

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

- 2.1.1 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 (EH&S). Please visit <http://www.ehs.pitt.edu/biosafety/biochemreg.htm> 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 EH&S.
- 2.1.2 EH&S will coordinate the Federal registration with the Select Agent Program for all University 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.
- 2.1.3 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 the University RO. The RO will coordinate all requests for CDC or USDA approval regarding the procurement, transfer, or destruction of Select Agents.

3. Toxin Exemptions

- 3.1.1 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):

Abrin	100 mg
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Botulinum neurotoxin	0.5 mg
<i>Clostridium perfringens</i> epsilon toxin	100 mg
Conotoxins	100 mg
Diacetoxyscirpenol	1000 mg
Ricin	100 mg
Saxitoxin	100 mg
Shiga-like ribosome inactivating proteins	100 mg
Shigatoxin	100 mg
Staphylococcal enterotoxin	5 mg
Tetrodotoxin	100 mg
T-2	1,000 mg

- 3.1.2 Investigators in possession of any the toxins listed above, but in a quantity below the applicable limits are still required to [register with EHS](#).
- 3.1.3 All principal investigators in possession of any the toxins listed above (in any quantity) must sign and date the attached *Toxin Declaration Form*. Completed forms must be returned to the Department of Environmental Health & Safety, 4th Floor Public Safety Building, 3412 Forbes Avenue or faxed to 624-8524.
- 3.1.4 The Department of Environmental Health and Safety must be notified prior to each toxin acquisition, purchase or transfer, regardless of quantity procured or transferred. The notification must include the identity, quantity and source of the agent and should be submitted via email to biosafe@ehs.pitt.edu. The investigator must wait for a response before the acquisition or purchase is initiated.
- 3.1.5 An inventory log must be accurately maintained 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.
- 3.1.6 EH&S will conduct periodic audits to verify the maintenance of the toxin inventory logs, and to verify appropriate storage and use of the toxin.
- 3.1.7 The investigator must take precautions to ensure the security of the toxins by limiting access to the toxin storage and use locations.
- 3.1.8 Investigators must notify EH&S if they will no longer be in possession of select agent toxins.
- 3.1.9 If an investigator seeks to possess more toxin than the exemption quantity, prior approval from University EH&S and the Federal Select Agent Program, as coordinated through EH&S, must be obtained before acquiring the material

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 (EH&S).
- 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 EH&S prior to any new toxin(s) acquisition, purchase or transfer.
- I agree to notify EH&S when I am no longer in possession of any select agent toxin(s).

Signature

Date

Name (Print)

Return completed forms to the Department of Environmental Health & Safety, 4th Floor Public Safety Building, 3412 Forbes Avenue or fax to 624-8524. For questions, please call 624-9505.

Select Agents and Toxins

CDC – Regulated under 42 CFR Part 73
USDA – Regulated under 9 CFR Part 121
USDA Plant Pathogen – Regulated under 7 CFR Part 331

Bacteria

- *Bacillus anthracis* (CDC / USDA)
- *Brucella abortus* (CDC / USDA)
- *Brucella melitensis* (CDC / USDA)
- *Brucella suis* (CDC / USDA)
- *Burkholderia mallei* (formerly *Pseudomonas mallei*) (CDC / USDA)
- *Burkholderia pseudomallei* (formerly *Pseudomonas pseudomallei*) (CDC / USDA)
- Botulinum neurotoxin producing species of *Clostridium* (CDC / USDA)
- *Coxiella burnetii* (CDC / USDA)
- *Cowdria ruminantium* (Heartwater) (USDA)
- *Francisella tularensis* (CDC / USDA)
- *Liberobacter africanus* (USDA Plant Pathogen)
- *Liberobacter asiaticus* (USDA Plant Pathogen)
- *Mycoplasma capricolum*/ *M. F38*/*M. mycoides capri* (contagious caprine pleuropneumonia) (USDA)
- *Mycoplasma mycoides mycoides* (contagious bovine pleuropneumonia) (USDA)
- *Ralstonia solanacearum*, race 3, biovar 2 (USDA Plant Pathogen)
- *Rickettsia prowazekii* (CDC)
- *Rickettsia rickettsii* (CDC)
- *Xanthomonas oryzae* pv. *oryzicola* (USDA Plant Pathogen)
- *Xylella fastidiosa* (citrus variegated chlorosis strain) (USDA Plant Pathogen)
- *Yersinia pestis* (CDC)

Toxins (Below quantity in parentheses, toxin is exempt)

- Abrin (100 mg) (CDC)
- Botulinum neurotoxin (0.5 mg) (CDC / USDA)
- *Clostridium perfringens* epsilon toxin (100 mg) (CDC / USDA)
- Conotoxins (100 mg) (CDC)
- Diacetoxyscirpenol (1 g) (CDC)
- Ricin (100 mg) (CDC)
- Saxitoxin (100 mg) (CDC)
- Shiga-like ribosome inactivating proteins (100 mg) (CDC)
- Shigatoxin (100 mg) (CDC / USDA)
- Staphylococcal enterotoxins (5 mg) (CDC / USDA)
- T-2 toxin (1 g) (CDC / USDA)
- Tetrodotoxin (100 mg) (CDC)

Viruses

- African horse sickness virus (USDA)
- African swine fever virus (USDA)
- Akabane virus (USDA)
- Avian influenza virus (highly pathogenic) (USDA)
- Bluetongue virus (exotic) (USDA)
- Camel pox virus (USDA)
- Cercopithecine herpesvirus 1 (Herpes B virus) (CDC)
- Classical swine fever virus (USDA)

- Crimean-Congo haemorrhagic fever virus (CDC)
- Eastern Equine Encephalitis virus (CDC / USDA)
- Ebola viruses (CDC)
- Foot-and-mouth disease virus (USDA)
- Goat pox virus (USDA)
- Hendra virus (CDC / USDA)
- Japanese encephalitis virus (USDA)
- Lassa fever virus (CDC)
- Lumpy skin disease virus (USDA)
- Malignant catarrhal fever virus (Alcelaphine herpesvirus type 1) (USDA)
- Marburg virus (CDC)
- Menangle virus (USDA)
- Monkeypox virus (CDC)
- Newcastle disease virus (Velogenic) (USDA)
- Nipah virus (CDC / USDA)
- Peste des petits ruminants virus (USDA)
- Reconstructed replication competent forms of the 1918 pandemic influenza virus containing any portion of the coding regions of all eight gene segments (Reconstructed 1918 Influenza virus) (CDC)
- Rift Valley fever virus (Vaccine strain MP-12 exempt) (CDC / USDA)
- Rinderpest virus (USDA)
- Sheep pox virus (USDA)
- South American Haemorrhagic Fever viruses [Junin (Candid #1 vaccine strain exempt) Machupo, Sabia, Flexal, Guanarito] (CDC)
- Swine vesicular disease virus (USDA)
- Tick-borne encephalitis complex (flavi) viruses (Central European Tick-borne encephalitis, Far Eastern Tick-borne encephalitis, Russian Spring and Summer encephalitis, Kyasanur Forest disease, Omsk Hemorrhagic Fever) (CDC)
- Variola major virus (Smallpox virus) and Variola minor virus (Alastrim) (CDC)
- Venezuelan Equine Encephalitis virus (Vaccine strain TC-83 exempt) (CDC / USDA)
- Vesicular stomatitis virus (exotic) (USDA)

Fungi

- *Coccidioides immitis* (CDC / USDA)
- *Coccidioides posadasii* (CDC)
- *Peronosclerospora philippinensis* (USDA Plant Pathogen)
- *Sclerophthora rayssiae var. zae* (USDA Plant Pathogen)
- *Synchytrium endobioticum* (USDA Plant Pathogen)

Prions

- Bovine spongiform encephalopathy agent (USDA)

Genetic Elements and Recombinant Organisms considered as Select Agents

- Nucleic acids that can produce infectious forms of any of the select agent viruses.
- Recombinant nucleic acids that encode for the functional form(s) of any of the select agent toxins (i) can be expressed *in vivo* or *in vitro* or (ii) are in a vector or recombinant host genome and can be expressed *in vivo* or *in vitro*
- Viruses, bacteria, fungi, and toxins listed that have been genetically modified.
- Experiments involving deliberate formation of recombinant DNA containing genes for the biosynthesis of listed toxin lethal for vertebrates at an LD50 <100 ng/kg body weight

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.