sup>
Australia TWA	10 mg/m <sup>3</sup>
Belgium OEL - TWA	10 mg/m <sup>3</sup>
Estonia OEL - TWA	10 mg/m <sup>3</sup>
France OEL - TWA	10 mg/m <sup>3</sup>
Ireland OEL - TWAs	10 mg/m <sup>3</sup>
	4 mg/m <sup>3</sup>
Latvia OEL - TWA	2 mg/m <sup>3</sup>
OSHA - Final PELs - TWAs:	15 mg/m <sup>3</sup>
Portugal OEL - TWA	10 mg/m <sup>3</sup>
Romania OEL - TWA	10 mg/m <sup>3</sup>
Spain OEL - TWA	10 mg/m <sup>3</sup>

#### Glyceryl monostearate

ACGIH Threshold Limit Value (TWA)	10 mg/m <sup>3</sup>
Lithuania OEL - TWA	5 mg/m <sup>3</sup>
Sweden OEL - TWAs	5 mg/m <sup>3</sup>

#### Talc (non-asbestiform)

ACGIH Threshold Limit Value (TWA)	2 mg/m <sup>3</sup>
Australia TWA	2.5 mg/m <sup>3</sup>
Austria OEL - MAKs	2 mg/m <sup>3</sup>
Belgium OEL - TWA	2 mg/m <sup>3</sup>
Bulgaria OEL - TWA	1.0 fiber/cm <sup>3</sup>
	6.0 mg/m <sup>3</sup>
	3.0 mg/m <sup>3</sup>
Czech Republic OEL - TWA	2.0 mg/m <sup>3</sup>
Denmark OEL - TWA	0.3 fiber/cm <sup>3</sup>
Finland OEL - TWA	0.5 fiber/cm <sup>3</sup>
Greece OEL - TWA	10 mg/m <sup>3</sup>
	2 mg/m <sup>3</sup>
Hungary OEL - TWA	2 mg/m <sup>3</sup>
Ireland OEL - TWAs	10 mg/m <sup>3</sup>
	0.8 mg/m <sup>3</sup>
Lithuania OEL - TWA	2 mg/m <sup>3</sup>
	1 mg/m <sup>3</sup>
Netherlands OEL - TWA	0.25 mg/m <sup>3</sup>
OSHA - Final PELs - Table Z-3 Mineral D:	20 mppcf
Poland OEL - TWA	4.0 mg/m <sup>3</sup>
	1.0 mg/m <sup>3</sup>
Portugal OEL - TWA	2 mg/m <sup>3</sup>
Romania OEL - TWA	2 mg/m <sup>3</sup>
Slovakia OEL - TWA	2 mg/m <sup>3</sup>
	10 mg/m <sup>3</sup>
Slovenia OEL - TWA	2 mg/m <sup>3</sup>
Spain OEL - TWA	2 mg/m <sup>3</sup>
Sweden OEL - TWAs	2 mg/m <sup>3</sup>
	1 mg/m <sup>3</sup>

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### Titanium dioxide

ACGIH Threshold Limit Value (TWA)	10 mg/m <sup>3</sup>
ACGIH OELs - Notice of Intended Changes	Listed
Australia TWA	10 mg/m <sup>3</sup>
Austria OEL - MAKs	5 mg/m <sup>3</sup>
Belgium OEL - TWA	10 mg/m <sup>3</sup>
Bulgaria OEL - TWA	10.0 mg/m <sup>3</sup>
Denmark OEL - TWA	6 mg/m <sup>3</sup>
Estonia OEL - TWA	5 mg/m <sup>3</sup>
France OEL - TWA	10 mg/m <sup>3</sup>
Greece OEL - TWA	10 mg/m <sup>3</sup>
	5 mg/m <sup>3</sup>
Ireland OEL - TWAs	10 mg/m <sup>3</sup>
	4 mg/m <sup>3</sup>
Latvia OEL - TWA	10 mg/m <sup>3</sup>
Lithuania OEL - TWA	5 mg/m <sup>3</sup>
OSHA - Final PELs - TWAs:	15 mg/m <sup>3</sup>
Poland OEL - TWA	10.0 mg/m <sup>3</sup>
Portugal OEL - TWA	10 mg/m <sup>3</sup>
Romania OEL - TWA	10 mg/m <sup>3</sup>
Spain OEL - TWA	10 mg/m <sup>3</sup>
Sweden OEL - TWAs	5 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.

### Disodium Hydrogen Phosphate, Dihydrate

Manufacturer OEB: OEB5 (control exposure to <1ug/m<sup>3</sup>)

### 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 gloves 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 protective clothing is recommended if skin contact with drug product is possible and for bulk processing operations.

**Respiratory protection:** 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.

## 9. PHYSICAL AND CHEMICAL PROPERTIES

Physical State:	Tablet	Color:	Tan, White, or Yellow to Beige
Molecular Formula:	Mixture	Molecular Weight:	Mixture

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### 9. PHYSICAL AND CHEMICAL PROPERTIES

### 10. STABILITY AND REACTIVITY

**Chemical Stability:** Stable under normal conditions of use.  
**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

### 11. TOXICOLOGICAL INFORMATION

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

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

##### **Sirolimus**

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

##### **Sodium lauryl sulfate**

Rat Oral LD50 1288 mg/kg

##### **Microcrystalline cellulose**

Rat Oral LD50 > 5000 mg/kg  
Rabbit Dermal LD50 > 2000 mg/kg

##### **Mannitol**

Rat Oral LD 50 13500 mg/kg  
Mouse Oral LD 50 22 g/kg

##### **Talc (non-asbestiform)**

Rat Oral LD50 > 1600 mg/kg

##### **Glyceryl monostearate**

Mouse IP LD50 200 mg/kg

##### **Polysorbate 80**

Rat Oral LD50 25 g/kg

##### **Titanium dioxide**

Rat Oral LD50 > 7500 mg/kg  
Rat Subcutaneous LD50 50 mg/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)

##### **Sodium lauryl sulfate**

Eye Irritation Rabbit Moderate  
Skin Irritation Rabbit Mild Moderate

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### 11. TOXICOLOGICAL INFORMATION

Skin Sensitization - GPMT Guinea Pig Negative  
Skin Sensitization - LLNA Mouse Negative

#### Microcrystalline cellulose

Skin Irritation Rabbit Non-irritating  
Eye Irritation Rabbit Non-irritating

#### 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

##### Sodium lauryl sulfate

Bacterial Mutagenicity (Ames) *Salmonella* 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:** None of the components of this formulation are listed as a carcinogen by IARC, NTP or OSHA.

##### Talc (non-asbestiform)

**IARC:** Group 3 (Not Classifiable)

##### Titanium dioxide

**IARC:** Group 2B (Possibly Carcinogenic to Humans)

**OSHA:** Listed

### 12. ECOLOGICAL INFORMATION

**Environmental Overview:** See aquatic toxicity data, below:

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

##### Sirolimus

*Pseudokirchneriella subcapitata* (Green Alga) OECD EC50 72 Hours 0.063 mg/L

##### Sodium lauryl sulfate

*Oncorhynchus mykiss* (Rainbow Trout) LC50 96 Hours 3.6 mg/L

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### 12. ECOLOGICAL INFORMATION

### 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.

This material is regulated for transportation as a hazardous material/dangerous good.

**UN number:** UN 3077  
**UN proper shipping name:** Environmentally Hazardous Substance, Solid, n.o.s (Sirolimus) Marine Pollutant  
**Transport hazard class(es):** 9  
**Packing group:** III  
Exception: Non-bulk packages of this product are not regulated for transport by road or air within the US and Puerto Rico, per 49 CFR 171.4(c).

### 15. REGULATORY INFORMATION

**EU Symbol:** T N  
**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.

**OSHA Label:**  
DANGER  
May damage fertility or the unborn child.

#### Canada - WHMIS: Classifications

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



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## 15. REGULATORY INFORMATION



### Hydroxypropyl cellulose

California Proposition 65	Not Listed
Inventory - United States TSCA - Sect. 8(b)	Present
Australia (AICS):	Present

### Microcrystalline cellulose

California Proposition 65	Not Listed
Inventory - United States TSCA - Sect. 8(b)	Present
Australia (AICS):	Present
EU EINECS/ELINCS List	232-674-9

### Polysorbate 80

California Proposition 65	Not Listed
Inventory - United States TSCA - Sect. 8(b)	Present
Australia (AICS):	Present

### Sirolimus

California Proposition 65	Not Listed
Standard for the Uniform Scheduling for Drugs and Poisons:	Schedule 4

### Disodium Hydrogen Phosphate, Dihydrate

California Proposition 65	Not Listed
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### Lactose NF, monohydrate

California Proposition 65	Not Listed
Australia (AICS):	Present

### Sodium lauryl sulfate

California Proposition 65	Not Listed
Inventory - United States TSCA - Sect. 8(b)	Present
Australia (AICS):	Present
Standard for the Uniform Scheduling for Drugs and Poisons:	Schedule 6
EU EINECS/ELINCS List	205-788-1

### Water, purified

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	231-791-2

### Glyceryl monostearate

California Proposition 65	Not Listed
Inventory - United States TSCA - Sect. 8(b)	Present

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### 15. REGULATORY INFORMATION

<b>Australia (AICS):</b>	Present
<b>EU EINECS/ELINCS List</b>	250-705-4
<b>Talc (non-asbestiform)</b>	
<b>California Proposition 65</b>	Not Listed
<b>Inventory - United States TSCA - Sect. 8(b)</b>	Present
<b>Australia (AICS):</b>	Present
<b>EU EINECS/ELINCS List</b>	238-877-9
<b>Titanium dioxide</b>	
<b>California Proposition 65</b>	carcinogen initial date 9/2/11 airborne, unbound particles of respirable size
<b>Inventory - United States TSCA - Sect. 8(b)</b>	Present
<b>Australia (AICS):</b>	Present
<b>EU EINECS/ELINCS List</b>	236-675-5
<b>Triethyl Citrate</b>	
<b>California Proposition 65</b>	Not Listed
<b>Inventory - United States TSCA - Sect. 8(b)</b>	Present
<b>Australia (AICS):</b>	Present
<b>EU EINECS/ELINCS List</b>	201-070-7
<b>Mannitol</b>	
<b>California Proposition 65</b>	Not Listed
<b>Inventory - United States TSCA - Sect. 8(b)</b>	Present
<b>Australia (AICS):</b>	Present
<b>REACH - Annex IV - Exemptions from the obligations of Register:</b>	Present
<b>EU EINECS/ELINCS List</b>	200-711-8

### 16. OTHER INFORMATION

#### Text of R phrases and GHS Classification abbreviations mentioned in Section 3

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:** 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 14 - Transport Information.

**Prepared by:** Product Stewardship Hazard Communication  
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**