



Rapamycin

Description

This standard operating procedure outlines the handling and use of rapamycin. Review this document and supply the information required in order to make it specific to your facility. In accordance with this document, laboratories should use appropriate controls, personal protective equipment, and disposal techniques when handling rapamycin.

Rapamycin is an immunosuppressant drug used to prevent rejection in organ transplantation; it is especially useful in kidney transplants. Rapamycin is not a calcineurin inhibitor. However, it has a similar suppressive effect on the immune system. Rapamycin inhibits the response to interleukin-2 (IL-2) and thereby blocks activation of T- and B-cells. The health effects from long-term usage could include increase the risk of developing an infection or cancer, especially lymphoma (cancer of a part of the immune system) or skin cancer.

Synonyms: RAPA, RPM, Rapamune, Sirolimus, "macrocyclic polyketide", "macrocyclic triene antibiotic", antirestenotic, immunosuppressant, "mTOR inhibitor"

Potential Hazards

- Toxic: danger of serious damage to health by prolonged exposure if swallowed.
- Possible carcinogenic effect.
- Biologically active compounds may produce idiosyncratic effects which are entirely unpredictable on the basis of literature searches and prior clinical experience (both recent and past).
- Ingestion of the material may be damaging to the health of the individual.

Macrolides comprise a large group of antibiotics derived from *Streptomyces* spp. having in common a macrocyclic lactone ring to which one or more sugars are attached. They are all weak bases. The most common side effect produced by the family of macrolide antibiotics is gastrointestinal discomfort. Supra-infections may occur although these are rare. Several macrolides produced allergic sensitization but, again, these are rare. Symptoms include watery eyes, shortness of breath, nasal congestion, choking, coughing and wheezing. Allergic skin reactions have also occurred. Exposure to at least one member of the family, erythromycin, at high concentrations, has produced reversible deafness (ototoxicity). Systemic reactions including fever, rash, and lymph-node pain or swelling have been produced by the avermectin group. Ivermectin has produced ataxia (incoordination), lethargy, bradypnea (slowed breathing), vomiting, mydriasis (dilated pupils), sedation, tremors and death in animals. The avermectin group (anthelmintics, insecticides and acaricides) mediate the transmission of gamma-butyric acid (GABA), an inhibitory neurotransmitter, in mammals thus causing paralysis. Hepatotoxic effects with transient disturbances and jaundice have resulted from the use of oleandomycin. Transient alterations in heart rate/ rhythm have also been produced by several members of the family (notably tilmicosin). Heart muscle degeneration, characterized by small areas of cell death has also been reported in animals exposed to tilmicosin. Cross-resistance is often observed between the macrolide, lincosamide and streptogramin group of antibiotics.

Eye:
Although the material is not thought to be an irritant, direct contact with the eye may cause transient discomfort characterized by tearing or conjunctival redness (as with windburn). Slight abrasive damage may also result. The material may produce foreign body irritation in certain individuals.

Skin:

The material is not thought to produce adverse health effects or skin irritation following contact (as classified using animal models). Nevertheless, good hygiene practice requires that exposure be kept to a minimum and that suitable gloves be used in an occupational setting.

Open cuts, abraded or irritated skin should not be exposed to this material. Entry into the blood-stream through, for example, cuts, abrasions or lesions, may produce systemic injury with harmful effects. Examine the skin prior to the use of the material and ensure that any external damage is suitably protected.

Inhaled:

The material is not thought to produce either adverse health effects or irritation of the respiratory tract following inhalation (as classified using animal models). Nevertheless, adverse effects have been produced following exposure of animals by at least one other route and good hygiene practice requires that exposure be kept to a minimum and that suitable control measures be used in an occupational setting.

Persons with impaired respiratory function, airway diseases and conditions such as emphysema or chronic bronchitis, may incur further disability if excessive concentrations of particulate are inhaled.

Engineering Controls

- Enclosed local exhaust ventilation is required at points of dust, fume or vapor generation.
- Work should be performed in a fume hood or Biological Safety Cabinet.

Work Practice Controls

Decontamination should consist of surface cleaning with water and detergent followed by thorough rinsing. The use of detergent is recommended because there is no single accepted method of chemical deactivation for all agents involved. A plastic backed absorbent pad should be placed under the work area during the process. This should be changed at the end of each procedure or when a spill occurs.

Personal Protective Equipment (PPE)

Personal protective equipment includes a lab coat, eye protection and disposable gloves. Gloves should be changed frequently and should be pulled up over sleeves if possible to reduce the likelihood of any exposed skin. Wash hands and arms immediately after working with the substance. Particulate respirator protection should be assessed where incidental or accidental exposure is anticipated.

Transportation and Storage

- Keep containers tightly closed and store in a dry and ventilated area.
- Store away from strong oxidizing agents.
- Store according with information on product insert.
- Rapamycin is NOT REGULATED by DOT or IATA.

Waste Disposal

All hazardous chemical agent contaminated waste should be placed in a 5 gallon white pail. The container should be closed except when actively adding waste. The container must be located in the area where hazardous drugs are

being used. All items contaminated by hazardous drugs, including gloves, syringes, vials needles, and solution containers should be disposed according to EHS guidelines.

Sharps – place needles, syringes with needles attached and other breakable items into appropriately labeled sharps containers.

Empty stock vials, reagent bottles, etc. – triple rinse with copious amounts of water. Deface label with black magic marker or scraper. Place in a cardboard box for disposal.

Because most spent, unused and expired chemicals/materials are considered hazardous wastes, they must be properly disposed of. ***Do not dispose of chemical wastes by dumping them down a sink, flushing in a toilet or discarding in regular trash containers, unless authorized by UM Flint EHS.*** Contact Environment, Health and Safety (EHS) at (810) 766-6763 for waste containers, labels, manifests, waste collection and for any questions regarding proper waste disposal. Also refer to UM-Flint Hazardous Waste Management Program and EHS webpage <http://www.umflint.edu/ehs/environment-health-and-safety> for more information.

If animals are administered rapamycin in their food or water, both the food and water container must be labeled. Food or water that is not consumed by the animals must be collected, labeled and submitted for disposal as a hazardous material.

Exposures/Unintended Contact



If the employee is in need of emergency medical attention, call 911 immediately.



SWALLOWED

- Seek medical advice.
- Give water to rinse out mouth.
- If swallowed do NOT induce vomiting, unless directed to do so by medical personnel.
- If vomiting occurs, lean patient forward or place on left side (head-down position, if possible) to maintain open airway and prevent aspiration.

EYE

If this product comes in contact with the eyes:

- Wash out immediately with fresh running water.
- Ensure complete irrigation of the eye by keeping eyelids apart and away from eye and moving the eyelids by occasionally lifting the upper and lower lids.
- If pain persists or recurs seek medical attention.
- Removal of contact lenses after an eye injury should only be undertaken by skilled personnel.

SKIN

If skin or hair contact occurs:

- Flush skin and hair with running water (and soap if available).
- Seek medical attention in event of irritation.

INHALED

- If inhaled remove from contaminated area.
- Consult a physician.

Contact EHS for advice on symptoms of chemical exposure, or assistance in performing an exposure assessment.

Report all work related accidents, injuries, illnesses or exposures to UM-Flint DPS. Additionally, employees and supervisors must be sure to report the injury to EHS and complete and submit the [Illness and Injury Report Form](#) to WorkConnections within 24 hours. Follow the directions on the WorkConnections website [Forms Instructions](#) to obtain proper medical treatment and follow-up.

If you were involved in or observed an incident or near miss, please complete the [EHS Laboratory Incident and Near-Miss Report Form](#). This will be valuable in improving laboratory safety on UM-Flint campus.

TREATMENT FACILITIES:

<u>MAJOR INJURIES</u>	<u>MINOR INJURIES –During Business Hours</u>	<u>MINOR INJURIES –After Business Hours</u>
Genesys Hospital One Genesys Parkway Grand Blanc, MI 48439 (810) 606-5710 Hurley Medical Center One Hurley Plaza Flint, MI 48503 (810) 262-9000 McLaren Hospital Flint 401 South Ballenger Hwy Flint, MI 48532 (810) 342-2000	Genesys Occupational Health Network 1460 Center Rd. Burton, MI 48509 (810) 715-4620 Mon. to Fri. 7:30 am to 10 pm Sat. & Sun. Noon to 8 pm McLaren Flint-Burton OCC Center 1459 S. Center Rd. Burton, MI 48509 (810) 496-0900 Mon. - Fri. 8 am to 8 pm Sat & Sun 10 am to 2 pm	Downtown Flint 420 S. Saginaw St. Flint, MI 48502 (810) 762-1550 Genesys East 1096 S. Belsay Rd, Suite F Burton, MI 48509 (810) 743-3351 Genesys North 4154 W. Vienna Rd Clio, MI 48420 (810) 686-7397 Genesys South 8447 N. Holly Rd Grand Blanc, MI 48439 (810) 603-0856 Mon. - Fri. 6 to 10pm / Sat. & Sun. 1-10pm

Click [here](#) for more information on the UM – Flint Emergency Preparedness and Response Plan.

Spill Procedure

- When a spill occurs, **personal safety should always come first**.
- Alert and clear everyone in the immediate area where the spill occurred.

A **minor (small) chemical spill** is one of a known chemical that the laboratory staff is capable of handling safely without the assistance of safety and emergency personnel. A **major/large chemical spill** requires active assistance from emergency personnel.

Spill Response Steps:

MINOR CHEMICAL SPILL

- Alert people in immediate area of spill.
- Open outside windows, if possible.
- Use proper personal protective equipment (PPE) as indicated above.
- Avoid breathing vapors from spill.
- Confine spill to as small an area as possible.
- **Do not wash spill down the drain.**
- Use appropriate spill kits/sorbents to absorb spill. Collect contaminated materials and residues and place in container. For powdered chemicals sweep carefully to avoid generation of dust or, if appropriate, use moist sorbent pads or wet the powder with a suitable solvent and then wipe with a dry cloth. Contact EHS at (810) 766-6763 for proper disposal.
- Clean spill area with water.

MAJOR CHEMICAL SPILL

- Attend to injured or contaminated persons and remove them from exposure.
- Alert people in the laboratory to evacuate.
- If spilled material is flammable, turn off ignition and heat sources. Don't light Bunsen burners or turn on other switches.
- **Call University of Michigan – Flint Public Safety Department (DPS) at 911 immediately for assistance.**
- Close doors to affected area.
- Post warnings to keep people from entering the area.
- Have person available that has knowledge of incident and laboratory to assist emergency personnel.

Additional Spill Links:

- www.oseh.umich.edu/pdf/chemspil.pdf
- <http://www.oseh.umich.edu/emer-chemical.shtml>

Report all emergencies, suspicious activity, injuries, spills, and fires to the UM-Flint Department of Public Safety (DPS) at 911 from any university telephone or (810) 762-3333 from cell phone or non-university telephone. Register with the [University of Michigan-Flint Emergency Alert System](#) via Wolverine Access. Also, preprogram the UM-Flint DPS telephone number (810) 762-3333 into your cell phone for quick, easy use.

Training of personnel

All personnel are required to complete Laboratory Safety Training. Documentation of the training is required. This training can be accomplished by completing the **Comprehensive Laboratory Safety** session (**BLS009** or equivalent) via [MyLINC](#), or UM-Flint EHS on-line training or other equivalent approved by EHS. Furthermore, all personnel shall read and fully adhere to this SOP when handling rapamycin.

Certification

I have read and understand the above SOP. I agree to contact my Supervisor or Lab Manager if I plan to modify this procedure.

Name	Signature	UM ID #	Date

Prior Approval required – Is this procedure hazardous enough to warrant prior approval from the Principal Investigator? YES NO

Principal Investigator _____

Revision Date _____