Update: Regulation of Select Agents and Toxins in the U.S.

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Centers for Disease Control & Prevention
Evolution of Select Agent and Toxin Regulations

- Antiterrorism Act
- Select Agent Program Established 1996
- Patriot Act 2001
- Bioterrorism Act 2002
- Select Agent Final Rule March 2005
- Amerithrax Attacks Oct. 2001
- BSAT Congressional Hearing Oct. 2007
October 2012 HHS Select Agents and Toxins Final Rule

- Tiered/Reduced Select Agent List
- Updated Responsible Official requirements
- Specific physical and cyber security requirements for Tier 1 Biological Select Agents and Toxins (BSAT)
- Personnel Suitability Programs for Tier 1 BSAT
- Occupational Health Programs for Tier 1 BSAT
- Broader Definition of Restricted Experiments
- Updated Transfer Requirements
### Effective Dates

<table>
<thead>
<tr>
<th>Effective Date</th>
<th>Section</th>
</tr>
</thead>
<tbody>
<tr>
<td>December 4, 2012</td>
<td>1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 13, 16, 17, 18, 19, 20, and 21</td>
</tr>
<tr>
<td>April 3, 2013</td>
<td>11, 12, 14, and 15</td>
</tr>
</tbody>
</table>
Additions & Removals
HHS Select Agent List

● Additions
  - SARS-associated coronavirus (SARS-CoV)
  - Lujo virus
  - Chapare virus

● Removals
  - Cercopithecine Herpesvirus 1 (Herpes B virus)
  - Clostridium perfringens epsilon toxin
  - Coccidioides posadasii/Coccidioides immitis
  - Eastern Equine Encephalitis virus (South American type only)
  - Flexal virus
  - West African clade of Monkeypox viruses
  - Rickettsia rickettsii
Removals
HHS & Overlap Select Agent List

- **Removals from HHS List**
  - Conotoxins, except short, paralytic alpha conotoxins containing the following nucleic acid sequence
  - Shigatoxins
  - Shiga-like ribosome inactivating proteins
  - Staphylococcal Enterotoxins, except A, B, C, D, and E subtypes
  - Tick-borne encephalitis complex viruses (Central European subtype)

- **Removals from Overlap List**
  - Venezuelan Equine Encephalitis virus (subtypes 1D and 1E). All other subtypes to remain regulated.
Tier 1 Select Agents and Toxins

- Ebola and Marburg viruses
- Variola minor and Variola major viruses
- *Francisella tularensis*
- *Yersinia pestis*
- *Bacillus anthracis**
- *Burkholderia mallei* and *B. pseudomallei*
- Botulinum neurotoxin and neurotoxin-producing strains of *Clostridium botulinum*
- Foot-and-Mouth Disease virus*
- Rinderpest virus*

*USDA-regulated  **Pasteur strain exempt
Specific security requirements for Tier 1 Select Agent Possessors

- **Suitability assessments**
  - Pre-access suitability assessments
  - On-going assessment of the suitability of personnel

- **Physical security standards: access control**
  - Minimum of three security barriers to reach space that contains Tier 1 BSAT
  - Intrusion Detection System
Occupational Health Programs for Tier 1 BSAT

The biosafety plan must include an occupational health program for individuals with access to Tier 1 select agents and toxins, and those individuals must be enrolled in the occupational health program.
Broader definition of Restricted Experiments

(a) An individual or entity may not conduct or possess products resulting from a restricted experiment with a select agent or toxin unless approved by and conducted in accordance with any conditions prescribed by the HHS Secretary.

(b)(1) Experiments that involve the deliberate transfer of, or selection for, a drug resistance trait to select agents that are not known to acquire the trait naturally, if such acquisition could compromise the control of disease agents in humans, veterinary medicine, or agriculture.

(b)(2) Experiments involving the deliberate formation of synthetic or recombinant DNA containing genes for the biosynthesis of select toxins lethal for vertebrates at an LD[50] < 100 ng/kg body weight.
EXCLUSIONS
Exclusion, Naturally Occurring Select Agents and Toxin

• Select agent or toxin in its naturally occurring environment is excluded provided that it has not been intentionally introduced, cultivated, collected, or otherwise extracted from its natural source.
  – Non-human primates that are naturally infected with Herpes B virus;
  – Castor beans containing ricin.

• If the select agent or toxin has been intentionally introduced, cultivated, collected, or otherwise extracted from its natural source, then it is no longer excluded.
  – Tissues from non-human primates infected with Herpes B;
  – Ricin extracted from the castor bean.
Exclusions

• Non-viable select agents or non-functional toxins.

• Toxins under the control of a principal investigator, treating physician or veterinarian, or commercial manufacturer or distributor are excluded, if
  – Specific quantities of toxins if the aggregate amount under the control of a principal investigator, treating physician or veterinarian, or commercial manufacturer or distributor does not exceed the amount specified.
Exclusion of an Attenuated Strain

• An attenuated strain of a select agent or an inactive form of a select toxin may be excluded from the requirements of this part based upon a determination by the HHS Secretary or Administrator that the attenuated strain or inactivated toxin does not pose a severe threat to public health and safety, to animal health or to animal products.

• To apply, submit a request in writing to the Federal Select Agent Program—
  – Must provide documentation establishing that the attenuated strain is eligible for exclusion.

• The attenuated strain exclusion is effective upon notification to the applicant.


• No longer excluded if subjected to manipulations that restore or enhance virulence.
Federal Law Enforcement Exclusion

• Select agent or toxin seized by a Federal law enforcement agency provided that:
  – Report within 24 hours for Tier 1 BSAT
  – Report the seizure of known select agents or toxins (Report of Identification Form) within 7 calendar days
  – Secures and reports theft, loss, or release
  – As soon as practicable transfer to a registered entity (Request to Transfer Form) or destroy and report on the Report of Identification Form
EXEMPTIONS
Exemptions for Diagnostic Laboratories (42 CFR § 73.5)

- General Diagnostic Exemption (42 CFR 73.5(a))
- Proficiency Testing (42 CFR 73.5 (b))
- Possession of products licensed or cleared as an investigational drug by the FDA (42 CFR 73.5 (c)(d))
- Public health emergency (42 CFR 73.5 (e))
Exemptions
Clinical/Diagnostic

- Clinical or diagnostic laboratories and other entities that possess, use, or transfer a select agent or toxin contained in a specimen presented for diagnosis or verification, or proficiency testing, will be exempt from the requirements, provided that certain conditions are met.
<table>
<thead>
<tr>
<th>QA/QC strains</th>
<th>Tier 1</th>
<th>Select agent status</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>Bacillus anthracis</em> Pasteur</td>
<td>No</td>
<td>regulated</td>
</tr>
<tr>
<td><em>Bacillus anthracis</em> Sterne</td>
<td>No</td>
<td>excluded</td>
</tr>
<tr>
<td><em>Brucella suis</em> 1330 positive control strain</td>
<td>No</td>
<td>regulated</td>
</tr>
<tr>
<td><em>Brucella melitensis</em> 16 M strain</td>
<td>No</td>
<td>regulated</td>
</tr>
<tr>
<td><em>Francisella tularensis</em> LVS</td>
<td>No</td>
<td>excluded</td>
</tr>
<tr>
<td><em>Yersinia pestis</em> A1122</td>
<td>No</td>
<td>excluded</td>
</tr>
</tbody>
</table>
What must be done to qualify for a clinical/diagnostic exemption?

A select agent or toxin must be:
- Within 7 calendar days of identification (diagnosis/verification), or within 90 calendar days of receipt (proficiency testing):
  - Transferred (according to the provisions of Section 16)
  - Destroyed on-site by a recognized sterilization inactivation process
  - Retained if the entity is registered for the select agent or toxin
What must be done to qualify for a clinical/diagnostic exemption?

A select or toxin must also be:

• Secured against theft, loss, or release from the time it is identified to the time it is transferred or destroyed, and reported for any theft, loss, or release

• Identification must be reported to:
  – Federal Select Agent Program within 7 calendar days of identification (diagnosis/verification) or within 90 calendar days of receipt (proficiency testing)
  – Other appropriate authorities as required by Federal, State, or local law
  – Immediate Notification for Tier 1 BSAT

• Less stringent reporting may be allowed during extraordinary circumstances, such as a widespread outbreak.
• Clinical or Diagnostic Laboratories
  – Agents used only for diagnosis, verification, or proficiency testing

• Federal law enforcement agency
  – Seizures of known select agent or toxin
What are the requirements for a provider of proficiency samples?

• At least seven calendar days prior to the transfer, the sender of the proficiency samples must report to APHIS or CDC:
  • Select agent or toxin to be transferred
  • Name and address of the recipient
Shipping and Receiving (Section 16)

- Transportation in commerce starts when the select agent(s) or toxin(s) are packaged for shipment and ready for receipt by a courier transporting select agent(s) or toxin(s) and ends when the package is received by the intended recipient who is an individual approved by the HHS Secretary or Administrator to have access to select agents and toxins, following a security risk assessment by the Attorney General.
GUIDANCE
Guidance
(www.selectagents.gov)

- Frequently Asked Questions
- Incident Response
- Information Systems Security Control
- Inventory Requirements
- Long Term Storage
- Occupational Health Program
- Physical Security Control
- Responsible Official
- SA Grams
- Security Risk Assessment Tool
- Shipment and Receipt of Packages
- Suitability Assessment
- Toxin Due Diligence
- Training
Tour of www.selectagents.gov

National Select Agent Registry

What's New?

Website is being revamped based on Revised Select Agent regulations.

Influenza viruses containing the Hemagglutinin from the Goose/Guangdong/1/96 lineage, Request for Information and Comments

On October 17, 2012, the U.S. Department of Health and Human Services (HHS) posted in the Federal Register a notice seeking public comment regarding the classification of highly pathogenic avian influenza (HPAI) variants - specifically, influenza viruses that contain an HA from the A/goose/Guangdong/1/96 lineage. These variants have been shown to be transmissible in the ferret model and have been associated with infections in humans.

October 2012 Federal Register Notice (PDF) and February 2013 Federal Register Notice (PDF) seek the public's opinion as to whether HPAI should regulate such research to ensure labs follow appropriate biosafety controls.

PLEASE NOTE: We are reopening the comment period on February 8, 2013, to allow interested persons additional time to prepare and submit comments. Written or electronic comments must be received on or before March 11, 2013.

Those interested parties wishing to make a comment during the extended public comment period should visit http://www.regulations.com/RegulationsDetail.cfm?D=2012-0161

APHIS/USDA Select Agent Regulations

The U.S. Departments of Health and Human Services (HHS) and Agriculture (USDA) published final rules (24 C.F.R. Part 73, 7 C.F.R. Part 331, and 9 C.F.R. Part 121) in the

http://www.selectagents.gov/index.html
Resources

Agent and Toxin Laboratories: The videos describe how to prepare for an inspection and what transpires during and after an inspection.

Click here to view the videos online & download

Compliance Assistance

Please select from the below list of documents to assist in complying with the requirements of the Select Agents regulations:

Checklists
Comparative Analysis of the Fourth and Fifth Editions of RBRL
Containment Facility Design and Construction (Secondary Barriers)
Containment for Work with Eastern Equine Encephalitis Virus
Guidance for Completing the Shipper's Declaration for Dangerous Goods
Guidance for Meeting Training Requirements of the Select Agent Regulations
Guidance for Suitability Assessments
Guidance for the Inactivation of Select Agents and Toxins
Guidance on the Shipment and Receipt of Packages with Select Agents and Toxins
Guidance on the Use of Infectious Waste Treatment and Radiation Facilities Outside of Registered Space
Guidelines for Avian Influenza Viruses
Incident Response Plan
Information Systems Security Control Guidance Document
Long Term Storage
BFR Guidelines
Occupational Health Program Guidance Document for Working with Tier 1 Select Agents and Toxins
Select Agents and Toxins

The Public Health Security and Bioterrorism Preparedness and Response Act of 2002, Subtitle A of Public Law 107–188 requires the Department of Health and Human Services (HHS) to establish and regulate a list of biological agents and toxins that have the potential to pose a severe threat to public health and safety. The Agricultural Biotechnology Protection Act of 2009 requires the United States Department of Agriculture (USDA) to establish and regulate a list of biological agents that have the potential to cause a severe threat to animal health and safety, plant health and safety, or to the safety of animal or plant products (Select Agents). HHS and APHIS share responsibility for some agents because they potentially threaten both humans and animals (select agents). The laws require HHS and USDA to review and republish the lists of Select Agents and toxins on at least a biennial basis.

This page includes links to the list of Select Agents and toxins and information about additions or deletions that have been made to the list based on recommendations made from the biennial review or advances in research.

- Select Agents and Toxins List
- Select Agents and Toxins Exclusions
- Select Agents and Toxins Restricted Experiments
- Permissible Toxic Amounts

Addition of Reconstructed 1918 Influenza virus to the list of HHS Select Agents and Toxins

HHS published an interim final rule in the Federal Register on October 20, 2005 to add “Reconstructed replication competent forms of the 1918 pandemic influenza virus containing any portion of the coding regions of all eight gene segments” to the list of HHS Select Agents and toxins. The addition of the reconstructed 1918 pandemic influenza virus to the HHS Select Agents and toxins became effective on October 20, 2005.

The CDC/NIH Biosafety in Microbiological and Biomedical Laboratories, 5th edition includes information on the minimum containment for experiments involving this agent.

For more information on the biennial review of the lists of Select Agents and toxins, go to:
- CDC Federal Register Notice
- NIAID Notice
Frequently Asked Questions

Frequently Asked Questions

General FAQ's about Select Agents and Toxins
Legislation, Regulation, and Guideline FAQ's
Registration FAQ's
Report of the Identification of a Select Agent or Toxin FAQ's
Biological Safety FAQ's
Security FAQ's
Security Risk Assessments FAQ's
Training FAQ's
Transfer FAQ's
Use Dissemination FAQ's
BARS FAQ's
Responsible Official FAQ's

This site is best viewed in Internet Explorer version 6.0 or later.
For more information please contact Centers for Disease Control and Prevention

1600 Clifton Road NE, Atlanta, GA 30333
Telephone, 1-800-CDC-INFO (232-4636)/TTY: 1-888-232-6348
E-mail: cdcinfo@cdc.gov Web: www.cdc.gov

The findings and conclusions in this report are those of the authors and do not necessarily represent the official position of the Centers for Disease Control and Prevention.