SAFETY DATA SHEET

SECTION 1: PRODUCT IDENTIFICATION

PRODUCT NAME: TACROLIMUS, USP (Monohydrate)
PRODUCT CODE: 2698
SUPPLIER:
- MEDISCA Inc.
  Tel.: 1.800.932.1039 | Fax.: 1.855.850.5855
  661 Route 3, Unit C, Plattsburgh, NY, 12901
  3955 W. Mesa Vista Ave., Unit A-10, Las Vegas, NV, 89118
  6641 N. Belt Line Road, Suite 130, Irving, TX, 75063

- MEDISCA Pharmaceutique Inc.
  Tel.: 1.800.665.6334 | Fax.: 514.338.1693
  4509 Rue Dobrin, St. Laurent, QC, H4R 2L8
  21300 Gordon Way, Unit 153/158, Richmond, BC V6W 1M2

- MEDISCA Australia PTY LTD
  Tel.: 1.300.786.392 | Fax.: 61.2.9700.9047
  Unit 7, Heritage Business Park
  5-9 Ricketty Street, Mascot, NSW 2020

EMERGENCY PHONE:
- CHEMTREC Day or Night Within USA and Canada: 1-800-424-9300
- NSW Poisons Information Centre: 131 126

USES: Immunosuppressant

SECTION 2: HAZARDS IDENTIFICATION

GHS CLASSIFICATION:
- Acute Toxicity - Oral (Category 3)
- Carcinogenicity (Category 1A)
- Toxic to Reproduction (Category 2) (Effects on or via lactation)
- Eye Irritation (Category 2B)
- Specific Target Organ Toxicity - Repeated Exposure (Category 1) - (Immune system)

PICTOGRAM:

SIGNAL WORD: Danger

HAZARD STATEMENT(S):
- Toxic if swallowed.
- May cause cancer.
- May cause harm to breast-fed children.
- Suspected of damaging fertility or the unborn child.
- Causes eye irritation.
- Causes damage to organs through prolonged or repeated exposure

AUSTRALIA-ONLY HAZARDS: Not Applicable

PRECAUTIONARY STATEMENT(S):
- Prevention: Wash thoroughly after handling.
  Do not eat, drink or smoke when using this product.
  Obtain special instructions before use.
  Do not handle until all safety precautions have been read and understood.
  Wear protective gloves, protective clothing, eye protection, face protection.
  Avoid contact during pregnancy/while nursing.
  Do not breathe dust/fume/gas/mist/ vapors/spray.

IF SWALLOWED: Immediately call a poison center or medical professional; Rinse mouth. IF EXPOSED OR CONCERNED: Get medical advice/attention. IF IN EYES: Rinse cautiously with water for several minutes. Remove contact lenses, if present and easy to do. Continue rinsing. If eye irritation persists: Get medical advice/attention.

Store locked up.

Disposal

Dispose of contents and/or container in accordance with local regulations.

**HMIS CLASSIFICATION**

<table>
<thead>
<tr>
<th>Health Hazard</th>
<th>Flammability</th>
<th>Reactivity</th>
<th>Personal Protection</th>
</tr>
</thead>
<tbody>
<tr>
<td>3</td>
<td>0</td>
<td>0</td>
<td>H</td>
</tr>
</tbody>
</table>

**SECTION 3: COMPOSITION-INFORMATION ON INGREDIENTS**

**CHEMICAL NAME**

15,19-Epoxy-3H-pyrido[2,1-c][1,4]oxazacyclotricosine-1,7,20,21(4H,23H)-tetrone-5,6,8,11,12,13,14,15,16,17,18,19,24,25,26,26a-hexadecahydro-5,19-dihydroxy-3-[2-(4-hydroxy-3-methoxycyclohexyl)-1-methylethenyl]-14,16-dimethoxy-4,10,12,18-tetramethyl-8-(2-propenyl)-, monohydrate, [3S-[3R*,E(1S*,3S*,4S*)],4S*,5R*,8S*,9E,12R*,14R*,15S*,16R*,18S*,19S*,26aR*]]-

**BOTANICAL NAME**

Not applicable

**SYNONYM**

Not applicable

**CHEMICAL FORMULA**

C₄₄H₆₉NO₁₂·H₂O

**CAS NUMBER**

109581-93-3

**ALTERNATE CAS NUMBER**

Not applicable

**MOLECULAR WEIGHT**

822.0389

**COMPOSITION**

<table>
<thead>
<tr>
<th>CHEMICAL NAME</th>
<th>CAS NUMBER</th>
<th>% BY WEIGHT</th>
</tr>
</thead>
<tbody>
<tr>
<td>TACROLIMUS (monohydrate)</td>
<td>109581-93-3</td>
<td>100</td>
</tr>
</tbody>
</table>

There are no additional ingredients present which, within the current knowledge of the supplier and in the concentrations applicable, are classified as health hazards and hence require reporting in this section.

**NOTES**

Chemical family: Macrolide.

**SECTION 4: FIRST-AID MEASURES**

**IN CASE OF EYE CONTACT**

Flush with copious amounts of water for 15 minutes, separating eyelids with fingers. If irritation persists seek medical aid.

**IN CASE OF SKIN CONTACT**

Wash with soap & water for 15 minutes. If irritation persists seek medical aid.

**IF SWALLOWED**

Call a physician. Wash out mouth with water. Do not induce vomiting without medical advice.

**IF INHALED**

Remove to fresh air. If not breathing, give artificial respiration. If breathing is difficult, give oxygen. Call a physician.

**SYMPTOMS AND EFFECTS**

Not expected to present a significant hazard under anticipated conditions of normal use.

**SECTION 5: FIREFIGHTING MEASURES**

**SPECIFIC HAZARDS ARISING FROM THE CHEMICAL**

Not applicable

**FLAMMABLE PROPERTIES**

May be combustible at high temperature

**HAZARDOUS COMBUSTION PRODUCTS**

Under fire conditions, hazardous fumes will be present.
SAFETY DATA SHEET

SECTION 6: ACCIDENTAL RELEASE MEASURES

PERSONAL PRECAUTIONS
Wear respiratory protection. Avoid dust formation. Avoid breathing vapours, mist or gas. Ensure adequate ventilation. Evacuate personnel to safe areas. Avoid breathing dust.

METHODS & MATERIAL FOR CONTAINMENT
On land, sweep or shovel into suitable containers. Minimize generation of dust.

CLEANUP PROCEDURE
Do not touch damaged containers or spilled material unless wearing appropriate protective clothing. Wear respirator, chemical safety goggles, rubber boots and heavy rubber gloves. Stop leak if you can do it without risk. Prevent entry into waterways, sewers, basements or confined areas. Shut off all sources of ignition. Evacuate the area. If necessary, employ water fog to disperse the vapors. Absorb the matter with compatible vermiculite or other absorbing material. Place in a suitable container and retain for disposal. Ventilate and clean the affected area. Do not flush into sewerage system or to drains.

SECTION 7: HANDLING AND STORAGE

PRECAUTIONS FOR SAFE HANDLING
Do not inhale. Avoid contact with eyes, skin and clothing. Avoid prolonged or repeated exposure. Wash thoroughly after handling.

STORAGE CONDITIONS
Store in original container, tightly sealed container, protected from direct sunlight, in a dry and well-ventilated area, away from incompatible materials. Store in accordance with local regulations. Eliminate all ignition sources. Separate from oxidizing materials. Containers that have been opened must be carefully resealed and kept upright to prevent leakage. Do not store in unlabelled containers. Use appropriate containment to avoid environmental contamination. Controlled room temperature indicates a temperature 20° to 25°C (68° to 77°F); that results in a mean kinetic temperature calculated to be not more than 25°C; and that allows for excursions between 15° and 30°C (59° and 86°F) that are experienced in pharmacies, hospitals, and warehouses. Provided the mean kinetic temperature remains in the allowed range, transient spikes up to 40°C (104°F) are permitted as long as they do not exceed 24 hours. Preserve in tight containers, protected from light. Store at controlled room temperature.

SECTION 8: EXPOSURE CONTROLS/ PERSONAL PROTECTION

<table>
<thead>
<tr>
<th>Chemical Name: TACROLIMUS</th>
<th>CAS #: 109581-93-3</th>
</tr>
</thead>
<tbody>
<tr>
<td>OSHA PEL</td>
<td>TWA: N/L</td>
</tr>
<tr>
<td></td>
<td>Ceiling: N/L</td>
</tr>
<tr>
<td></td>
<td>STEL: -</td>
</tr>
<tr>
<td></td>
<td>REL: -</td>
</tr>
<tr>
<td></td>
<td>IDLH: -</td>
</tr>
<tr>
<td></td>
<td>Remarks: -</td>
</tr>
<tr>
<td>ACGIH TLV</td>
<td>TWA: N/L</td>
</tr>
<tr>
<td></td>
<td>Ceiling: N/L</td>
</tr>
<tr>
<td></td>
<td>STEL: N/L</td>
</tr>
<tr>
<td></td>
<td>REL: -</td>
</tr>
<tr>
<td></td>
<td>IDLH: -</td>
</tr>
<tr>
<td></td>
<td>Remarks: -</td>
</tr>
<tr>
<td>NIOSH</td>
<td>TWA: N/L</td>
</tr>
<tr>
<td></td>
<td>Ceiling: N/L</td>
</tr>
<tr>
<td></td>
<td>STEL: N/L</td>
</tr>
<tr>
<td></td>
<td>REL: N/L</td>
</tr>
<tr>
<td></td>
<td>IDLH: N/L</td>
</tr>
<tr>
<td></td>
<td>Remarks: -</td>
</tr>
<tr>
<td>AIHA WEEL</td>
<td>TWA: N/L</td>
</tr>
<tr>
<td></td>
<td>Ceiling: N/L</td>
</tr>
<tr>
<td></td>
<td>STEL: N/L</td>
</tr>
<tr>
<td></td>
<td>REL: -</td>
</tr>
<tr>
<td></td>
<td>IDLH: -</td>
</tr>
<tr>
<td></td>
<td>Remarks: -</td>
</tr>
<tr>
<td>Safe Work Australia HSIS</td>
<td>TWA: N/L</td>
</tr>
<tr>
<td></td>
<td>Ceiling: N/L</td>
</tr>
<tr>
<td></td>
<td>STEL: N/L</td>
</tr>
<tr>
<td></td>
<td>REL: -</td>
</tr>
<tr>
<td></td>
<td>IDLH: -</td>
</tr>
<tr>
<td></td>
<td>Remarks: -</td>
</tr>
<tr>
<td>HSE</td>
<td>TWA: N/L</td>
</tr>
<tr>
<td></td>
<td>Ceiling: N/L</td>
</tr>
<tr>
<td></td>
<td>STEL: N/L</td>
</tr>
<tr>
<td></td>
<td>REL: -</td>
</tr>
<tr>
<td></td>
<td>IDLH: -</td>
</tr>
<tr>
<td></td>
<td>Remarks: -</td>
</tr>
</tbody>
</table>

N/L = Not Listed

EXPOSURE GUIDELINES
Consult local authorities for provincial or state exposure limits. Particulates not otherwise regulated, respirable fraction: 5 mg/m³
SAFETY DATA SHEET

PERSONAL PROTECTIVE EQUIPMENT
Eyes: Wear appropriate protective eyeglasses or chemical safety goggles as described by WHMIS or OSHA's eye and face protection regulations in 29 CFR 1910.133 or European Standard EN166. Skin: Wear appropriate gloves to prevent skin exposure. Clothing: Wear appropriate protective clothing to minimize contact with skin. Respirators: Follow WHMIS or OSHA respirator regulations found in 29 CFR 1910.134 or European Standard EN 149. Use a NIOSH/MSHA or European Standard EN 149 approved respirator if exposure limits are exceeded or if irritation or other symptoms are experienced.

SPECIFIC ENGINEERING CONTROLS
Adequate mechanical ventilation. Fume hood, eye wash station, and safety shower.

NOTES
USP: ELV: Industrial use: TWA: 0.2 micrograms/m³

SECTION 9: PHYSICAL AND CHEMICAL PROPERTIES

<table>
<thead>
<tr>
<th>PHYSICAL STATE</th>
<th>Solid</th>
</tr>
</thead>
<tbody>
<tr>
<td>DESCRIPTION</td>
<td>White to off-white powder.</td>
</tr>
<tr>
<td>SOLUBILITY</td>
<td>Insoluble in water; soluble in acetone, chloroform and ethyl acetate.</td>
</tr>
<tr>
<td>ODOR</td>
<td>Not available.</td>
</tr>
<tr>
<td>FLAMMABILITY</td>
<td>May be combustible at high temperature</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>ODOR THRESHOLD</th>
<th>Not available</th>
</tr>
</thead>
<tbody>
<tr>
<td>pH</td>
<td>Not available</td>
</tr>
<tr>
<td>MELTING POINT</td>
<td>(127 - 133)°C, (260.6-271.4)°F</td>
</tr>
<tr>
<td>FREEZING POINT</td>
<td>(127 - 133)°C, (260.6-271.4)°F</td>
</tr>
<tr>
<td>EVAPORATION RATE</td>
<td>Not available</td>
</tr>
<tr>
<td>EXPLOSIVE LIMIT</td>
<td>Not available</td>
</tr>
<tr>
<td>VAPOR PRESSURE</td>
<td>Not available</td>
</tr>
<tr>
<td>RELATIVE DENSITY</td>
<td>(WATER = 1)</td>
</tr>
<tr>
<td>log P</td>
<td>(OCTANOL-WATER)</td>
</tr>
<tr>
<td>VISCOSITY</td>
<td>Not available</td>
</tr>
</tbody>
</table>

SECTION 10: STABILITY AND REACTIVITY

<table>
<thead>
<tr>
<th>REACTIVITY</th>
<th>Not established</th>
</tr>
</thead>
<tbody>
<tr>
<td>STABILITY</td>
<td>Stable under recommended storage conditions</td>
</tr>
<tr>
<td>MATERIALS TO AVOID</td>
<td>Strong oxidants</td>
</tr>
<tr>
<td>HAZARDOUS DECOMPOSITION PRODUCTS</td>
<td>Toxic fumes of carbon monoxide, carbon dioxide, nitrogen oxides and other gases may occur</td>
</tr>
<tr>
<td>HAZARDOUS POLYMERIZATION</td>
<td>Will not occur</td>
</tr>
<tr>
<td>POSSIBILITY OF HAZARDOUS REACTION</td>
<td>Not established</td>
</tr>
<tr>
<td>CONDITIONS TO AVOID</td>
<td>Moisture, sunlight and extreme temperatures</td>
</tr>
</tbody>
</table>
SECTION 11: TOXICOLOGICAL INFORMATION

ACUTE TOXICITY

Oral: Rat: LD50: (mg/kg): 134
Dermal: Rabbit LD50: (mg/kg): Not available
Inhalation: Rat: LD50: (mg/L/4hr): Not available

SKIN CORROSION/IRRITATION

Based on available data, the classification criteria are not met.
Local effects:
Irritancy test
Result: Non-Irritant.
Species: Rabbit
Organ: Skin.

SERIOUS EYE DAMAGE/EYE IRRITATION

Causes eye irritation.
Local effects:
Irritancy test
Result: Irritant.
Species: Rabbit
Organ: Eye.

RESPIRATORY OR SKIN SENSITIZATION

Respiratory sensitization: Due to lack of data the classification is not possible.
Skin sensitization: Due to lack of data the classification is not possible.

GERM CELL MUTAGENICITY

Due to lack of data the classification is not possible.

CARCINOGENICITY

OSHA
TACROLIMUS is not listed.
NTP
TACROLIMUS is not listed.
IARC
TACROLIMUS is not evaluated.
California
Proposition 65
This product does not contain any chemicals known to the State of California to cause cancer, birth defects, or any other reproductive harm.

ADDITIONAL CARCINOGENICITY INFORMATION

The systemic use of tacrolimus increases the risk of malignancy. Carcinogenicity studies in animals have also reported an increase in the incidence of malignancies associated with the topical tacrolimus. As of December 2004 the FDA had received reports of 19 cases of lymphoma or cutaneous tumours associated with topical tacrolimus, of which 4 cases were a recurrence or aggravation of a pre-existing malignancy, and 3 other cases were confounded by other possible risk factors. In general, longterm data are still needed to determine the carcinogenic risk, if there is any, from topical tacrolimus.

REPRODUCTIVE TOXICITY

Suspected of damaging fertility or the unborn child. Tacrolimus is distributed into breast milk. Tacrolimus concentrations were measured in milk from a liver transplant recipient on a dose of 100 micrograms/kg daily. The authors estimated that the infant would ingest only 0.06% (0.06 micrograms/kg daily) of the mother’s weight-adjusted dose. No adverse effects were noted in the infant at 2.5 months of age.

SPECIFIC TARGET ORGAN TOXICITY - SINGLE EXPOSURE

Based on available data, the classification criteria are not met.

SPECIFIC TARGET ORGAN TOXICITY - REPEATED EXPOSURE

Causes damage to organs (Immune system) through prolonged or repeated exposure.

ASPIRATION HAZARDS

Based on available data, the classification criteria are not met.

SIGNS AND SYMPTOMS OF EXPOSURE

May produce nephrotoxicity and neurotoxicity, tremor, headache, paraesthesias, nausea, diarrhoea, hypertension, leucocytosis, impaired renal function, anaemia, luccopenia, hyperkalaemia, mood changes, sleep disturbances, confusion, tinnitus, visual disturbances, convulsions, constipation, gastrointestinal haemorrhage, skin rash, cramps, peripheral oedema liver dysfunction and coagulation disorders.

Symptoms related to the physical, chemical, and toxicological characteristics

POTENTIAL HEALTH EFFECTS

Inhalation: May be harmful if inhaled. May cause respiratory tract irritation.
Ingestion: Toxic if swallowed.
Skin: May be harmful if absorbed through skin. May cause skin irritation
Eyes: Causes eye irritation.
SECTION 12: ECOLOGICAL INFORMATION

**TOXICITY**
EC50: 48 Hr: Crustacea: (mg/L): Not available
LC50: 96 Hr: Fish: (mg/L): Not available
IC50: 72 Hr: Algae: (mg/L): Not available

**PERSISTENCE AND DEGRADABILITY**
Not available

**BIOACCUMULATIVE POTENTIAL**
Not available

**MOBILITY IN SOIL**
Insoluble in water

**OTHER ADVERSE EFFECTS**
This product is not intended to be released into the environment

SECTION 13: DISPOSAL CONSIDERATIONS

**WASTE DISPOSAL**
Dispose of in accordance with federal / local laws and regulations. Avoid release into the environment.

SECTION 14: TRANSPORT INFORMATION

**UNITED STATES & CANADA**
UN PROPER SHIPPING NAME: TOXIC SOLID, ORGANIC, N.O.S.
UN NUMBER: 2811
CLASS: 6.1
PACKING GROUP: III

**AUSTRALIA**
UN PROPER SHIPPING NAME: TOXIC SOLID, ORGANIC, N.O.S.
UN NUMBER: 2811
CLASS: 6.1
PACKING GROUP: III
HAZCHEM: 2X

**ENVIRONMENTAL HAZARDS**
Not available

**SPECIAL SHIPPING INFORMATION**
Not applicable

SECTION 15: REGULATORY INFORMATION

<table>
<thead>
<tr>
<th>Chemical Name &amp; CAS</th>
<th>CERCLA 40 CFR Part 302.4</th>
<th>SARA (Title III) 40 CFR Part 372.65</th>
<th>EPA 40 CFR Part 355 Appendix A</th>
<th>Pennsylvania</th>
<th>Right-to-know New Jersey</th>
<th>Massachusetts</th>
<th>California Prop 65</th>
</tr>
</thead>
<tbody>
<tr>
<td>TACROLIMUS 109581-93-3</td>
<td>N/L</td>
<td>N/L</td>
<td>N/L</td>
<td>N/L</td>
<td>N/L</td>
<td>N/L</td>
<td>N/L</td>
</tr>
</tbody>
</table>

N/L = Not Listed; X = Listed

Last Revision: 09/2016
**SAFETY DATA SHEET**

**AUSTRALIAN REGULATIONS**

<table>
<thead>
<tr>
<th>Chemical Name &amp; CAS</th>
<th>Poisons and Therapeutic Goods Regulation</th>
<th>Therapeutic Goods Act</th>
<th>Code of Practices - Illicit Drug Precursors</th>
</tr>
</thead>
<tbody>
<tr>
<td>TACROLIMUS 109581-93-3</td>
<td>N/L</td>
<td>Listed as Schedule 4</td>
<td>N/L</td>
</tr>
</tbody>
</table>

**SECTION 16: OTHER INFORMATION**

**REFERENCES**
Available upon request

**ABBREVIATIONS AND ACRONYMS**
CAS – Chemical Abstract Service; GHS – Global Harmonized System; OSHA PEL – Occupational Safety & Health Administration Permissible Exposure Limits; TWA – Time Weighted Average; HSIS – Hazardous Substances Information System; STEL – Short Term Exposure Limit; AIHA WEEL – American Industrial Hygiene Association Workplace Environment Exposure Levels; LD50 – Lethal Dose, 50%; IARC – International Agency for Research on Cancer; NTP – National Toxicology Program; WHMIS – Workplace Hazardous Materials Information System; SARA – Superfund Amendments and Reauthorization Act; EPA – Environmental Protection Agency; CERCLA – Comprehensive Environmental Response, Compensation, and Liability Act; HMIS – Hazardous Materials Information System; NIOSH – National Institute for Occupational Safety and Health; MSHA - Mine Safety and Health Administration; ACGIH - American Conference of Governmental Industrial Hygienists; IDHL - Immediately Dangerous to Health or Life; TLV – Threshold Limit Value; HSE – Health and Safety Executive; REL - Recommended Exposure Limit

**LAST REVISION**
09/2016

**SUPERSEDES**
07/2015

**DISCLAIMER**
This document was created in accordance with OSHA, Safe Work Australia and WHMIS regulations. The above information is believed to be correct but does not purport to be all inclusive and shall be used only as a guide. The information in this document is based on the present state of our knowledge and is applicable to the product with regard to appropriate safety precautions. It does not represent any guarantee of the properties of the product. MEDISCA® shall not be held liable for any damage resulting from handling or from contact with the above product. Recipients of the product must take responsibility for observing existing laws and regulations.