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GUIDELINES FOR WORKING WITH SELECT AGENT TOXINS

1. Scope

The Department of Health and Human Services (DHHS)/Centers for Disease Control and Prevention (CDC) and the U.S. Department of Agriculture (USDA) have regulations for the possession, use and transfer of select biological agents and toxins that could pose a threat to human, animal and plant health and safety. The complete list of agents currently regulated under the Select Agent Program is attached.

These regulations implement the Public Health Security and Bioterrorism Preparedness Response Act of 2002, which became effective February 7, 2003 with full compliance due before November 12, 2003. The rules establish a registration process for facilities possessing select agents and toxins, safety and physical security compliance requirements, exemption criteria, and restrictions upon persons eligible to be granted access to a select agent or toxin in accordance with the US Patriot Act. More information about the Select Agent Program may be found at <http://www.cdc.gov/od/sap/>.

These Guidelines pertain to toxins on the Select Agent list, which may be exempt from Federal registration due to possession of quantities below federally established thresholds.

2. Requirements

- 2.1. All investigators at the University of Pittsburgh in possession of any select agents (including toxins) must be registered with the Department of Environmental Health and Safety. Please visit <http://www.ehs.pitt.edu/biological/workbook.html> to download this MS Excel-based workbook and follow the associated instructional guide to submit your registration. Upon successful submittal, you will receive an email notification of receipt from EHS.
- 2.2. EHS will coordinate the federal registration with the Select Agent Program for those investigators requiring registration. Federal regulations require the designation of a Responsible Official (RO) for Select Agents in each organization possessing such materials. The RO for the University of Pittsburgh is Jay Frerotte, Director of Environmental Health and Safety.
- 2.3. All investigators must notify the RO prior to acquiring or purchasing any amount of material on the attached list of select agents, including toxins. The notification must include the identity, quantity and source of the agent and should be submitted via email to biosafe@ehs.pitt.edu No select agents may be transferred to or from the University of Pittsburgh without prior registration with the CDC and with the RO. The RO will coordinate all requests for CDC or USDA approval regarding the procurement, transfer, or destruction of Select Agents.

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3. Toxin Exemptions

- 3.1. Under the Regulations, certain listed toxins are exempt from the Select Agent registration with the Federal government provided that the *principal investigator does not at any time possess more than the following aggregate amount of any toxin* (in the purified form or in combinations of pure and impure forms):

Toxin	Maximum Exempt Aggregate Amount
Abrin	1,000 mg
Botulium neurotoxin	1 mg
Conotoxins	100 mg
Diacetoxyscirpenol	10,000 mg
Ricin	1,000 mg
Saxitoxin	500 mg
Staphylococcal Enterotoxins (Subtypes A, B, C, D, and E)	100 mg
T-2 Toxin	10,000 mg
Tetrodotoxin	500 mg

- 3.2. Investigators in possession of any the toxins listed above, but in a quantity below the applicable limits are still required to **register with EHS**.
- 3.3. All principal investigators in possession of any the toxins listed above must sign and date the attached *Toxin Declaration Form*. Completed forms must be returned to the Biosafety Officer, 4th Floor Jerome Cochran Public Safety Building or faxed to 412-624-8524.
- 3.4. The Biosafety Officer must be notified prior to each toxin acquisition purchase or transfer, regardless of quantity, procured or transferred. The notification must include the recipient's identity including the recipient's name, institution name, address, telephone number and email address; the name of the toxin and the total amount to be transferred; and the recipient's intended use of the toxin (to demonstrate a legitimate need), and must be submitted via email to biosafe@ehs.pitt.edu. The investigator must wait for a response before the acquisition or purchase is initiated. **No amount of toxin may be transferred to an investigator either within the University of Pittsburgh or at another institution without prior authorization from the Biosafety Officer.**
- 3.5. An inventory log must be kept for each toxin listed above. The inventory log must reflect the date and quantity of each purchase, acquisition or transfer of toxin. The log must also reflect any toxin usage or destruction.
- 3.6. EHS will conduct periodic audits to verify the maintenance of the toxin inventory logs, and to verify appropriate storage and use of the toxin.

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- 3.7. The investigator must take precautions to ensure the security of the toxins by limiting access to the toxin storage and use locations. EH&S recommends that toxin samples be secured in a locking refrigerator/freezer or a locking box within the refrigerator/freezer, to which physical access (key or combination) is restricted. Toxin use locations should be secured by locking lab doors. Access should be limited to lab personnel.
- 3.8. The investigator must take the following steps **PRIOR** to discontinuing work with select agent toxins, relocating a laboratory, or leaving the university:
- 3.8.1. The University BSO must be notified via email at biosafe@ehs.pitt.edu. The investigator must note the date that work with toxin is scheduled to be complete.
- 3.8.2. The investigator must fill out the "Request to Discontinue Select Agent Toxin Registration" form. Completed forms must be returned to the Biosafety Officer, 4th Floor Public Safety Building or faxed to 412-624-8524.
- 3.8.3. If the investigator is in possession of unwanted/excess toxin, the agent must be properly deactivated, the deactivation witnessed by a representative of EH&S, and the "Select Agent Toxin Destruction" form completed. Appropriate means of deactivation are as follows:

Toxin	Chemical Inactivation Agent	Contact time
Abrin	1:10 bleach	30 minutes
Botulinum neurotoxin	1:10 bleach	30 minutes
Conotoxins	Contact EH&S	
Diacetoxyscirpenol	1:1 bleach +0.25N NaOH	30 minutes
Ricin	1:5 bleach	30 minutes
Saxitoxin	1:10 bleach	30 minutes
Staphylococcus enterotoxin A, B, C, D, or E	1:10 bleach	15 minutes
Tetrodotoxin	1:1 bleach 1:10 bleach + 1N NaOH	30 minutes
T-2	1:1 bleach + 0.25 N NaOH	4 hours

- 3.9. If an investigator seeks to possess more toxin than the exemption quantity, prior approval from University EHS and the Federal Select Agent Program, as coordinated through EHS, must be obtained before acquiring the material.

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TOXIN DECLARATION FORM

The University of Pittsburgh requires all investigators in possession of toxins listed in the Select Agent Regulation (42 CFR 73) to complete this form. If the investigator always possesses less than the exemption quantity, no Federal registration is necessary.

By signing below, I indicate the following:

- I am in possession of a toxin(s) found on the attached Select Agent List.
- I have registered the toxin(s) in my possession with the University of Pittsburgh Department of Environmental Health and Safety (EHS).
- I understand the quantity exemption limit for the toxin(s) in my possession and **I agree to never exceed the applicable possession limit without prior approval from the Department of Environmental Health and Safety and the Federal government.**
- I understand that failure to abide by these quantity limits for specified toxins will result in a Federal violation of the Select Agent Regulation, which may have serious consequences including criminal penalties.
- I agree to maintain an accurate inventory log for the toxin(s) in my possession.
- I agree to notify EHS prior to any new toxin(s) acquisition, purchase or transfer, including transfers to another investigator at the University of Pittsburgh or at another institution.
- I agree to notify EH&S when discontinuing work with the toxin(s), relocating the laboratory, or leaving the University of Pittsburgh. I understand that if I am leaving the university or discontinuing work with select agent, I will need to complete the "Request to Discontinue Select Agent Toxin Registration" form.
- I understand that unwanted/excess toxin must be inactivated by an approved means, the inactivation must be witnessed by a representative of EH&S, and that the "Select Agent Toxin Destruction" form must be completed and submitted to EH&S.

Name (Print)

Signature

Date

**Return completed form to: Biosafety Officer, 400 Public Safety Building or fax to 624-8524.
For questions call: 412-624-8919**

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Select Agents and Toxins

Bacteria

- § *Bacillus anthracis**
- § *Bacillus anthracis* Pasteur strain
- § Botulinum neurotoxin producing species of *Clostridium**
- § *Brucella abortus*
- § *Brucella melitensis*
- § *Brucella suis*
- § *Burkholderia mallei**
- § *Burkholderia pseudomallei**
- § *Coxiella burnetii*
- § *Francisella tularensis**
- § *Mycoplasma capricolum*
- § *Mycoplasma mycoides*
- § *Ralstonia solanacearum*
- § *Rathayibacter toxicus*
- § *Rickettsia prowazekii*
- § *Xanthomonas oryzae*
- § *Yersinia pestis**

Toxins (Below quantity in parentheses, toxin is exempt)

- § Abrin (1,000 mg)
- § Botulinum neurotoxin (1 mg)*
- § Conotoxins (Short, paralytic alpha conotoxins containing the following amino acid sequence: X₁CCX₂PACGX₃X₄X₅X₆CX₇) (100 mg)
- § Diacetoxyscirpenol (10,000 mg)
- § Ricin (1,000 mg)
- § Saxitoxin (500 mg)
- § Staphylococcal enterotoxins A, B, C, D, and E subtypes(100 mg)
- § T-2 toxin (10,000 mg)
- § Tetrodotoxin (500 mg)

Viruses

- § African horse sickness virus
- § African swine fever virus
- § Avian influenza virus
- § Classical swine fever virus
- § Crimean-Congo haemorrhagic fever virus
- § Eastern Equine Encephalitis virus
- § Ebola virus*
- § Foot-and-mouth disease virus*
- § Goat pox virus
- § Hendra virus
- § Lassa fever virus
- § Lujo virus
- § Lumpy skin disease virus

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Viruses, continued

- § Marburg virus*
- § Monkeypox virus
- § Newcastle disease virus¹
- § Nipah virus
- § Peste des petits ruminants virus
- § Rift Valley fever virus
- § Rinderpest virus*
- § Sheep pox virus
- § South American Haemorrhagic Fever viruses (Chapare, Guanarito, Junin, Machupo, and Sabia)
- § Swine vesicular disease virus
- § Tick-borne encephalitis complex (flavi) viruses (Far Eastern subtype, Siberian subtype, Kyasanur Forest disease virus, Omsk hemorrhagic fever virus)
- § Variola major virus (Smallpox virus)*
- § Variola minor virus (Alastrim)*
- § Venezuelan Equine Encephalitis virus
- § Vesicular stomatitis virus (exotic)

Fungi

- § *Peronosclerospora philippinensis* (*Peronosclerospora sacchari*)
- § *Phoma glycinicola* (formerly *Pyrenochaeta glycines*)
- § *Sclerophthora rayssiae*
- § *Synchytrium endobioticum*

*Denotes Tier 1 Agent

Genetic Elements and Recombinant Organisms considered as Select Agents

- § Nucleic acids that can produce infectious forms of any of the select agent viruses listed above.
- § Recombinant and/or synthetic nucleic acids that encode for the functional form(s) of any of the toxins listed above if the nucleic acids:
 - can be expressed in vivo or in vitro, or
 - are in a vector or recombinant host genome and can be expressed in vivo or in vitro.
- § Select agents and toxins that have been genetically modified.

Exclusions

- § Any select agent or toxin that is in its naturally occurring environment provided it has not been intentionally introduced, cultivated, collected, or otherwise extracted from its natural source.
- § Non-viable select agent organisms or nonfunctional toxins.
- § Fixed tissues that bear or contain select agents or toxins.
- § Genetic elements or sub-units of agents or toxins, if the genetic elements or sub-units are not capable of causing disease.
- § An animal inoculated with or exposed to a select toxin