

MU Policy on Research Use of Acute Biological Toxins and Select Agents

(June 12 2019)

1. General Description of Biological Toxins

Biological toxins are toxic substances produced by microorganisms, animals, and plants that have the capability of causing harmful effects when inhaled, ingested, injected or absorbed. The health effects of exposure can vary greatly depending on the toxin, the amount, and the route of exposure, ranging from minor (skin or eye irritation, headache, nausea) to severe (respiratory distress, muscle weakness, seizures, death).

The MU Institutional Biosafety Committee (IBC) oversees the possession, use, and transfer of unfractionated mixtures and purified preparations of acute biological toxins which are mammalian toxins with an LD50 less than 100 µg/kg body weight. The IBC also oversees the use and possession of organisms, both natural and recombinant, which produce these toxins. **A Listing of Biological Toxins can be found on the Marshall University Institutional Biosafety Committee (IBC) website.** Please note that this list may not be complete and that any biological toxins with LD50 values < 100 µg/kg body weight that will require registration. If you are uncertain about LD50 of your toxin or need additional guidance, please contact Mark Buchanan in Environmental Health and Safety 304-696-3461 or Don Primerano IBC Chair 304-696-7338.

Modes of Transmission

Biological toxins may be transmitted via surface contact with contaminated object(s) and subsequently spread to mucous membranes (eyes, nose, and mouth) and/or to open sores on skin. Some biological toxins can be absorbed through intact skin, especially if solubilized in substances such as dimethyl sulfoxide (DMSO).

Accidental needle-stick is a mode of transmission within research laboratories. Accidental ingestion of contaminated materials and inhalation are other routes of transmission.

Laboratory Practices

- Biosafety Level 2 practices and facilities shall be used for activities involving biological toxins.
- Biohazard signs and labels must be displayed in areas and on equipment where biological toxins are used and stored. This includes, but is not limited to, laboratory entrance doors, biological safety cabinets, chemical fume hoods, refrigerators, and freezers.
- Use a biological safety cabinet (BSC) (a.k.a. tissue culture hood) or a chemical fume hood for resuspension of biological toxins or manipulation of stock solutions of toxins that can generate aerosols, such as pipetting, harvesting, infecting cells, filling tubes/containers, and opening sealed centrifuge canisters.
- Some toxins come in sealed glass ampoules that must be snapped open to access to the powder within for resuspension. Use great care in cracking the ampoule to avoid an accidental cut or exposure to the toxin powder.

- Some toxins arrive in rubber septum sealed vials. If using a needle and syringe to plunge through the septum to resuspend, then use a hands-free device to stabilize the vial to avoid an accidental needle stick. Use great care.
- Whenever possible, use needle-free techniques to resuspend biological toxins. If you must weigh a quantity of powder-form toxin, then the scale must be located in a certified chemical fume hood.

Personal Protective Equipment

Work with biological toxins shall be conducted using the following PPE within a BSL2 facility:

- Disposable gloves (Consider the use of double gloves for enhanced protection.) Ensure your gloves are compatible with any solvent your toxin may be dissolved in.
- Lab coat or back-closing disposable gown
- Eye protection (safety glasses or goggles) is recommended, but not required when working within a biosafety cabinet or a chemical fume hood.

Inactivation and Disposal

Toxin stability varies considerably outside of physiological conditions depending upon the temperature, pH, ionic strength, and other characteristics. Inactivation is not always a linear function of heating time, and some protein toxins possess a capacity to re-fold, and partially reverse inactivation caused by heating. In addition, the conditions for denaturing toxins in aqueous solutions are not necessarily applicable for inactivating dry, powdered toxin preparations. Please contact Mark Buchanan or Don Primerano for information on methods of toxin inactivation. If the toxin cannot be inactivated on site, contact Mark Buchanan to arrange for a waste pickup. Solid and liquid materials that are potentially contaminated with toxins shall be disposed of as biohazardous waste. These materials must be decontaminated by inactivation on site or picked up as biohazardous waste.

Employee Exposure

All personnel working with biological toxins or accessing a toxin laboratory should be familiar with the signs and symptoms of toxin exposure. Researchers working with a toxin should be vaccinated if a vaccine is available for the biological toxin (e.g. diphtheria toxin, tetanus toxin). Antitoxins are available for some biological toxins and immediate medical "first-aid" interventions may help prevent or lessen the severity of the reaction.

If you know or suspect a biological toxin exposure...

- Irrigate the site of exposure
If exposure was by needle stick or other route which breaks the skin, wash with soap and water for 5-15 minutes and cover with a bandage.
If exposure was by splash to eyes or mucus membranes, irrigate thoroughly for 15 minutes at an appropriate eye wash station.
- Seek medical attention immediately then report to your Laboratory Supervisor and biosafety officer.

2. Registration of Projects Involving Acute Toxins

All acute toxins must be registered with the MU IBC by completing the rDNA Infectious Agent Form and the Biological Toxin/Select Agent Forms. **In addition to the registration forms, you must also submit lab-specific Standard Operating Procedures (SOPs) for work with and handling of acute toxins at the time you submit your acute toxin registration document.** You cannot begin work with the toxin until your project and SOPs have been approved.

Note that the deliberate formation of recombinant or synthetic nucleic acid molecules containing genes for the biosynthesis of toxin molecules with an LD50 less than 100 ng/kg body weight (e.g. botulinum toxins, tetanus toxin, diphtheria toxin, and Shigella dysenteriae neurotoxin) is subject to the NIH Guidelines and must be approved by NIH/OBA and the IBC prior to initiation.

3. Toxins Classified as Select Agents

Some biological toxins are classified by the Federal Government as Select Agents due to their potential to pose a severe threat to public health and safety. Possession, use and transfer of these toxins are highly regulated and all Select Agent Toxins must be registered with the Institutional Biosafety Committee. Information on Select Agents and the Select Agent Program can be found at www.selectagents.gov/index.html.

Some Select Agents when present in small quantities are exempt from Select Agent regulations, provided the amount under control of a principal investigator, treating physician or veterinarian does not exceed, at any time or in any form, the amounts indicated in the table below. **However, any Select Agent regardless of amount must still be registered with the IBC.**

Permissible Toxin Amounts: (from the Select Agent Website)
<https://www.selectagents.gov/PermissibleToxinAmounts.html>

The following toxins are not regulated by the Select Agent Program if the amount under the control of a principal investigator, treating physician or veterinarian, or commercial manufacturer or distributor does not exceed, at any time, the amounts indicated in the table below.

HHS Toxins [§73.3(d)(7)]	Amount
Abrin	1000 mg
Botulinum neurotoxins	1 mg
Short, paralytic alpha conotoxins	100 mg
Diacetoxyscirpenol (DAS)	10,000 mg
Ricin	1000 mg
Saxitoxin	500 mg
Staphylococcal Enterotoxins (Subtypes A, B, C, D, and E)	100 mg
T-2 toxin	10,000 mg
Tetrodotoxin	500 mg

4. Export Controlled Toxins

Several biological toxins are restricted for export by the U.S. Department of Commerce and require an export license prior to any shipment out of the U.S. Relevant regulations and the list of toxins and subject to export controls may be found on the US Department of Commerce Bio-agent export control list:

<http://www.bis.doc.gov/index.php/regulations/export-administration-regulations-ear>