12 Select Agents

Select agents are materials that have been identified by the U.S. Government as agents with potential for use in biological terrorism or warfare. The Department of Health and Human Services (DHHS), through the U.S. Centers for Disease Control and Prevention (CDC), and the Animal Plant Health Inspection Service (APHIS), through the United States Department of Agriculture (USDA), regulate select agents in the United States and its territories. Each agency has developed and maintains a list of select agents, including human, animal, and plant pathogens, high-risk toxins of biological origin, and prions. The list of select agents is below is current as of January 2013, and can also be accessed from CDC and USDA web sites at: http://www.selectagents.gov/SelectAgentsandToxins.html. The Select Agent Registry page may be accessed at: http://www.selectagents.gov/index.html.

The federal select agent regulations were updated and changes have taken effect as of December 4, 2012. The most significant changes are an update of the select agents and toxins list (as reflected in Appendix A of this plan) and the establishment of Tier 1 select agents and toxins. The list of Tier 1 select agents and toxins are also included in Appendix A. Institutions that possess or work with Tier 1 agents will have to implement additional personnel screening and ongoing personal screening requirements beyond the current federal background checks. Yale University is not currently registered for Tier 1 agents. A personnel screening program will be developed prior to the receipt of Tier 1 agents. In addition to the enhanced screening requirements for personnel with access to Tier 1 select agents, additional physical security measures have been added for locations where Tier 1 select agents are either stored or used. Yale University’s current select agent laboratory is in conformity with the additional physical security measures that are required for research with Tier 1 select agents and toxins.

National concerns over select agents have led to an expansion in security requirements for these materials. As a result, entities and researchers in possession of these materials have additional obligations and responsibilities for their safe storage, use, transfer, and disposal.

12.1 Possession, Use, or Transfer of Select Agents

In order to possess, use, send or receive Select Agents, an institution and each individual who will have access to the Select Agent(s) must first satisfy the following requirements. Each requirement must be approved prior to possession, use or transfer.

- Register with the applicable U.S. Governing bodies (CDC, APHIS, and/or USDA) through the Yale Office of Environmental Health & Safety (EHS).
- Register with the State of Connecticut Department of Public Health through Yale EHS. This is required for those Select Agents that are human pathogens.
- Official authorization granted for each individual requesting access to Select Agents provided by the U.S. Federal Bureau of Investigation, the applicable U.S. Governing body, and Yale University.

Please note that violations of Select Agent rules and regulations can lead to severe criminal or civil penalties. Imprisonment and fines up to $250,000.00 may be levied against individuals who are found in violation of these laws.
12.2 List of Select Agents and Regulated Toxins

The current list of Select Agents below is current as of January 2013. The Select Agent List is available online at: http://www.selectagents.gov/SelectAgentsandToxins.html.

Select Agent Regulations may be found at: http://www.selectagents.gov/regulations.html.

The list of excluded agents and toxins can be found at: http://www.selectagents.gov/SelectAgentsandToxinsExclusions.html

**HHS Select Agents and Toxins**

- Abrin
- Botulinum neurotoxins*
- Botulinum neurotoxin producing species of Clostridium*
- Short, paralytic alpha Conotoxins
- Coxiella burnetii
- Crimean-Congo haemorrhagic fever virus
- Diacetoxyscirpenol
- Eastern Equine Encephalitis virus
- Ebola virus*
- Francisella tularensis*
- Lassa fever virus
- Lujo virus
- Marburg virus*
- Monkeypox virus
- 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)
- Ricin
- Rickettsia prowazekii
- Saxitoxin
- South American Haemorrhagic Fever viruses
  - Chapare
  - Guanarito
  - Junin
  - Machupo
  - Sabia
- Staphylococcal enterotoxins T-2 toxin
- Tetrodotoxin
- Tick-borne encephalitis complex (flavi) viruses
  - Far Eastern Tick-borne encephalitis
  - Siberian subtype
  - Kyasanur Forest disease
  - Omsk Hemorrhagic Fever
  - Variola major virus (Smallpox virus)*
  - Variola minor virus (Alastrim)*
  - Yersinia pestis*

**Overlap Select Agents and Toxins**

- Bacillus anthracis*
- Bacillus anthracis Pasteur strain
- Brucella abortus
- Brucella melitensis
- Brucella suis
- Burkholderia mallei*
- Burkholderia pseudomallei*
- Hendra virus
- Nipah virus
- Rift Valley fever virus
- Venezuelan Equine Encephalitis virus

**USDA Veterinary Services (VS) Select Agents and Toxins**

- African horse sickness virus
- African swine fever virus
- Akabane virus
- Avian influenza virus (highly pathogenic)
- Bluetongue virus (exotic)
- Camel pox virus
- Classical swine fever virus
- Ehrlichia ruminantium (Heartwater)
- Foot-and-mouth disease virus
- Goat pox virus
- Lumpy skin disease virus
- Malignant catarrhal fever virus (Alcelaphine herpesvirus type 1)
- Menangle virus
Mycoplasma capricolum  
Mycoplasma mycoides  
Newcastle disease virus (virulent)  
Peste des petits ruminants virus  
Rinderpest virus  
Sheep pox virus  
Swine vesicular disease virus  

USDA Plant Protection and Quarantine (PPQ) Select Agents and Toxins  
Peronosclerosporaphilippinensis  
(Peronosclerosporasacchari)  

Phoma glycinicola (formerly Pyrenochaeta glycines)  
Ralstonia solanacearum Rathayibacter toxicus  
Rathayibacter toxicus  
Sclerophthora rayssiae  
Synchytrium endobioticum  
Xanthomonas oryzae  

* Denotes Tier 1 Agent

12.3 Tier 1 Select Agents

A subset of select agents and toxins have been designated as Tier 1 because these biological agents and toxins present the greatest risk of deliberate misuse with significant potential for mass casualties or devastating effect to the economy, critical infrastructure, or public confidence, and pose a severe threat to public health and safety:

<table>
<thead>
<tr>
<th>Tier 1 Select Agents and Toxins</th>
<th>HHS Agents and Toxins</th>
<th>Overlap Agents</th>
<th>USDA Agents</th>
</tr>
</thead>
<tbody>
<tr>
<td>Botulinum neurotoxins</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Botulinum neurotoxin producing species of Clostridium</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ebola virus</td>
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<td></td>
<td></td>
</tr>
<tr>
<td>Francisella tularensis</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Marburg virus</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Variola major virus (Smallpox virus)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Variola minor virus (Alastrim)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yersinia pestis</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bacillus anthracis</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Burkholderia mallei</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Burkholderia pseudomallei</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Foot-And-Mouth Disease virus</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Rinderpest virus</td>
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</tbody>
</table>

Entities that possess, use, or transfer Tier 1 select agents and toxins must adhere to the additional personnel screening and ongoing personal screening requirements. Additional physical requirements are also required for Tier 1 Select Agents.

The Yale Select Agent laboratory has been designed to meet the additional physical security requirements. However, the finalized program for personnel screening has not been set forth as of this version of the manual as Yale University is not currently registered for experiments involving Select Agents.

12.4 Permissible Toxin Amounts

The following toxins are not regulated 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)(3)]

<table>
<thead>
<tr>
<th>Toxin</th>
<th>Amount</th>
</tr>
</thead>
<tbody>
<tr>
<td>Abrin</td>
<td>100 mg</td>
</tr>
<tr>
<td>Botulinum neurotoxins</td>
<td>0.5 mg</td>
</tr>
<tr>
<td>Short, paralytic alpha conotoxins</td>
<td>100 mg</td>
</tr>
<tr>
<td>Diacetoxyscirpenol (DAS)</td>
<td>1000 mg</td>
</tr>
<tr>
<td>Ricin</td>
<td>100 mg</td>
</tr>
<tr>
<td>Saxitoxin</td>
<td>100 mg</td>
</tr>
<tr>
<td>Staphylococcal Enterotoxins (Subtypes A, B, C, D, and E)</td>
<td>5 mg</td>
</tr>
<tr>
<td>T-2 toxin</td>
<td>1000 mg</td>
</tr>
<tr>
<td>Tetrodotoxin</td>
<td>100 mg</td>
</tr>
</tbody>
</table>

Note: Toxin quantities shown are maximum quantities of toxins, in aggregate per PI, allowed by USDA/CDC. Note: Yale’s internal watch list limits PIs to only 50% of the quantities shown here.

### 12.4.1 Toxin Due Diligence Requirements

All Yale Principal Investigators in possession of ANY QUANTITY of the 9 Select Agent Toxins listed above must retain a record of ALL transfers of ANY QUANTITY of these toxins outside their laboratory. The required documentation must include the following information:

- Name of the recipient
- Toxin and quantity transferred
- Purpose of use (knowledge of recipient’s legitimate need for the toxins)

### 12.4.2 Reporting Suspected Violations or Suspicious Activity

If a Yale Principal Investigator in possession of ANY QUANTITY of the 9 Select Agent Toxins listed above detects suspicious activity associated with a request for toxin or suspicious activity associated with a shipped toxin, s/he must immediately notify the Yale University Responsible Official or Alternate Responsible Official and the Federal Select Agent program at the contact information below:

Yale Responsible Official: Mr. Rob Klein: 203-737-2131 (office) 203-410-6202 (cell)

Email CDC: LRSAT@cdc.gov
CDC Select Agent Office: 404-718-2000
Anonymous OIG Hotline: 1-800-447-8477 (voice) or 1-800-223-8164 (FAX)

### 12.5 Registration of Possession, Use or Transfer of Select Agents.

All activity involving Select Agents must be registered with the Yale Office of Environmental Health & Safety prior to initiation. Please contact the Biosafety Office with Yale EHS or contact your EHS Safety Advisor at 785-3550 to initiate a registration for your proposed Select Agent activity. The following bullets summarize the Select Agent registration and compliance pathway at Yale University.

- Notify Yale EHS of your intent to possess, use or transfer Select Agents.
- Complete an update of your Yale EHS FORM 01 Registration with the new agents. (If the Select Agent is a human pathogen, Yale will help you also register with the State of CT Dept. of Public Health).
- Complete FBI Form FD961 and file with Yale EHS for registration with applicable federal entity
- Complete 2 sets of FBI fingerprint cards for initiation of background investigation check
- Complete all Yale EHS applicable training programs (Biosafety, Bloodborne Pathogens, Laboratory Safety, Biosafety Level 3, Select Agent Biosecurity, and Shipping/Transport of Hazardous Biological Agents).
- Complete a Yale EHS Request to Use Infectious Agents Form(s) and Researcher Experience Form.
- Complete the Yale EHS researcher experience requirements (for BL2+ or BL3 agents)
- Satisfactory completion of EHS laboratory inspection of proposed work practices, safety equipment, and facility for Yale, CDC/NIH, and Select Agent regulatory requirements. (Safety and Security)

Receive final approval and authorization from Yale EHS, FBI, and the applicable governing body that you and each individual requesting access to Select Agents, the proposed storage location for Select Agents, and the Select Agent research areas have been cleared. (This is provided in the form of an approval letter from the Yale Biological Safety Committee).

Your laboratory will be subject to Yale and federal inspection or audit prior to initiation of work and at any time during your possession of Select Agents.

### 12.6 Discovery of Select Agents or Unknown Samples

Please notify EHS immediately if:
- You identify any Select Agent pathogen or toxin listed on the current federal list that was not previously registered by your lab.
- You discover a toxin not previously reported by your laboratory in excess of either the Yale Watch List or the federal maximum allowable quantities listed above.
- You discover any unknown materials in your laboratory for assistance with identification. These discoveries must be reported to the applicable governmental institution.

### 12.7 Intrafacility Transfer of Select Agents

Select agent pathogens and toxins may not be transferred outside of, to, or within Yale University unless EHS and federal approval has been granted. An intrafacility transfer is defined as the transfer of a Select Agent from one EHS and federally registered Select Agent lab to a similarly registered laboratory. Select Agents may not be transferred to a laboratory that is not registered with EHS and the applicable governmental institution. Once approved, intrafacility transfers will be overseen by EHS. Please contact the EHS Biosafety Office for additional information.

### 12.8 Destruction of Select Agents or Unknown Samples

Select Agent pathogens or toxins may not be destroyed until Yale EHS and the applicable government institution has provided approval for the destruction. Once approval has been granted for the destruction of Select Agents, Yale EHS will officially assume possession of the material and record its destruction. The governing institution will alert Yale if witnesses are required.

If you have any questions regarding the Yale of Federal Select Agent process, please don’t hesitate to contact the EHS Biosafety Office or your EHS Safety Advisor at 785-3550.
12.9 Additional Information

Information on the Select Agent Program may be found at the following web sites:

Yale EHS: http://ehs.yale.edu.


Centers for Disease Control and Prevention: http://www.cdc.gov/biosafety/publications/bmbl5/.


Notice of Exclusion for attenuated strains SAs: http://www.cdc.gov/od/sap/exclusion.htm

United States Department of Agriculture: http://www.usda.gov/